PROGRAMME GRANTS FOR APPLIED RESEARCH

VOLUME 4 ISSUE 12 AUGUST 2016
ISSN 2050-4322

Improving patients' experience and outcome of total joint replacement: the RESTORE programme

Ashley W Blom, Neil Artz, Andrew D Beswick, Amanda Burston, Paul Dieppe, Karen T Elvers, Rachael Gooberman-Hill, Jeremy Horwood, Paul Jepson, Emma Johnson, Erik Lenguerrand, Elsa Marques, Sian Noble, Mark Pyke, Catherine Sackley, Gina Sands, Adrian Sayers, Victoria Wells and Vikki Wylde

DOI 10.3310/pgfar04120

NHS
National Institute for Health Research

Improving patients' experience and outcome of total joint replacement: the RESTORE programme

Ashley W Blom,[1]* Neil Artz,[2] Andrew D Beswick,[1] Amanda Burston,[1] Paul Dieppe,[3] Karen T Elvers,[1] Rachael Gooberman-Hill,[1] Jeremy Horwood,[4] Paul Jepson,[5] Emma Johnson,[1] Erik Lenguerrand,[1] Elsa Marques,[4] Sian Noble,[4] Mark Pyke,[6] Catherine Sackley,[7] Gina Sands,[8] Adrian Sayers,[1] Victoria Wells[1] and Vikki Wylde[1]

[1]Musculoskeletal Research Unit, School of Clinical Sciences, University of Bristol, Bristol, UK
[2]School of Health Professions, Faculty of Health and Human Sciences, Plymouth University, Plymouth, UK
[3]Medical School, University of Exeter, Exeter, UK
[4]School of Social and Community Medicine, University of Bristol, Bristol, UK
[5]School of Sport, Exercise and Rehabilitation Sciences, Birmingham, UK
[6]North Bristol NHS Trust, Bristol, UK
[7]Department of Physiotherapy, King's College London, London, UK
[8]School of Health Sciences, Faculty of Medicine and Health Sciences, University of East Anglia, Norwich, UK

*Corresponding author

Declared competing interests of authors: Ashley Blom reports grants from National Institute for Health research during the conduct of the study; and grants from Stryker, Orthimo and Azellon outside the programme.

Published August 2016
DOI: 10.3310/pgfar04120

This report should be referenced as follows:

Blom AW, Artz N, Beswick AD, Burston A, Dieppe P, Elvers KT, *et al*. Improving patients' experience and outcome of total joint replacement: the RESTORE programme. *Programme Grants Appl Res* 2016;**4**(12).

Programme Grants for Applied Research

ISSN 2050-4322 (Print)

ISSN 2050-4330 (Online)

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: nihredit@southampton.ac.uk

The full PGfAR archive is freely available to view online at www.journalslibrary.nihr.ac.uk/pgfar. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

Criteria for inclusion in the *Programme Grants for Applied Research* journal

Reports are published in *Programme Grants for Applied Research* (PGfAR) if (1) they have resulted from work for the PGfAR programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Programme Grants for Applied Research programme

The Programme Grants for Applied Research (PGfAR) programme, part of the National Institute for Health Research (NIHR), was set up in 2006 to produce independent research findings that will have practical application for the benefit of patients and the NHS in the relatively near future. The Programme is managed by the NIHR Central Commissioning Facility (CCF) with strategic input from the Programme Director.

The programme is a national response mode funding scheme that aims to provide evidence to improve health outcomes in England through promotion of health, prevention of ill health, and optimal disease management (including safety and quality), with particular emphasis on conditions causing significant disease burden.

For more information about the PGfAR programme please visit the website: http://www.nihr.ac.uk/funding/programme-grants-for-applied-research.htm

This report

The research reported in this issue of the journal was funded by PGfAR as project number RP-PG-0407-10070. The contractual start date was in December 2008. The final report began editorial review in September 2014 and was accepted for publication in August 2015. As the funder, the PGfAR programme agreed the research questions and study designs in advance with the investigators. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The PGfAR editors and production house have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the final report document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, CCF, NETSCC, PGfAR or the Department of Health. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the PGfAR programme or the Department of Health.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).

Programme Grants for Applied Research Editor-in-Chief

Professor Paul Little Professor of Primary Care Research, University of Southampton, UK

NIHR Journals Library Editor-in-Chief

Professor Tom Walley Director, NIHR Evaluation, Trials and Studies and Director of the EME Programme, UK

NIHR Journals Library Editors

Professor Ken Stein Chair of HTA Editorial Board and Professor of Public Health, University of Exeter Medical School, UK

Professor Andree Le May Chair of NIHR Journals Library Editorial Group (EME, HS&DR, PGfAR, PHR journals)

Dr Martin Ashton-Key Consultant in Public Health Medicine/Consultant Advisor, NETSCC, UK

Professor Matthias Beck Chair in Public Sector Management and Subject Leader (Management Group), Queen's University Management School, Queen's University Belfast, UK

Professor Aileen Clarke Professor of Public Health and Health Services Research, Warwick Medical School, University of Warwick, UK

Dr Tessa Crilly Director, Crystal Blue Consulting Ltd, UK

Dr Eugenia Cronin Senior Scientific Advisor, Wessex Institute, UK

Ms Tara Lamont Scientific Advisor, NETSCC, UK

Professor Elaine McColl Director, Newcastle Clinical Trials Unit, Institute of Health and Society, Newcastle University, UK

Professor William McGuire Professor of Child Health, Hull York Medical School, University of York, UK

Professor Geoffrey Meads Professor of Health Sciences Research, Health and Wellbeing Research and Development Group, University of Winchester, UK

Professor John Norrie Health Services Research Unit, University of Aberdeen, UK

Professor John Powell Consultant Clinical Adviser, National Institute for Health and Care Excellence (NICE), UK

Professor James Raftery Professor of Health Technology Assessment, Wessex Institute, Faculty of Medicine, University of Southampton, UK

Dr Rob Riemsma Reviews Manager, Kleijnen Systematic Reviews Ltd, UK

Professor Helen Roberts Professor of Child Health Research, UCL Institute of Child Health, UK

Professor Jonathan Ross Professor of Sexual Health and HIV, University Hospital Birmingham, UK

Professor Helen Snooks Professor of Health Services Research, Institute of Life Science, College of Medicine, Swansea University, UK

Professor Jim Thornton Professor of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, University of Nottingham, UK

Professor Martin Underwood Director, Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, UK

Please visit the website for a list of members of the NIHR Journals Library Board:
www.journalslibrary.nihr.ac.uk/about/editors

Editorial contact: nihredit@southampton.ac.uk

Abstract

Improving patients' experience and outcome of total joint replacement: the RESTORE programme

Ashley W Blom,[1]* Neil Artz,[2] Andrew D Beswick,[1] Amanda Burston,[1] Paul Dieppe,[3] Karen T Elvers,[1] Rachael Gooberman-Hill,[1] Jeremy Horwood,[4] Paul Jepson,[5] Emma Johnson,[1] Erik Lenguerrand,[1] Elsa Marques,[4] Sian Noble,[4] Mark Pyke,[6] Catherine Sackley,[7] Gina Sands,[8] Adrian Sayers,[1] Victoria Wells[1] and Vikki Wylde[1]

[1]Musculoskeletal Research Unit, School of Clinical Sciences, University of Bristol, Bristol, UK
[2]School of Health Professions, Faculty of Health and Human Sciences, Plymouth University, Plymouth, UK
[3]Medical School, University of Exeter, Exeter, UK
[4]School of Social and Community Medicine, University of Bristol, Bristol, UK
[5]School of Sport, Exercise and Rehabilitation Sciences, Birmingham, UK
[6]North Bristol NHS Trust, Bristol, UK
[7]Department of Physiotherapy, King's College London, London, UK
[8]School of Health Sciences, Faculty of Medicine and Health Sciences, University of East Anglia, Norwich, UK

*Corresponding author ashley.blom@bristol.ac.uk

Background: Total hip replacements (THRs) and total knee replacements (TKRs) are common elective procedures. In the REsearch STudies into the ORthopaedic Experience (RESTORE) programme, we explored the care and experiences of patients with osteoarthritis after being listed for THR and TKR up to the time when an optimal outcome should be expected.

Objective: To undertake a programme of research studies to work towards improving patient outcomes after THR and TKR.

Methods: We used methodologies appropriate to research questions: systematic reviews, qualitative studies, randomised controlled trials (RCTs), feasibility studies, cohort studies and a survey. Research was supported by patient and public involvement.

Results: Systematic review of longitudinal studies showed that moderate to severe long-term pain affects about 7–23% of patients after THR and 10–34% after TKR. In our cohort study, 10% of patients with hip replacement and 30% with knee replacement showed no clinically or statistically significant functional improvement. In our review of pain assessment few research studies used measures to capture the incidence, character and impact of long-term pain. Qualitative studies highlighted the importance of support by health and social professionals for patients at different stages of the joint replacement pathway. Our review of longitudinal studies suggested that patients with poorer psychological health, physical function or pain before surgery had poorer long-term outcomes and may benefit from pre-surgical interventions. However, uptake of a pre-operative pain management intervention was low. Although evidence relating to patient outcomes was limited, comorbidities are common and may lead to an increased risk of adverse events, suggesting the possible value of optimising pre-operative management. The evidence base on clinical effectiveness of pre-surgical interventions, occupational therapy and

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

physiotherapy-based rehabilitation relied on small RCTs but suggested short-term benefit. Our feasibility studies showed that definitive trials of occupational therapy before surgery and post-discharge group-based physiotherapy exercise are feasible and acceptable to patients. Randomised trial results and systematic review suggest that patients with THR should receive local anaesthetic infiltration for the management of long-term pain, but in patients receiving TKR it may not provide additional benefit to femoral nerve block. From a NHS and Personal Social Services perspective, local anaesthetic infiltration was a cost-effective treatment in primary THR. In qualitative interviews, patients and health-care professionals recognised the importance of participating in the RCTs. To support future interventions and their evaluation, we conducted a study comparing outcome measures and analysed the RCTs as cohort studies. Analyses highlighted the importance of different methods in treating and assessing hip and knee osteoarthritis. There was an inverse association between radiographic severity of osteoarthritis and pain and function in patients waiting for TKR but no association in THR. Different pain characteristics predicted long-term pain in THR and TKR. Outcomes after joint replacement should be assessed with a patient-reported outcome and a functional test.

Conclusions: The RESTORE programme provides important information to guide the development of interventions to improve long-term outcomes for patients with osteoarthritis receiving THR and TKR. Issues relating to their evaluation and the assessment of patient outcomes are highlighted. Potential interventions at key times in the patient pathway were identified and deserve further study, ultimately in the context of a complex intervention.

Study registration: Current Controlled Trials ISRCTN52305381.

Funding: This project was funded by the NIHR Programme Grants for Applied Research programme and will be published in full in *Programme Grants for Applied Research*; Vol. 4, No. 12. See the NIHR Journals Library website for further project information.

Contents

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

List of tables

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

List of figures

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

List of boxes

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

List of abbreviations

3D	three-dimensional
6MWT	6-metre walk test
Ab-A	Aberdeen activity limitation subscale
Ab-I	Aberdeen impairment subscale
Ab-IAP	Aberdeen impairment, activity limitation and participation restriction measure
Ab-P	Aberdeen participation restriction subscale
ADAPT	Assessing Disability After Partial and Total joint replacement
ADL	activities of daily living
AIMS	Arthritis Impact Measure Score
AIMS2	Arthritis Impact Measure Score 2
AKSS	American Knee Society Score
AMED	Allied and Complementary Medicine Database
ANOVA	analysis of variance
AOC	Avon Orthopaedic Centre
APEX	Arthroplasty Pain EXperience
ARENA	Activity orientated REhabilitation following kNee Arthroplasty
BCI	bootstrapped confidence interval
BMI	body mass index
CEAC	cost-effectiveness acceptability curve
CI	confidence interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CIRRIE	Center for International Rehabilitation Research Information and Exchange
CONSORT	Consolidated Standards of Reporting Trials
CSRI	Client Service Receipt Inventory
DIRUM	Data Instruments for Resource Use Measurement
EQ-5D	European Quality of Life-5 Dimensions
EQ-5D-3L	European Quality of Life-5 Dimensions 3-Level version
ERIC	Education Resources Information Center
FNB	femoral nerve block
GP	general practitioner
HADS	Hospital Anxiety and Depression Scale
HADS-A	Hospital Anxiety and Depression Scale – anxiety subscale
HADS-D	Hospital Anxiety and Depression Scale – depression subscale
HHS	Harris Hip Score
HOOS	Hip Disability and Osteoarthritis Outcome Score
HRQoL	health-related quality of life
HSS	Hospital for Special Surgery Knee Score
i.v.	intravenous
IASP	International Association for the Study of Pain
ICD	*International Classification of Diseases*
ICECAP	ICEpop CAPability measure
ICECAP-O	ICEpop CAPability measure for Older people
ICF	International Classification of Functioning, Disability and Health
ICOAP	Measure of Intermittent and Constant Osteoarthritis Pain
ILAS	Iowa Level of Assistance Scale
IMMPACT	Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

INMB	incremental net monetary benefit
IPA	interpretative phenomenological analysis
IQR	interquartile range
ITT	intention to treat
ITT-CC	intention-to-treat complete cases
ITT-imputed	intention-to-treat imputed
KOOS	Knee Injury and Osteoarthritis Outcome Score
LEFS	Lower Extremity Functional Scale
MCII	minimum clinical important improvement
MD	mean difference
MLM	multivariate linear mixed
MOOSE	Meta-analysis of Observational Studies in Epidemiology
MRC	Medical Research Council
MRU	Musculoskeletal Research Unit
MYMOP2	Measure Yourself Medical Outcome Profile 2
NEADL	Nottingham Extended Activities of Daily Living
NHP	Nottingham Health Profile
NICE	National Institute for Health and Care Excellence
OHS	Oxford Hip Score
OKS	Oxford Knee Score
OLS	ordinary least squares
OR	odds ratio
OT	occupational therapist
PCA	patient-controlled analgesia
PCS	physical component score
PEDro	Physiotherapy Evidence Database
PEP-R	Patient Experience Partnership in Research
PI	principal investigator
PICOS	participants, interventions, comparisons, outcomes, and study design
PP	per protocol complete cases
PPI	patient and public involvement
PPT	pressure pain threshold
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROM	patient-reported outcome measure
PROOF-THR	Pilot Randomised controlled trial Of Occupational therapy For–Total Hip Replacement
PROSPECT	PROcedure SPECific postoperative pain managemenT
PSS	Personal Social Services
QALY	quality-adjusted life-year
QoL	quality of life
QST	quantitative sensory testing
RCT	randomised controlled trial
RESTORE	REsearch STudies into the ORthopaedic Experience
ROM	range of motion
SD	standard deviation
SEM	structural equation modelling
SF-12	Short Form questionnaire-12 items
SF-36	Short Form questionnaire-36 items
SMD	standardised mean difference
SPIRAL	Self-managing Pain In aRthritis and ArthropLasty
STAI	State–Trait Anxiety Inventory
THR	total hip replacement
TKR	total knee replacement
UCLA	University of California at Los Angeles
ULM	univariable linear mixed
VAS	visual analogue scale
WHO	World Health Organization
WOMAC	Western Ontario and McMaster Universities Arthritis Index

Plain English summary

Many people with pain and disability caused by osteoarthritis receive hip or knee replacement. In around 10% of patients with hip replacement and 20% with knee replacement, pain and disability persist.

In the REsearch STudies into the ORthopaedic Experience (RESTORE) programme, we applied appropriate research methods including literature reviews, interviews with patients and health-care professionals, studies observing patient recovery over time, and randomised trials to assess new methods. Research studies were developed in collaboration with patient representatives.

Patients with worse psychological health, disability or pain before surgery are more likely to have a poor long-term recovery. Patients describe the importance of support by health and social professionals throughout the joint replacement pathway and may benefit from education, pain management, counselling, exercise and management of health conditions before surgery.

Previous small randomised trials suggested that patients might have short-term benefit from exercise or education before surgery, and supply of aids and home modifications and physiotherapy after surgery. We conducted studies that demonstrated the feasibility of trials evaluating the provision of aids and home modifications before surgery and group-based exercise after surgery.

In a literature review and randomised trial we assessed whether or not local anaesthetic injections during surgery improve recovery. In patients with hip replacement, long-term pain was reduced and the treatment was cost-effective. In patients receiving knee replacement, we could not confirm a reduction in pain, probably because patients receive extensive pain control during surgery.

In conclusion, the RESTORE programme has provided important information to guide the development of methods to improve long-term recovery after hip and knee replacement.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Scientific summary

Background

Total hip replacement (THR) and total knee replacement (TKR) are common elective procedures with over 150,000 performed annually in the NHS. For many patients with advanced osteoarthritis, THR and TKR are effective in treating pain and restoring physical function. However, some patients report little functional benefit and long-term pain.

Objectives

Recognising the presence of long-term pain and disability in some patients after joint replacement, the REsearch STudies into the ORthopaedic Experience (RESTORE) programme explored the care and experiences of patients at key times in the pathway from being listed for THR and TKR to the time after surgery when an optimal outcome should be expected. RESTORE consisted of a series of interrelated work packages with systematic reviews, qualitative studies, randomised controlled trials (RCTs), cohort studies and economic evaluations.

Specific objectives were to:

1. Synthesise research in THR and TKR on long-term pain prevalence and assessment methods, and review the impact of comorbidities and pre-surgical factors on long-term patient outcomes.
2. Characterise the patient pathway through THR and TKR and study the experience of trial involvement for health-care professionals and patients.
3. Compare outcome measures over time in patients with hip or knee replacement and assess how well they measure impairment, activity limitation and participation.
4. Evaluate in a RCT the clinical effectiveness and cost-effectiveness of perioperative local anaesthetic infiltration on long-term pain after THR and TKR.
5. Assess relationships between radiographic measures of osteoarthritis severity and patient-reported pain and function. Explore associations between pre-operative patient factors and patient outcomes after THR and TKR.
6. Review the effectiveness of pre-surgical education and exercise.
7. Assess feasibility and acceptability of pain self-management for patients undergoing THR.
8. Review existing evidence on effectiveness of occupational therapy and evaluate the feasibility and acceptability of pre-surgical provision in patients waiting for THR.
9. Update previous reviews of physiotherapy exercise, assess current provision and explore the feasibility of group-based physiotherapy with individualised exercises for patients with TKR.

Methods

To ensure patient and public involvement throughout the programme, work packages were discussed and developed in collaboration with patient representatives and a patient forum.

We appraised existing research using systematic review methods and meta-analysis in accordance with appropriate guidelines.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

In a qualitative study, 34 patients receiving THR and TKR were interviewed before surgery, 2–4 weeks and 6 and 12 months after surgery. Interviews elicited patients' experiences of preparing for, undergoing and recovering from surgery. Interviews were audio-recorded, transcribed and analysed using a thematic approach or interpretive phenomenological analysis.

In the Assessing Disability After Partial and Total joint replacement (ADAPT) study, outcome measures were studied prospectively in 263 patients receiving joint replacement. Participants were assessed prior to surgery and at 3 and 12 months. Function was assessed using patient-completed questionnaires, clinician-administered tools and performance tests.

In the Arthroplasty Pain EXperience (APEX) RCTs, 322 patients receiving THR and 316 patients receiving TKR were randomised to receive 60 ml local anaesthetic infiltration (0.25% bupivacaine and 0.3 mg adrenaline) before wound closure or standard anaesthesia. All patients with TKR received a femoral nerve block (FNB). The primary outcome was the Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain score at 12 months. The primary health outcome for economic evaluation was the quality-adjusted life-year measured using the European Quality of Life-5 Dimensions 3-Level version.

The APEX RCTs were also analysed as cohort studies. Radiographic measures of osteoarthritis severity were correlated with pre-operative WOMAC pain and function. Associations between measures of pain over time were explored. Quantitative sensory testing was conducted to assess pre-operative widespread pain sensitisation. Qualitative interviews were conducted with 24 patients and 15 health-care professionals about involvement in the APEX trials and views about analgesics. Data were analysed using thematic methods.

Using systematic review and meta-analysis, we identified RCTs evaluating the effectiveness of pre-surgical education and exercise interventions.

To evaluate the feasibility of conducting a definitive RCT of a pain self-management programme for patients undergoing THR, the Self-managing Pain In aRthritis and ArthropLasty (SPIRAL) study assessed trial procedures and data collection, randomisation, recruitment and attrition rates.

The Pilot Randomised controlled trial Of Occupational therapy For – Total Hip Replacement (PROOF-THR) study evaluated the feasibility of pre-surgical occupational therapy in patients waiting for THR. Primary objectives were to assess patient identification, recruitment and retention, acceptability of allocation, and acceptability of health resource use and outcome measures.

Physiotherapy services were surveyed at 24 high-volume orthopaedic centres in England and Wales. In the Activity orientated REhabilitation following kNee Arthroplasty (ARENA) study, the feasibility of a RCT evaluating a 6-week activity-orientated rehabilitation programme for patients with TKR was assessed. Information was collected on uptake rates, reasons for non-attendance, patient satisfaction and outcomes, acceptability of exercises, outcomes measures and collection of costs.

Results

Prevalence of long-term pain

Studies in representative populations including 25,831 patients suggest that about 7–23% of patients have moderate or severe pain after THR and about 10–34% after TKR.

Outcome measures to assess long-term pain

Systematic review including 1164 research studies in patients with TKR identified extensive variation in pain outcome measures. Few studies attempted to capture the incidence, character and impact of long-term pain. A composite clinician assessment with a single question about pain was widely used but there was an increase in use of patient-reported outcomes over time.

Pre-surgical prediction

In prospective studies, patients with better pre-operative physical function and lower pain generally achieved a better recovery after surgery. Patients with poor physical function before surgery may have greater absolute improvement.

Patients with depression before THR and TKR had poorer long-term pain and functional outcomes. For patients with anxiety or poor general psychological health, there was evidence for a relationship with worse pain and functional outcomes in patients receiving TKR but evidence in THR was equivocal.

Patients with a broad range of body mass index benefited from THR and TKR but those with highest levels may not achieve good levels of function and pain control.

Comorbid conditions

About 64% and 71% of patients receiving THR and TKR, respectively, have comorbidities. In specific clinical conditions, we found little research on patient-reported outcomes. In studies looking at long-term patient outcomes according to diabetic status, research was inconclusive. However, studies show that patients with diabetes, previous heart disease and anaemia are at greater risk of post-surgical adverse events.

Patient experience

In qualitative interviews, patients noted that delays to NHS orthopaedic surgery are common. For patients undergoing joint replacement, changes to the date of surgery have implications for well-being and patients' experiences of time differ from the linear conceptualisation required to plan NHS services.

Undergoing surgery can increase feelings of vulnerability and alter a patient's trust in their own body; the influence of interactions with others on confidence levels and the fears that patients have concerning the potential of causing harm to their new prosthesis. Our research also highlights strategies that patients engage in to limit this. Patients rely extensively on, and value, both informal and formal support networks over the perioperative period and that transformation from a person living with osteoarthritis to a person recovering from a surgical intervention can lead to alterations in the assistance participants received from others. However, when patients are not offered the support of health and social professionals over the perioperative period, for example to aid recovery, negative consequences can ensue including distress and feelings of abandonment. The qualitative research also highlights the complexity of patient expectations for joint replacement surgery and how these expectations can be driven by previous personal experience, knowledge of others' experiences, and information resources provided by the hospital around the perioperative period.

Functional outcomes

In the ADAPT study, a clinically significant improvement occurred in about 90% of patients with THR and 70% of those with TKR. Compared with other outcomes, improvement of walking time was rarely large. Patients with very severe disease at the time of surgery were more likely to have substantial improvements in pain and functional ability. But the destination differs for the two joint sites; those with hip disease can have the similar good destination, irrespective of the starting point, whereas those with knee disease can never 'catch up' (i.e. have as good a final outcome or destination) if they start off with very severe disease at the time of surgery.

As pain and function measures were highly correlated and people with anxiety or depression may assess themselves as being worse off than objective measures suggest, measures of function may need adjustment for pain, psychological status, age and perhaps muscle strength to obtain a satisfactory picture of functional loss. Results suggested that physical function should be measured with a patient-reported outcome measure and a performance test. Range of motion is commonly assessed in clinical practice but correlated poorly with other measures of disease severity.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Perioperative pain management

Systematic review identified 36 RCTs evaluating local anaesthetic infiltration in patients receiving THR and TKR. Few reported long-term follow-up. Local anaesthetic infiltration was effective in reducing short-term pain when compared with no infiltration. Effectiveness was enhanced with the addition of post-closure analgesia. In TKR, there was no evidence of additional benefit if a FNB had already been sited.

In the APEX RCTs, local anaesthetic infiltration was associated with reduced pain 1-year after THR. Findings in patients receiving TKR provided no strong evidence that local anaesthetic infiltration reduced long-term pain additional to that provided by FNB. From the perspective of the NHS and Personal Social Services (PSS), local anaesthetic infiltration is a cost-effective treatment option in primary THR but evidence supporting its use in TKR was weaker.

Trial participation and views about medication

In qualitative interviews, patients and health-care professionals reported that they had weighed up the benefit and cost of involvement. They were interested in involvement in APEX RCTs because they considered the trials important and relevant. Patients expressed their desire to help others by contributing to the furthering of clinical knowledge. Many patients thought that they might benefit physically and psychologically from taking part.

The qualitative study also demonstrated the need for trials to ensure minimal burden. Health-care professionals wanted the trial to have minimal impact on daily clinical practice and patients wanted data collection and participation to be as easy as possible.

Further analysis of the qualitative data showed that the experience of joint replacement can temporarily alter patients' views of the acceptability, necessity and value of pain relief medication. This alteration is related to views about pain from intervention compared with pain from chronic condition, and is influenced by interactions with health-care professionals. However, once initial recovery from surgery has begun, long-standing beliefs about the appropriate use of pain relief medications may take prominence.

Radiographic osteoarthritis severity and pain

In the APEX cohort study, there was no relationship between the degree of radiographic damage and pain or function in patients waiting for THR. In patients waiting for TKR, those with the least severe radiographic damage reported more severe pain and poorer function.

Pain as a predictor of long-term pain

Long-term pain after THR was predominantly associated with pain at rest during the pre-operative and acute postoperative period. In contrast, long-term pain after TKR was predominantly associated with the severity of pain on movement during the pre-operative period.

Pre-operative widespread pain sensitisation and chronic pain

Pre-operative widespread pain sensitivity was not associated with change in pain severity from pre-operative to 12 months post operation in patients with THR and TKR.

Exercise and education interventions before surgery

Systematic review identified 36 interventions targeting optimisation of pre-surgical physical function before THR and TKR. Interventions showed benefit compared with controls for physical function, pain and anxiety. In 27 studies targeting in-hospital recovery, post-surgical anxiety was lower in intervention patients and mobilisation was earlier. In 18 studies, interventions targeting long-term outcomes showed no benefit.

Group-based pain self-management

Of 385 eligible patients with THR, 88 (23%) consented to participate in the SPIRAL study of group-based pain self-management. Common reasons for non-participation were views about the course and transport difficulties. Of the 43 patients randomised to the intervention, 28 attended pre-operative sessions and 11 attended postoperative sessions. Participant satisfaction was high and feedback highlighted that patients enjoyed the group format. Retention of participants in the RCT was acceptable (83%) with high questionnaire return rates except resource-use diaries.

Occupational therapy

In patients receiving THR, systematic review identified seven RCTs of occupational therapy, mainly combined with physiotherapy. There was a suggestion of improved function and reduced pain before surgery but this was not sustained after surgery. In the PROOF-THR study, 44 patients were randomised to pre-operative occupational therapy or usual care. Good recruitment rates, acceptability of randomisation of participants, successful intervention delivery, and reasonable attrition rates suggest a definitive trial would be feasible.

Physiotherapy exercise

Systematic review and meta-analysis identified a few small studies suggesting that physiotherapy exercise can have short-term benefits for patients with TKR. In the UK, physiotherapy is usually provided for patients with THR depending on clinical need. After TKR, group exercises focus on knee-specific strengthening, stretching and functional exercises. In the ARENA study a 6-week group-based activity-orientated rehabilitation programme for patients with TKR was evaluated. Of 124 eligible patients, 46 were randomised (37%). The intervention was generally well received and attendance was good (73%).

Conclusions

The RESTORE programme highlights the importance for patients of support by health and social professionals at different stages of the joint replacement pathway.

Feasibility studies in patients receiving THR and TKR provided information about the acceptability of interventions that might help patients achieve better long-term outcomes. Although participation in pre-operative pain management was low, those who attended provided positive feedback. Research into occupational therapy provision before surgery is feasible, and group-based post-surgical physiotherapy with individualised exercise was well received.

Perioperative care should include appropriate multimodal anaesthesia supported by evidence from adequately powered RCTs. For patients receiving THR, this should include local anaesthetic infiltration but this may not provide additional benefit to FNB in patients receiving TKR. Local anaesthetic infiltration is a cost-effective treatment in primary THR from a NHS and PSS perspective.

While specific intervention components should be evaluated in appropriately powered clinical trials, the best and most acceptable strategies may be complex interventions tailored to THR or TKR. These would include pre-operative assessment to guide treatment of comorbid conditions, psychological problems and pain, with support for exercises to prevent functional deterioration and education to prepare patients for surgery and recovery. Occupational therapy might be provided before hospital admission. Perioperatively, patients would receive multimodal pain management with evidence-based treatments. After hospital discharge, group-based and individualised physiotherapy exercise might be provided.

In conclusion, the RESTORE programme has provided important information to guide the development of new methods to improve long-term recovery after THR and TKR.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Study registration

This trial is registered as ISRCTN52305381.

Funding

Funding for this study was provided by the Programme Grants for Applied Research programme of the National Institute for Health Research.

Chapter 1 Background to the RESTORE programme

Osteoarthritis of the hip and knee joints

Osteoarthritis is the most common form of joint disease and causes significant pain and disability in about 10% of people aged > 55 years in the UK.[1] The joints most frequently affected include joints in the hands, feet and spine, but osteoarthritis of the hips and knees is particularly likely to cause chronic pain and severe physical disability. These two conditions result in a huge health burden worldwide,[2] particularly among older people, and are the main reason for the increasing utilisation of hip and knee joint replacements.[3]

The severity of osteoarthritis of the hips or knees varies considerably. It is often relatively mild, only causing modest, variable discomfort and some restriction of activities without disrupting the person's life in a major way. However, a significant minority of those who have these conditions develop more severe, progressive symptoms, which may result in their seeking professional help. Only about 50% of those with severe symptomatic lower limb osteoarthritis seek conventional medical help,[4] some prefer to rely on help from everyday folk remedies, complementary or alternative medicine interventions, and many seek no help at all, considering their aches and pains and disability as an inevitable part of the ageing process and something that are not treatable medical problems.[5,6] However, the prevalence of these diseases is so high, that while many do not seek professional help, there are enough that do to result in a huge workload for general practitioners (GPs), rheumatologists and physical therapists.[7] In addition, osteoarthritis is increasing in prevalence as our population gets older and the number of people with a high body mass index (BMI) increases,[8] and it is the major reason for lower limb joint replacement; thus, is a massive issue for orthopaedic service provision.

Who gets osteoarthritis of the hip and knee?

Osteoarthritis of the hip and knee are strongly age-related diseases. It is unusual for people to suffer from these before the age of 45 years and the prevalence then increases sharply with increasing age.[8] The three other main risk factors for osteoarthritis of the hip and knee are family history/genetic predisposition, previous injury to the joint and high BMI.

Given that age and high BMI are major risk factors for lower limb osteoarthritis, comorbidities related to age and obesity are very common in people receiving joint replacement for osteoarthritis.[9] Cardiovascular problems, sensory deficits (such as reduced sight or hearing) and diabetes are particularly common problems.[10]

Treatment options for osteoarthritis of the hip and knee

In the UK, those seeking help for lower limb osteoarthritis generally start with their GP and most of the management of hip and knee disease occurs in primary care. There is no known treatment able to alter the progression of osteoarthritis, or anything that can cause an improvement in joint structure – there is no 'cure' available. However, there is a wide range of both non-surgical and surgical interventions that can reduce pain and improve function. Conservative options available through primary care include education and access to self-help packages, including behavioural change; local or systemic drug therapies; physical therapies; and orthotics. National Institute for Health and Care Excellence (NICE) and international guidelines recommend that everyone should be offered simple options to begin with, while recognising that this will be insufficient to manage the pain and disability in some.[11–14]

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

If pharmacological and conservative treatments provide inadequate relief of symptoms, then total joint replacement is commonly recommended. The clinical effectiveness and cost-effectiveness of total joint replacement surgery as a treatment option for patients with advanced osteoarthritis is well established.[15,16] One of the challenges for patients and GPs dealing with osteoarthritis is who to refer to the surgeon and when surgical intervention is appropriate. There are no clear guidelines as to the severity of pain or disability that warrants moving from conservative management to surgery.[17] This difficulty is compounded by the knowledge that surgery is a dangerous, irreversible step that does not result in adequate relief of symptoms and restoration of function in everyone who undergoes it.[18]

Total hip and knee replacement

Total hip and knee replacements are undertaken to relieve pain and improve function in people with advanced osteoarthritis of the hip or knee joint, whose symptoms are not controlled by conservative treatment. They are two of the most common elective NHS procedures with 75,366 primary total hip replacements (THRs) and 76,497 primary total knee replacements (TKRs) performed in England and Wales between April 2012 and March 2013.[3] The main disease resulting in this need for joint replacement is osteoarthritis, with about 91% of total hip joint replacements and 98% of total knee joint replacements being carried out for this indication. In England, the number of THRs conducted annually increased by 54% between 2001 and 2011 and the number of TKRs by 108% over the same period.[19,20] Projections for total hip and knee replacement provision for the UK and the USA have largely underestimated current need.[21,22] This continued increase in provision adds to the burden of health-care budgets to cope with financial pressures while keeping waiting lists to a minimum.[23] Therefore, it is important to ensure that any technological innovations in the management of total joint replacement in relation to decreasing pain and increasing function are a good use of medical and societal resources.

Patients' experiences of hip and knee osteoarthritis, and of joint replacement

Qualitative studies have explored patients' experiences of living with and managing osteoarthritis,[5,24–27] decision-making about joint replacement,[28] patient pathways to surgery[4,29] and patient satisfaction with outcomes of joint replacement.[28,30] This body of research has highlighted the impact of lower limb osteoarthritis on individuals and the possibility that patients' priorities are not always uppermost in current planning and delivery of treatments, including joint replacement. Research has also highlighted the importance of patient expectations in relation to the outcomes after joint replacement,[31,32] the importance of what is said to patients about their treatment options[5] and the fact that patients may not be satisfied with the outcome of their joint replacements, even if they tell the surgeon that they are doing well.[30] It is clear that we need to understand much more about what patients think about joint replacement and its outcomes, and improve the evidence base in this area. We also need to know the patient experience of joint replacement from pre-operative care to postoperative recovery.

The outcomes of hip and knee joint replacement

Traditionally, the success of a total hip or knee replacement was judged predominantly by the length of time the implant remained in situ.[33] The key issues for surgeons and prosthesis-producing companies were seen to be the design and fixation of a prosthesis that would last for $\geq$ 10 years, precluding the need for complex revision surgery.[34] However, owing to advances in surgical technique and prosthetics design, joint replacement now has good survivorship and post-surgical complication rates are low.[35,36] Over 95% of hip and knee replacements remain unrevised at 9 years after surgery.[3] Severe adverse events are uncommon, but complications such as dislocation,[37] infection,[38,39] fracture,[40] thromboembolism[41] and neurovascular damage[42] may occur and can significantly impact on pain, function and quality of life (QoL). There is also a small mortality risk.[43,44]

Attention has turned in recent years towards patient-reported outcomes in addition to technical outcomes.[45] Studies using patient-reported outcome measures (PROMs) suggest that mean pain and function scores after initial recovery from surgery are generally good.[46–48] However a significant minority of patients have persistent moderate or severe long-term pain and functional difficulties after joint replacement despite what appears to be otherwise successful surgery.[49–53] This fact has been obscured by the reporting of mean changes and averages for groups, ignoring the fact that although most people improve after hip or knee joint replacement, some improve more than others and some get little or no improvement or are worse after surgery than they were before it.[54] Pain and functional problems can impact on a patient's usual activities and those suffering from chronic long-term pain may be unable to return to work or leisure activities, and require a higher level of care from relatives and friends. Long-term pain after joint replacement imposes a burden on service use and costs to the NHS for those seeking relief, and to patients, carers and society as a whole. It is a problem that has received little research or service attention in the past.[55,56]

Patients living with osteoarthritis see function as key to their experience of illness.[24,57] Restoring function, alongside alleviation of pain, is a main aim of joint replacement. As noted, application of instruments such as the Western Ontario and McMaster Universities Arthritis Index (WOMAC) has suggested that there is an improvement in function in most (but not all) cases.[46,58,59] But the WOMAC, a self-report measure, like most other self-report measures of function, has no sound theoretical basis.[60] There are many alternatives, including observed measures of function, and more objective techniques such as pedometry or accelerometry,[61] but very few data are available on what the most appropriate means of assessing function in the context of joint replacement might be.

Management of acute and chronic pain after joint replacement

Acute perioperative pain

The management of acute postoperative pain poses a significant challenge in all surgical specialties. It has been estimated that approximately 40% of surgical patients experience moderate or severe acute postoperative pain.[62] Poor management of pain can be distressing for patients and can significantly delay ambulation, lengthen hospital stay, increase the number of unanticipated hospital admissions and contribute to poor mental health.[63–65] Furthermore, severe acute postoperative pain is a risk factor for the development of chronic post-surgical pain.[66]

Good perioperative pain management after joint replacement surgery allows early mobilisation and rehabilitation,[67] which minimises risks of complications such as deep-vein thrombosis, pulmonary embolus, muscle and joint contractures, physical deconditioning, and chest infection.[68] Early mobilisation also facilitates early discharge with associated cost savings.[69] However, acute postoperative pain after joint replacement is often poorly managed[70] and many methods of achieving perioperative pain relief, such as spinal or epidural anaesthetics and the use of opioids, can preclude early mobilisation.[71,72] Although there has been much interest in the management of perioperative pain, research has largely looked at the first 24–48 hours after surgery alone and the likely longer-term effects of good perioperative pain control have not been explored.

Chronic post-surgical pain

Chronic post-surgical pain is a significant problem after different types of surgery. It has been defined by the International Association for the Study of Pain (IASP) as 'pain that has developed after surgery, and been present for at least three months, which is beyond the time for normal healing'.[73] Pain can be defined as chronic post-surgical pain if four criteria are fulfilled:[74]

1. pain developing after a surgical procedure
2. pain present for at least 2 months
3. other causes of pain have been excluded
4. the pain is not a continuation of a pre-existing condition.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

However, application of such criteria is difficult for procedures such as joint replacement, for which the primary aim is relief of pre-existing pain and it can be very difficult to be sure whether or not the chronic problem is a continuation of a pre-existing one (e.g. through pain sensitisation).[75]

There is considerable variation in the reported prevalence of chronic post-surgical pain, but it is clear that somewhere between 10% and 50% of patients experience the problem after different forms of surgery, including breast surgery, vasectomy, hernia repair and cardiac surgery.[76]

Perioperative medical care and rehabilitation

In the UK, if a patient is considered for joint replacement for their osteoarthritis and they agree to the procedure being carried out, they will generally be asked to attend a pre-operative clinic for assessment of their general medical status and to make sure that the surgical team is clear on what operation will be performed. The medical screening at this clinic usually involves looking for major health problems that might preclude anaesthesia or surgery. The patient is also likely to be given some information about joint replacement, but this does not usually indicate what they should expect, in terms of pain and disability, after the immediate postoperative period. It is unusual for any action to be taken as a result of this screening, other than delaying the surgery if a major problem is uncovered.

Postoperatively, attention is paid to the wound, pain control and general health, and patients are usually encouraged to become active as soon as possible after the operation, with the help of a physiotherapist. In the UK, it is usual for patients to be discharged from hospital after about 3–5 days. Physiotherapists are almost always involved in postoperative mobilisation and provide general advice on what patients should do when they get home. The ability to climb a step or stair is often used as a criterion of a patient having reached a satisfactory functional status for hospital discharge. In contrast with some other countries, such as Germany, further rehabilitation is not generally available to UK NHS patients after their hip of knee joint replacement. Furthermore, there are no agreed standards or guidelines as to what should or should not be done perioperatively to optimise outcomes (relief of pain and improvement of function), partly because of the deficiencies in the evidence base. Therefore, it is not surprising that in the UK service provision before and after joint replacement is perceived to vary in level of provision and content.[77,78] Supply of aids and appliances as well as other occupational therapies are widely offered during the hospital stay.[79]

The provision of adequate information and formal rehabilitation are potentially important adjuncts to joint replacement surgery that might both reduce the length of stay in hospitals and improve patient outcomes.

The rehabilitation process aims to support the patient in regaining pre-impairment levels of function and QoL, and reintegration into their social and personal environment. Ideally, for patients receiving joint replacement, rehabilitation should commence before surgery and be provided as appropriate throughout the different stages of recovery.

- Pre-surgical interventions target optimisation of physical health and preparation for hospitalisation and recovery.
- Occupational therapy and home modifications, provided pre- or postoperatively, help people perform activities of daily living (ADL) safely at home or at work.
- Postoperative rehabilitation during the hospital stay focuses on regaining range of motion (ROM), functional independence in ADL and improving mobility.
- Subsequent rehabilitation targets maintenance or improvements in muscle strength, joint range of movement, balance and co-ordination, mobility, and extended ADL.

According to the World Health Organization (WHO) International Classification of Functioning, Disability and Health (ICF) model, rehabilitation should be patient-centred and aim to maximise functional ability, facilitate activities and increase social participation.[80]

Evidence on the effectiveness of different aspects of rehabilitation is limited.[81] Early systematic reviews considered interventions relating to pre-operative exercise,[82] education[83] and physiotherapy exercise.[84,85] Recommendations were limited by issues of study size and quality and, since the publication of these trials, more trials have been reported. There is no published systematic review of occupational therapy interventions in joint replacement.

The economic implications

In the context of scarce NHS resources, the evaluation of the cost-effectiveness of interventions to improve the outcomes of patients with osteoarthritis are increasingly pertinent.[86] Despite the well-established cost-effectiveness of providing total joint replacement surgery for advanced osteoarthritis, little is known about the long-term cost-effectiveness of interventions to improve outcomes after total joint replacement surgery. Economic evaluations of interventions targeting acute postoperative pain are generally truncated at point of hospital discharge or a few weeks after surgery. Evaluations in such studies are restricted to differences in costs of anaesthesia provided.[87–91] Other interventions focus on postoperative rehabilitation programmes but, generally, only the differences in costs in delivering treatment between arms is evaluated for the duration of the intervention. Longer-term studies to improve outcomes after surgery with a health economic evaluation have typically focused on delivery of physiotherapy treatments.[92,93] However, these have not included informal care costs and productivity losses which are needed to examine the broader impact on society. Only the latter, by including patient expenses, estimated costs beyond the health-care provider perspective. None have included informal care costs and productivity losses which would be needed to examine the broader impact on society.

Complex package of care

Ultimately, interventions within the joint replacement pathway should combine within a complex package of care with interaction between components.[94] Key areas in the development of a complex intervention relate to:

- development
  - identifying the evidence base
  - identifying and developing theory
  - modelling process and outcomes
- feasibility/piloting
  - testing procedures
  - estimating recruitment/retention
  - determining sample size
- evaluation
  - assessing effectiveness
  - understanding change process
  - assessing cost-effectiveness

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

- implementation
    - dissemination
    - surveillance and monitoring
    - long-term follow-up.

Development of a complex package of care requires input from diverse specialities and research methodologies. The authors of the Medical Research Council (MRC) guidelines recognise the importance of developmental studies before large-scale evaluations.[94]

Overview of the 'RESTORE' programme

Recognising the presence of long-term pain and disability in many patients after total hip and knee replacement, we developed the REsearch STudies into the ORthopaedic Experience (RESTORE) programme of research. The aim of the RESTORE programme was to conduct research on methods to improve the experience and outcomes of people undergoing hip or knee replacement for osteoarthritis. As shown in *Figure 1*, the programme consisted of a series of interrelated work packages, all supported by appropriate patient and public involvement (PPI). Here we briefly overview the individual work packages.

FIGURE 1 The RESTORE programme.

Patient and public involvement

Patient and public involvement has been a major feature of RESTORE. Meaningful patient involvement has supported all aspects of the programme. This comprised collaboration with Arthritis Care, patient representation on the RESTORE management group throughout its duration, establishment of a patient forum, employment of a PPI co-ordinator and having patient partners on each project steering group.

Since 2010, the patient forum, Patient Experience Partnership in Research (PEP-R), has supported RESTORE. Through facilitated group sessions, the patient forum provided input into refinement of patient recruitment materials, intervention development, readability of outcome assessment tools and dissemination of findings. Individual projects also had their own oversight groups, each of which included patients with an interest in joint replacement surgery to monitor the progress of the project. Patient involvement was carried out in line with INVOLVE's guidance. We believe that this work might act as a good example of how to involve patients meaningfully and effectively in research studies in musculoskeletal disease.

Systematic literature reviews

Synthesis of evidence from previous research using systematic review methods and meta-analysis to:

- assess the prevalence of long-term pain after total hip or knee replacement
- identify methods used to measure chronic pain after TKR
- identify predictors of long-term patient outcomes after total hip or knee replacement
- evaluate the associations between comorbid conditions and patient outcomes after hip and knee replacement
- evaluate the effectiveness of pre-surgical education and exercise interventions
- support randomised controlled trials (RCTs) with reviews of perioperative pain management, occupational therapy and physiotherapy exercise.

Understanding the patient experience

To characterise and explore the patient pathway through total hip or knee replacement surgery in current routine NHS care.

Measuring functional outcomes in a cohort study of patients having joint replacement: the ADAPT study

In the Assessing Disability After Partial and Total joint replacement (ADAPT) longitudinal cohort study of patients with primary and revision hip and knee replacement, we compared the properties with responsiveness of a selection of commonly used outcome tools that assess function, examined how well they relate to the WHO ICF concepts, and explored the changes in the measures over time.

Randomised controlled trial of perioperative pain control: the APEX trial with full economic analysis and nested qualitative research

We examined the clinical effectiveness and cost-effectiveness of multimodal perioperative analgesia in total hip and knee replacement. The key intervention tested in the Arthroplasty Pain EXperience (APEX) RCT was an injection of local anaesthetic into the wound during total hip and knee replacement surgery to provide both short- and long-term pain relief. An economic evaluation was conducted to determine the

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

cost-effectiveness of the intervention from a NHS and Personal Social Services (PSS) perspective. Data were also collected to allow a future economic evaluation from a societal perspective.

The APEX cohort study

Data from the APEX study provided the opportunity to assess the relationships between radiographic measures of osteoarthritis severity and patient-reported pain and function. We were also able to explore the associations between pre-operative patient factors and perioperative pain, and long-term patient outcomes. Pre-operative pressure pain thresholds (PPTs) were measured before surgery and we explored their value in predicting long-term pain after total hip and TKR.

Pain self-management: the SPIRAL study

In the Self-managing Pain In aRthritis and ArthropLasty (SPIRAL) study we conducted a pilot RCT to assess the feasibility of delivering a pain self-management course, run by Arthritis Care, to patients undergoing THR.

Occupational therapy: PROOF-THR

To assess the feasibility of occupational therapy provided before surgery, we conducted the Pilot Randomised controlled trial Of Occupational therapy For – Total Hip Replacement (PROOF-THR) pilot RCT in patients undergoing primary THR.

Physiotherapy exercise rehabilitation

We surveyed physiotherapy provision after total hip and knee replacement in large orthopaedic centres in England and Wales. We also conducted the Activity orientated REhabilitation following kNee Arthroplasty (ARENA) pilot RCT of an activity-orientated rehabilitation programme for patients undergoing primary TKR.

Economic analyses

We conducted a full economic analysis of the APEX RCT. In addition, for each of the pilot studies within the complex package of care development work stream, methods to collect resource-use data from a societal perspective were developed and assessed. These will facilitate full economic analyses in future definitive studies.

Complex package of care

Based on literature reviews, cohort and qualitative studies and RCTs we aim to provide recommendations to support the development of a complex package of care for patients receiving total hip and knee replacement.

Chapter 2 General systematic review methods: systematic reviews of long-term pain after hip and knee replacement, methods used to assess chronic pain and pre-operative predictors of long-term patient outcomes

Parts of this chapter have been reproduced from Beswick and colleagues.[18] This is an open-access article distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license. See: http://creativecommons.org/licenses/by-nc/2.0/ and http://creativecommons.org/licenses/by-nc/2.0/legalcode. Parts of this chapter have also been reproduced from Wylde and colleagues[95] © 2013 The Authors. Arthritis Care & Research is published by Wiley Periodicals, Inc. on behalf of the American College of Rheumatology. This is an open access article under the terms of the Creative Commons Attribution NonCommercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

Abstract

Background

We conducted systematic literature reviews on chronic pain after joint replacement, pre-operative predictors of patient outcomes and the impact of comorbidities.

Methods

Systematic reviews conducted in accordance with appropriate guidelines.

Results

About 7–23% of patients have moderate or severe pain after THR and about 10–34% after TKR.

There was extensive variation in pain outcome measures used in TKR research. Although there was an increase in use of patient-reported outcomes over time, few studies attempted to capture the incidence, character and impact of long-term pain.

Better pre-operative physical function and lower pain was associated with a better recovery in terms of joint specific pain and function. However, patients with poor physical function before surgery may have greater absolute improvement. Patients with depression before joint replacement had poorer long-term pain and functional outcomes. In patients receiving TKR, anxiety and poor general psychological health were associated with worse pain and functional outcomes. Across a broad range of BMI, patients benefited from joint replacement but those with highest levels may not achieve good functional and pain outcomes.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Although approximately 64% and 71% of patients receiving joint replacement have comorbidities, research on their relationship with long-term patient outcomes was limited. The impact of diabetes, previous heart disease and anaemia on the risk of post-surgical adverse events is recognised.

Conclusions

Systematic reviews identified the potential value of intervention before joint replacement and highlight the importance of appropriate assessment of long-term pain.

Systematic review methods

Comprehensive, systematic literature reviews are an essential prelude to developing interventions and trials. Systematic reviews aim to appraise evidence from published studies and have two broad objectives:

- a synthesis of knowledge to guide decision-making
- identification of deficits in the evidence base that merit further research.

A literature review can be considered systematic if the methods are sufficiently transparent and unbiased that it can be reproduced on the basis of:

- sources of literature
- how it was searched
- why a study was included or excluded
- which data were analysed and how
- how study quality was assessed.

Numerous reviews of varying quality have been published on the care of patients receiving total hip or knee replacement. The first step in our systematic review was to identify previous systematic reviews. Reviews were updated or started anew depending on our assessment of the systematic nature of the methods used.

In the context of the RESTORE programme, we conducted systematic literature reviews of both cohort studies and evaluations of interventions in RCTs.

Reviews of cohort studies relate to assessment of chronic pain after hip or knee replacement, pre-operative determinants of patient centred outcomes, and comorbid conditions and patient outcomes after hip and knee replacement.

Reviews of interventions relate to pre-surgical exercise and education interventions, perioperative local anaesthetic infiltration, physiotherapy exercise after TKR, and occupational therapy in THR.

Methods and guidelines

Systematic reviews were conducted using methods based on those described in the Cochrane handbook of systematic reviews.[96] Guidelines appropriate to the study designs being reviewed were adhered to. In reviews of RCTs we referred to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[97] and in review of observational studies to Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines.[98] Composite PRISMA and MOOSE checklists for the eight systematic reviews conducted in the RESTORE programme are included in *Appendices 1* and *2*, respectively.

Each review was conducted following general structured methods as outlined here. Specific methods for each review are detailed in a separate table following the participants, interventions, comparisons, outcomes, and study design (PICOS) construct.[99]

Identification of studies

Studies were identified by searching appropriate online databases with tailored search strategies. MEDLINE and EMBASE electronic databases were searched via the Ovid SP platform. Additionally, PsycINFO was searched via Ovid SP, Cumulative Index to Nursing and Allied Health Literature (CINAHL) via EBSCO*host* and The Cochrane Library databases were searched if considered relevant to the topic. For the review of occupational therapy, Allied and Complementary Medicine Database (AMED) was searched via Ovid SP, Physiotherapy Evidence Database (PEDro), Education Resources Information Center (ERIC) via ProQuest, Center for International Rehabilitation Research Information and Exchange (CIRRIE) and OTDbase were also searched.

Search strategies as applied in MEDLINE and used in appropriate combinations are shown in *Appendix 3*. Searches were supplemented with hand-searching of reference lists from trials and review articles. Key articles were tracked in ISI Web of Science.

Criteria for including studies

Studies were included according to specific criteria described for each review. These covered patient inclusion, interventions, outcome measures and study type.

In evaluating the clinical effectiveness of interventions, we included studies that were RCTs with randomisation either at individual or cluster level. Because many relevant studies are not recent and conducted in diverse health-care settings, we also included studies with a quasi-randomised design (e.g. alternate allocation) but with no specific evidence of bias owing to allocation method. There were no language restrictions with the exception for our reviews of cohort studies looking at pre-surgical predictors and comorbidities.

Study selection

Bibliographic details of the articles identified were exported and managed in EndNote (Thomson Reuters, CA, USA) databases, where duplicates were removed. Titles and abstracts of articles were screened by one or two reviewers to exclude studies that were clearly not relevant. As recommended in the Cochrane handbook, studies were classified as potentially relevant if a reviewer had any doubts about relevance on the basis of title and abstract.

A final reading of potentially relevant articles and study selection based on defined eligibility criteria were carried out by two reviewers with further input of a relevant health-care professional, if required. Full papers for all potentially relevant studies were obtained electronically, from local libraries or through interlibrary loans. The progress of each review was recorded as a flow diagram.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Studies reported only as abstracts or for which we were unable to acquire full-text copies using interlibrary loans or e-mail contact with authors were excluded from the analyses. Reasons for exclusion at this stage were summarised in individual systematic review flow diagrams (see *Figures 2, 4, 7, 8, 21, 37, 42* and *48*).

Data extraction

Data were extracted from each paper by two reviewers or by one reviewer with data checked against source material by a second. For reviews of predictors and comorbidities, about 25% of articles were checked against source material by a second reviewer. Authors, colleagues and family helped to translate and interpret studies not published in English.

In reviews of observational cohort studies with no intervention reported, we extracted data relating to how representative the cohort is of the general population; variables and outcomes collected; methods of statistical analyses; as well as country, dates of data collection, and summaries of patient characteristics.

Data extracted from intervention studies included when and where the study was conducted; patient characteristics (mean age, percentage male/female, indication); inclusion criteria; description of interventions; timing, duration; health-care professionals providing care; and losses to follow-up and reasons. Results were recorded on piloted data extraction forms and Microsoft Excel® 2007 (Microsoft Corporation, Redmond, WA, USA) spreadsheets. If published reports did not contain the required data, authors were contacted. We also asked if any outcomes not reported in publications had been collected. If authors had provided information to other reviewers, then these data were included in our analyses and acknowledged appropriately. For continuous variables, means and standard deviations (SDs) were extracted. If outcomes were reported as means and confidence intervals (CIs), or medians and interquartile ranges (IQRs), appropriate conversions and estimations were used.[96]

Data analysis

Outcome data were extracted to Microsoft Excel spreadsheets and analysed in Stata 12 (StataCorp LP, College Station, TX, USA) or RevMan 5 (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark).

Studies were categorised according to our pre-specified criteria. If a sufficient number of intervention studies reported common outcomes, data were combined in meta-analyses. Combined outcomes were summarised as average mean difference (MD) if the outcome used a common measurement scale (e.g. length of hospital stay) or as average standardised mean difference (SMD) if different methods were used to assess a particular outcome. Generally we combined outcomes using random-effects meta-analysis[96,100] and reported 95% CIs, *p*-values for the magnitude of effect and tests of heterogeneity. When possible, results are shown as forest plots.

When two interventions were reported with a shared control group, in meta-analysis the number for controls was halved.

Quality assessment

For observational cohort studies our quality assessment was based on the diversity of centres (registry, multiple centres, single centre or surgeon), and losses to follow-up.

For RCTs, the Cochrane risk-of-bias table was used to assess study quality. Bias was assessed independently by two reviewers or assessed by one and checked by a second, with disagreements resolved by discussion. Risk of bias was based on random sequence generation, allocation concealment, blinding of outcome assessment, completeness of outcome data, selective reporting and other potential sources. In the context of the studies we reviewed, completeness of outcome data collection and blinding of outcome assessment were considered the key issues relating to risk of bias.

Systematic review of the severity of long-term pain after total hip or knee replacement

Background

We aimed to identify studies reporting the proportion of people with significant long-term pain after total hip or knee replacement. Eligible studies reported prospective follow-up of consecutive, unselected patients who were representative of the primary total hip or knee replacement population. We limited follow-up to 3 months to 5 years as this reflects the time when pain[48] and prosthesis-related outcomes[101] can be considered optimal.

Methods

General methods	As described in *Systematic review methods*
Databases and dates	MEDLINE and EMBASE from inception to 31 January 2011. Citations of key articles in ISI Web of Science and reference lists
Search strategy	Total hip or knee replacement/osteoarthritis/epidemiological study design/PROM. MEDLINE search strategy based on terms in *Appendix 3*
Study design	Prospective follow-up of consecutive, unselected patients
Patients	Patients with primary total hip or knee replacement
Follow-up	3 months to 5 years
Data extraction	Indication, pain outcome, baseline dates, country, study design, follow-up, how group selected, age, number of patients recruited, number who died and the number lost to follow-up
Outcomes	Patient-reported pain in the operated knee. Proportions of people with different severities of pain at follow-up were summarised as: • 'favourable': no pain or mild pain at follow-up • 'unfavourable': moderate to severe pain or for whom surgery had not relieved pain • 'uncertain': patients who had died, had revision surgery, contralateral surgery or dislocation and were not followed up with questionnaires, and those lost to follow-up
Quality assessment	Representativeness of study population. Losses to follow-up

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Results

Review progress is summarised in *Figure 2*. Searches identified 1308 studies reporting patient-centred outcomes in patients with osteoarthritis. Of these, 115 studies were potentially eligible. After detailed evaluation, 14 articles describing 17 cohorts presented results classifiable as proportions of people with different extents of pain at follow-up. Six cohorts reported outcomes in hip replacement,[49,51,58,102–104] and 11 in knee replacement patients.[47,49,50,58,102,105–110] The main reasons for exclusion at this stage were lack of a pain outcome separate from an overall outcome score or the presentation of results as means only. Patient and study characteristics are summarised briefly in *Table 1* and in more detail with outcome data in *Appendix 4*.

Studies ordered within hip and knee replacement groups by decreasing representativeness (multiple compared with single centre); and by increasing losses to follow-up.

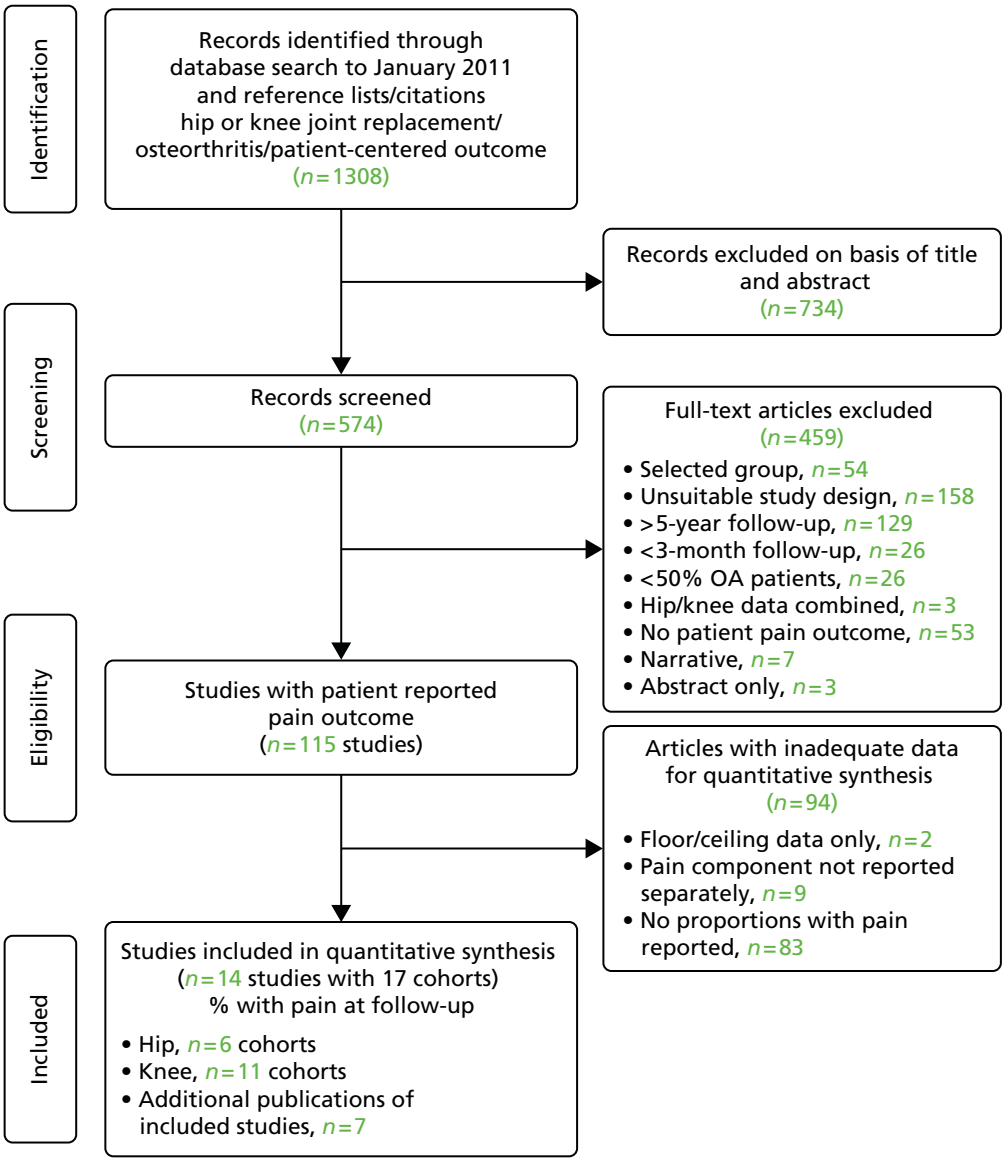


FIGURE 2 Systematic review of long-term pain after hip or knee replacement: flow diagram. OA, osteoarthritis.

TABLE 1 Systematic review of long-term pain after hip or knee replacement: included studies

Author	Population	Pain outcome measure; follow-up time
THR		
Nikolajson and colleagues 2006[51]	1231 consecutive patients in a national joint registry	Authors' own scale; 12–18 months
Jones and colleagues 2000[58]	Estimated 242 consecutive patients with hip replacement in health region	WOMAC pain; 6 months
Quintana and colleagues 2006[102]	784 consecutive patients scheduled for THR in seven teaching hospitals	WOMAC pain; 6 months
Nilsdotter and colleagues 2003[103]	92 consecutive patients with two surgical methods at single centre	WOMAC pain; mean 43 months
Singh and Lewallen 2010[104]	9154 consecutive patients from joint registry	Authors' own scale; 24 and 60 months
Wylde and colleagues 2011[49]	1401 consecutive patients at single centre	WOMAC pain; median 41 months
TKR		
Baker and colleagues 2007[105]	9417 random sample of patients in joint registry	OKS pain; 12 months or latest available
Jones and colleagues 2000[58]	Estimated 292 patients in health region	WOMAC pain; 6 months
Quintana and colleagues 2006[102]	792 consecutive patients in seven centres	WOMAC pain; 6 months
Núñez and colleagues 2007[47]	88 consecutive patients at a single centre	WOMAC pain; 36 months
Stephens and colleagues 2002[106]	68 patients aged $\geq$ 50 years	WOMAC pain; 6 months
Lundblad and colleagues 2008[107]	69 patients scheduled for knee replacement	VAS pain; 18 months
Nilsdotter and colleagues 2009[108]	102 responders to postal survey on waiting list for knee replacement	KOOS pain; 60 months
Vuorenmaa and colleagues 2008[109]	51 patients referred for knee replacement	VAS pain; 3 months
Czurda and colleagues 2010[110]	411 consecutive patients with computer assisted or conventional surgery	WOMAC pain; mean 26 months (range 18–42 months)
Wylde and colleagues 2011[49]	1394 consecutive patients at single centre	WOMAC pain; median 28 months (range 14–43 months)
Brander and colleagues 2003[50]	116 consecutive patients operated on by one surgeon	VAS pain; 12 months

KOOS, Knee Injury and Osteoarthritis Outcome Score; OKS, Oxford Knee Score; VAS, visual analogue scale.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Total hip replacement

Systematic searches identified six studies including a total of 13,031 patients.[49,51,58,102–104] Pain outcome assessments were based on the WOMAC pain scale or authors' own methods.

One study was in patients recruited from a national joint registry.[51] Two studies were in multiple centres,[58,102] and three were studies in single centres.[49,103,104] Cohorts were generally similar with regard to patient age (range of means or medians 65.0–73.0 years) and sex (range of percentage female 48.3–63%). Losses to follow-up ranged from 5.8% to 47.6%. We considered two markers of study quality: multiple compared with single centres and lower losses to follow-up.

Overall, an unfavourable pain outcome was seen in at least 4.8% and up to 20.5% of patients after THR (*Figure 3*). However these are likely to be underestimates as we do not have information on the outcomes in between 5.8% and 52.7% of patients.

Proportion of patients with outcome

Applying the conservative assumption that an equal proportion of patients with missing data had an unfavourable pain outcome, we estimate that at least 7–23% of patients experienced long-term pain after hip replacement. In three higher-quality, more representative studies conducted in multiple centres, this would reflect an unfavourable pain outcome in 9%,[58] 13%[51] and 20%[102] of patients, and in three studies with low losses to follow-up in 9%,[58] 13%[51] and 23%[103] of patients. Data from two studies considered more representative and with low losses to follow-up suggested that 9%[58] to 13%[51] of patients had an unfavourable pain outcome after THR.

Total knee replacement

Searches identified 11 studies including a total of 12,800 patients.[47,49,50,58,102,105–110] Pain outcome measures were based on the WOMAC and Knee Injury and Osteoarthritis Outcome Score (KOOS) pain scales, the Oxford Knee Score (OKS) pain dimension or pain measured on a visual analogue scale (VAS). One study was in patients recruited from a national joint registry.[105] Two studies were in patients from multiple centres,[58,102] six studies were in patients treated at a single centre[47,106–110] and one study reported all patients operated on by one surgeon.[50] Cohorts were generally similar with regard to patient age (range of means or medians 66–76 years) and sex (range of percentage female 54–86%), and the indication was osteoarthritis in ≥ 94% of patients when specified. Losses to follow-up ranged from 0% to 43.5%.

Overall, after TKR, an unfavourable pain outcome was seen in at least 8.0% and up to 26.5% of patients (see *Figure 3*). Assuming conservatively that the patients with missing data had similar pain outcomes, studies suggested that at least 10% to 34% of patients experience long-term pain after knee replacement. Applying this assumption in the higher-quality studies with potentially more representative populations, at least 19%,[105] 20%[58] and 31%[102] of patients had an unfavourable pain outcome after TKR. In four studies with low losses to follow-up, 10%,[47] 13%,[105] 17%[106] and 20%[58] of patients reported an unfavourable pain outcome at follow-up. In one study conducted in multiple centres with low losses to follow-up, 20% of patients reported an unfavourable pain outcome at follow-up.[58]

Discussion

Well-conducted studies in representative populations of patients with primary total hip and knee replacement suggest that a significant proportion of people continue to have painful joints after surgery. Our analyses were limited by the small number of studies and different pain outcome measures. These precluded meta-analysis, calculation of a summary estimate and exploration of sources of heterogeneity.

The proportion of people with an unfavourable long-term pain outcome in studies ranged from about 7% to 23% after hip replacement, and 10% to 34% after knee replacement. In the best quality studies an unfavourable pain outcome was reported in ≥ 9% of patients after total hip and about 20% of patients after TKR.

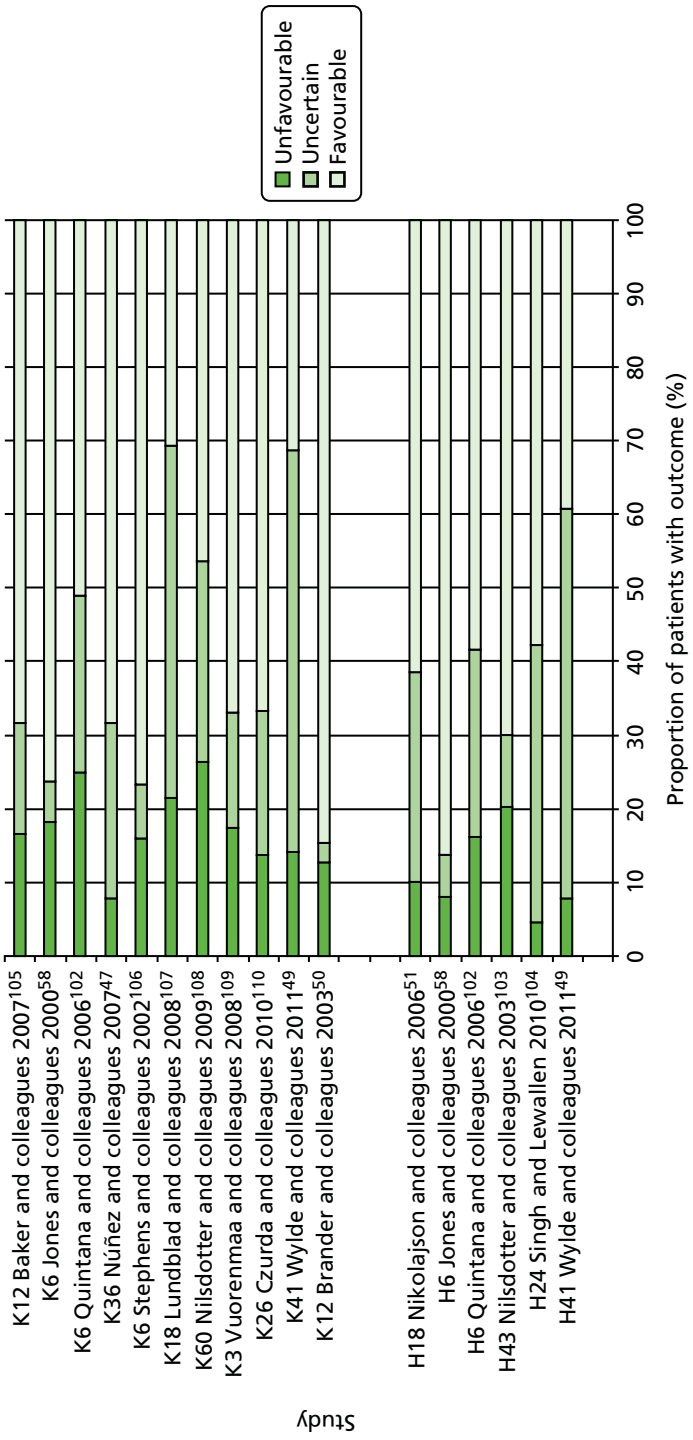


FIGURE 3 Systematic review of long-term pain after hip or knee replacement: proportion of patients with pain at follow-up. Preceding study author: H (hip) or K (knee) and months (follow-up). Studies ordered within hip and knee replacement groups by decreasing representativeness (multiple compared with single centre) and by increasing losses to follow-up.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Conclusion

For many people, total hip or knee replacement is effective in treating osteoarthritis pain. However, a significant proportion of people have painful joints after surgery.

Systematic review of methods used to assess chronic pain after total knee replacement

Background

Pain is a key outcome after TKR[111] and our systematic review showed that 10–34% of patients report long-term pain. However, there is little guidance about which aspects of pain should be assessed. For clinical trials investigating efficacy of chronic pain treatments, the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) recommends that the assessment of pain should include an assessment of pain intensity, pain medication usage, pain quality and the temporal aspects of pain.[112] The aim of this review was to determine which outcome measures have been used to assess chronic pain after TKR by reviewing all original research articles published over a 10-year period.

Methods

General methods	As described in *Systematic review methods*
Databases and dates	MEDLINE, EMBASE, PsycINFO, The Cochrane Library and CINAHL databases from 1 January 2002 to 22 November 2011
Search strategy	Knee replacement/pain. MEDLINE search strategy based on terms in *Appendix 3*
Study design	Study design filters were not applied. Empirical studies
Patients	Patients with knee replacement
Data extraction	Pain at $\geq$ 3 months
Outcomes	Study objective, study design, setting, country of the first author, number of study participants recruited, timings of assessments and outcome measures that contained pain items
Quality assessment	No assessment conducted

Results

Characteristics of included studies

The review process and reasons for exclusion are summarised in *Figure 4*. A total of 8486 articles were identified in the literature searches and screened for potential eligibility by one reviewer. A second reviewer performed duplicate screening on a random 1000 articles but no relevant articles had been missed by the first reviewer. After screening, 1164 articles met the eligibility criteria for the review. Studies included in the review used a variable number of outcome measures that incorporated pain items (range 1–14), with 506 studies (43%) using two or more measures.

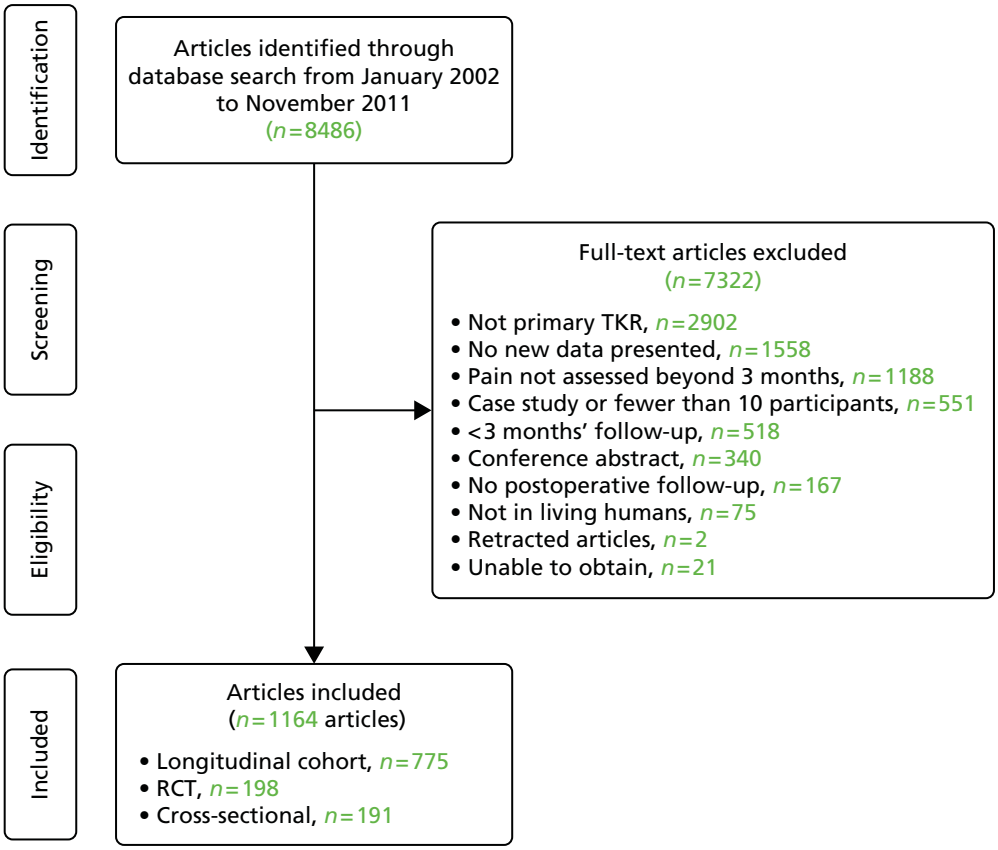


FIGURE 4 Systematic review of methods used to assess chronic pain after TKR: flow diagram.

Multi-item tools

Overall, 54 different multi-item tools containing pain questions were used in the studies of TKR. Five multi-item tools were used in > 5% of the studies and these included the American Knee Society Score (AKSS),[113] WOMAC,[114] Hospital for Special Surgery Knee Score (HSS),[115] Short Form questionnaire-36 items (SF-36)[116] and OKS.[117] Details of the multi-item tools that were used in more than five studies and the number of items which assessed pain within each of these tools are provided in *Table 2*.

Geographical trends in the use of multi-item tools

The use of multi-item tools by countries that contributed > 50 articles to the review were compared (*Figure 5*). Nation-specific preferences for particular tools were apparent, with the AKSS being the most commonly used tool in studies from the USA, UK, Germany, South Korea and Australia. The HSS was most commonly used in studies from China, whereas the WOMAC was the most frequently used in Canadian studies.

Temporal trends in the use of multi-item tools

The percentage of studies using the five most commonly used multi-item tools over a 10-year period is displayed in *Figure 6*. From 2006 to 2011 there was a reduction in the proportion of studies that have used the AKSS, from 66% in 2006–7 to 52% in 2010–11. Over the same time period, there has been an increase in the proportion of studies that have used the WOMAC, from 19% in 2006–7 to 32% in 2010–11.

Single-item questions

Single-item questions were used 333 times to assess chronic pain after TKR. The aspects of pain assessed by the single-item questions, based on the framework provided by IMMPACT, are shown in *Table 3*. Pain severity was the most frequently assessed aspect of pain and the VAS was the most commonly used question format to assess pain severity.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 2 Systematic review of methods used to assess chronic pain after TKR: multi-item tools

Multi-item tool	Number of studies (%) that used tool	Number of items in tool	Number of items that assess pain
AKSS	675 (58)	10	1
WOMAC	267 (23)	24	5
HSS	184 (16)	7	2
SF-36	165 (14)	36	2
OKS	101 (9)	12	5
SF-12	54 (5)	12	1
KOOS	26 (2)	42	9
EQ-5D	25 (2)	5	1
Feller Patellar Score	20 (2)	4	1
ADL Scale of the Knee Outcome Survey	14 (1)	17	1
Lequesne Index	11 (< 1)	12	5
Tegner and Lysholme score	9 (< 1)	8	1
Total Knee Function Questionnaire	9 (< 1)	55	1
NHP	7 (< 1)	45	8
Self-Administered Patient Satisfaction Scale	6 (< 1)	4	1
Stern and Insall Patellar Score	6 (< 1)	1	1
Bristol Knee Score	6 (< 1)	9	1
15D	6 (< 1)	15	1

EQ-5D, European Quality of Life-5 Dimensions; NHP, Nottingham Health Profile; SF-12, Short Form questionnaire-12 items.

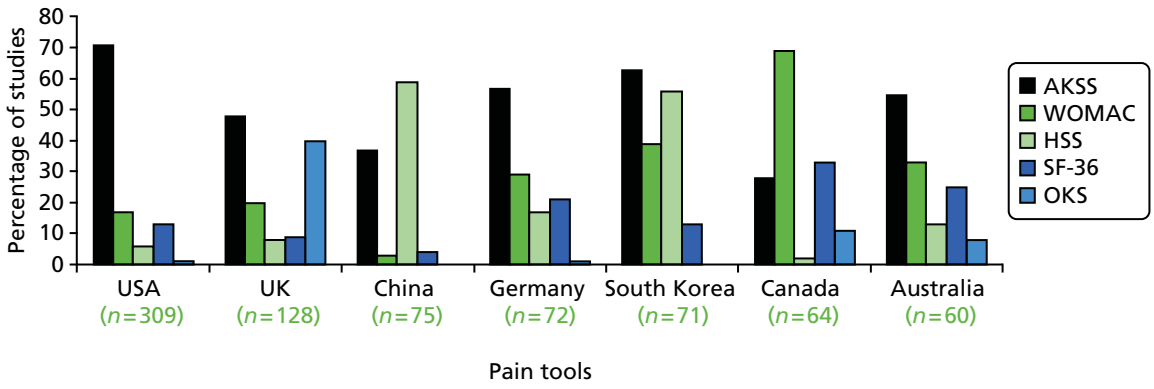


FIGURE 5 Systematic review of methods used to assess chronic pain after TKR: geographical trends in use of multi-item tools.

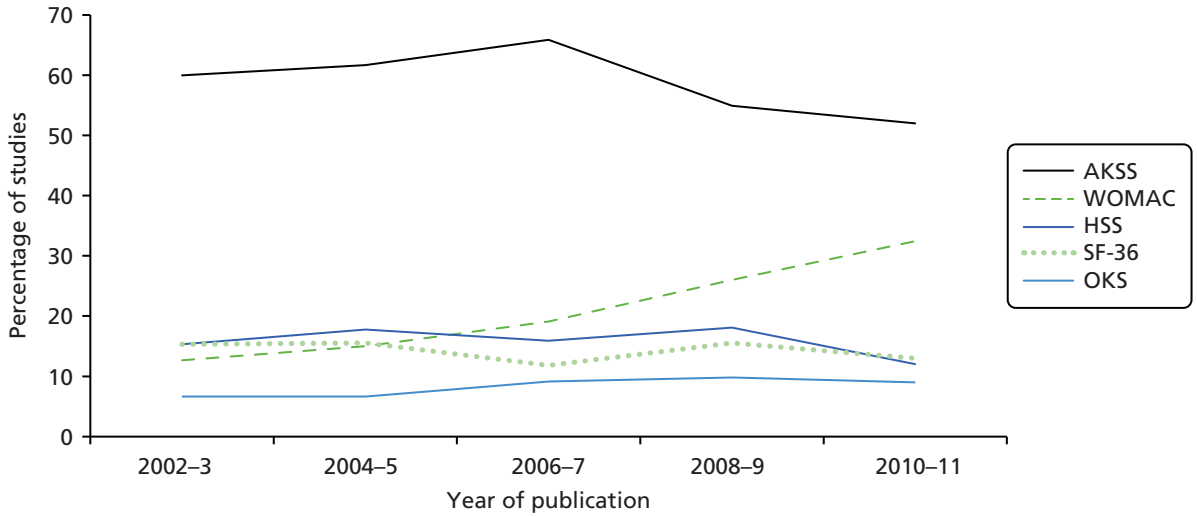


FIGURE 6 Systematic review of methods used to assess chronic pain after TKR: temporal trends in the use of multi-item tools.

TABLE 3 Systematic review of methods used to assess chronic pain after TKR: aspects of pain assessed by the single-item questions

Pain domain	Examples of codes	Number (%) of single-item questions
Pain intensity	General pain intensity	227 (68)
	Average pain intensity	
	Worst pain intensity	
	Presence/absence of pain	
Use of pain medication	Frequency of use	8 (2)
	Adherence	
	Decreased need	
Pain quality	Location of pain (e.g. anterior knee pain)	57 (17)
Temporal aspects of pain	Pain frequency	33 (10)
	Night pain	
	Constant pain	
	Intermittent pain	
Physical functioning	Pain on walking	98 (29)
	Pain on climbing stairs	
	Pain during sports	
	Pain at rest	
Emotional functioning	Unbearable pain	5 (1.5)
	Bothersome pain	
	Emotional well-being	
Participant ratings of global improvement	Satisfaction with pain relief	26 (8)
	Reduction in pain from operation	
	Fulfilment of expectations	

Each single-item pain question could be coded into more than one pain domain.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Discussion

Numerous tools are available to assess general health and functional outcomes after TKR.[118] Despite a growing interest in investigating the burden, character and impact of long-term pain, we found that assessment has been inconsistent with extensive variation in the outcome measures used after TKR.

The AKSS is widely used in orthopaedic research,[119,120] and was the most common method to assess long-term pain used in 58% of studies. The scale involves a clinician-conducted assessment and a composite score based on functional ability and measurements such as ROM and joint stability, and a single question about pain.

Our review showed a reduction over time in the use of the AKSS, accompanied by an increase in the use of the WOMAC. This may reflect increased awareness of the assessment of outcomes from a patient's perspective.[121,122] There was also international variation in the use of multi-item tools.

Strengths of this review were the systematic and rigorous methods used to search and screen eligible articles, the wide inclusion criteria with diverse epidemiological and experimental study designs, and the inclusion of studies irrespective of language. Owing to the high volume of literature, it was not feasible to assess whether or not particular methods were used in studies of different quality.

Conclusion

Our systematic review shows that the assessment of long-term pain after TKR could be improved. Despite the availability of many validated pain-related instruments, few studies have attempted to capture the incidence, character and impact of chronic pain after TKR. Future research is needed to develop consensus and standardisation on which pain domains should be assessed after TKR.

Systematic review of pre-operative predictors of patient-centred outcomes after total hip and knee replacement

Background

Identification of pre-operative determinants and predictors of poor outcomes can guide the development of interventions and help target the provision of care. For factors that are determinants, the possibility exists that an intervention may alter the level of the factor and that this may lead to improved outcomes. Other variables cannot be changed by an intervention but may have value in predicting outcomes with care tailored for specific patient groups.

Associations between variables measured before joint replacement and post-surgical outcomes have been studied extensively. Establishment of a cohort study in an orthopaedic setting is relatively straightforward in the context of routine data collection and follow-up. However, it is important that analyses are conducted with robust statistical methods taking into account possible confounding factors.

The aim of this review was to identify high-quality systematic reviews and cohort studies that have assessed the predictive value of pre-surgical factors in relation to long-term post-surgical outcomes. In keeping with the themes of the RESTORE programme, we considered patient-reported outcomes.

Pre-surgical factors studied in detail were:

- BMI
- mental health status including anxiety and depression
- pain
- physical function.

Methods

General methods	As described in *Systematic review methods*
Databases and dates	MEDLINE and EMBASE from inception to 15 October 2013
Search strategy	Joint replacement/osteoarthritis/specified patient centred outcomes. MEDLINE strategy based on terms in *Appendix 3*
Study design	Cohort studies with multivariable regression analysis or ANCOVA
Patients	Total hip or knee replacement. If both reported, included only if analysed separately and with at least 100 patients per analysis
Follow-up	At least 12 months
Data extraction	Date of publication, hip or knee, country, baseline dates, follow-up duration, pre-surgical measures
Outcomes	Patient-reported outcomes

ANCOVA, analysis of covariance.

All titles and abstracts of articles published in 2010 were checked for inclusion by two reviewers experienced in orthopaedic research and systematic reviews. Comparison of inclusion decisions showed good agreement between reviewers. Subsequently titles and abstracts were checked by one reviewer but with oversampling in the event of uncertainty.

At an early stage, it became apparent that the literature base for the review was very large. We limited our inclusion to studies with ≥ 100 patients with at least 12 months' follow-up and to studies published in English.

Quality assessment

A level of good quality of studies was implicit with study selection based on seven MINORS criteria:[123]

- clear stated aim – multivariable analysis
- inclusion of consecutive patients – cohort study
- prospective collection of data – prospective
- end points appropriate to aim of study – pain, function, satisfaction
- unbiased assessment of end point – patient-reported outcomes
- follow-up period appropriate to aim of study – at least 12 months
- prospective calculation of study size – estimated at least 100.

For the eighth criterion we considered:

- per cent follow-up of those at baseline (eligible) – $>80\%$ good quality.

Furthermore we included one classification modified from the Newcastle-Ottawa quality assessment scale:[124]

- representativeness of the cohort – registry or multiple centres good quality.

These last two classifications were used to assess quality of the studies relating to generalisability.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Results

Review progress is summarised as flow diagrams for total hip and TKR in *Figures 7* and *8*. We identified one systematic review and 53 cohort studies that explored the relation between pre-surgical factors and long-term outcomes in multivariable analysis.

Total hip replacement

Searches identified 26 studies reporting multivariable analyses including patients with THR. In this section we summarise results from 14 studies of pre-operative BMI, mental health, pain and physical function as predictors of long-term patient-reported outcomes.[31,103,104,125–135] Study characteristics are summarised in *Appendix 5* with brief details in *Table 4*.

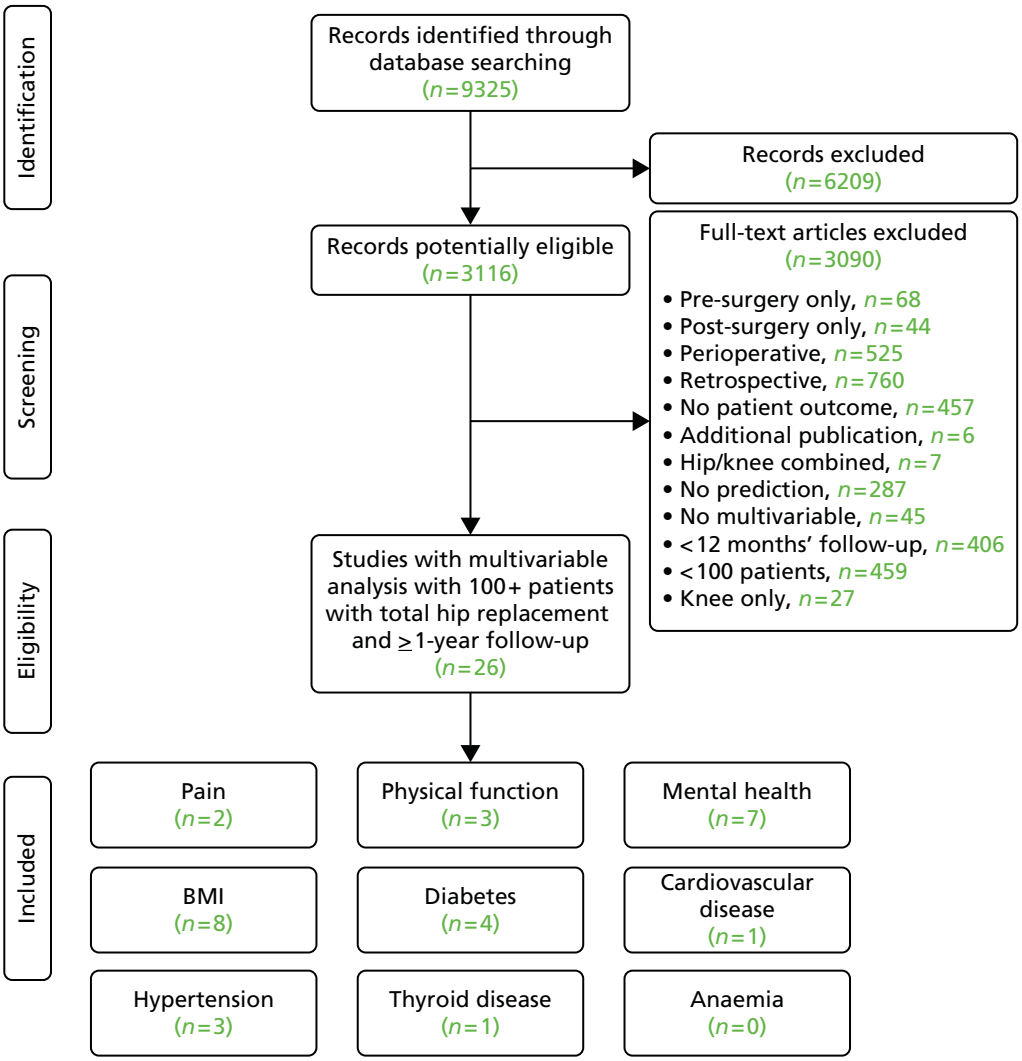


FIGURE 7 Systematic review of pre-operative predictors of patient-centred outcomes after THR: flow diagram.

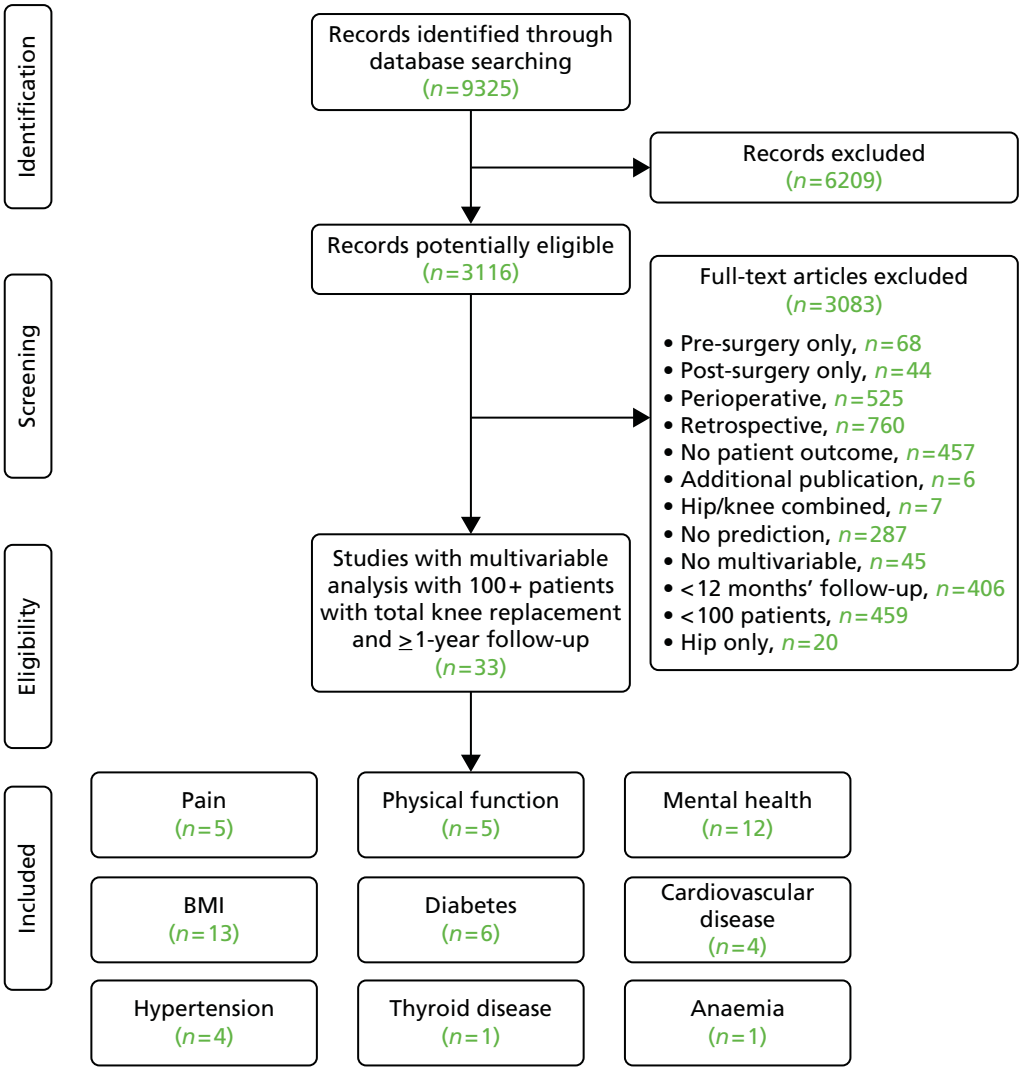


FIGURE 8 Systematic review of pre-operative predictors of patient-centred outcomes after TKR: flow diagram.

TABLE 4 Systematic review of pre-operative predictors of patient-centred outcomes after THR: included studies

Study	Number of patients; follow-up	Predictors	Outcome measures
Registry			
Rolfson and colleagues 2009[125]	6158; 12 months	Mental health	VAS pain, satisfaction, EQ-5D domains
Multiple centres			
Hajat and colleagues 2002[126]	3600; 12 months	Physical function	OHS
Jones and colleagues 2012[127]	Estimated 167; 3 years	BMI	WOMAC
Judge and colleagues 2011[31]	845; 12 months	Physical function	WOMAC
Judge and colleagues 2013[128]	1375; 60 months	BMI, mental health, physical function	OHS
Stevens and colleagues 2012[129]	653; 12 months	BMI	WOMAC, SF-36

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 4 Systematic review of pre-operative predictors of patient-centred outcomes after THR: included studies (*continued*)

Study	Number of patients; follow-up	Predictors	Outcome measures
Single centre			
Anakwe and colleagues 2011[130]	850; 12 months	Mental health, physical function	Satisfaction
Clement and colleagues 2011[131]	1312; 12 months	Mental health, physical function	OHS
Davis and colleagues 2011[132]	1095; 60 months	BMI	SF-36
Gandhi and colleagues 2010[133]	636; 12 months and up to 72 months (mean 39 months)	BMI, mental health	WOMAC, SF-36 physical function
Garbuz and colleagues 2006[134] and Xu and colleagues 2005[136]	147; 12 months	Pain, physical function	WOMAC pain
Moran and colleagues 2005[135]	687; minimum 18 months	BMI	SF-36
Nilsdotter and colleagues 2003[103]	198; 12 months and at mean 43 months	BMI, mental health, pain	WOMAC function
Singh and Lewallen 2010[104]	5707; 24 months	BMI, mental health	Pain (five-response scale)

EQ-5D, European Quality of Life-5 Dimensions; OHS, Oxford Hip Score.

Body mass index

There is no clear evidence linking high BMI with the development of hip osteoarthritis,[137] but people with higher BMI are more likely to require THR. For example, in a UK study including over 490,000 women, those with a BMI of > 30 kg/m^2 had nearly 2.5 times the risk of requiring a THR of those with a BMI of < 22.5 kg/m.[138] Patients included in the National Joint Registry for England and Wales in 2012 had an average BMI of 28.71 kg/m^2 (SD 5.29 kg/m^2) and about 39% had a BMI of ≥ 30 kg/m^2.[3] In the RESTORE APEX RCT, the mean BMI in 322 patients receiving THR was 29.1 kg/m^2 (SD 5.5 kg/m^2, range 18.6 to 47.8 kg/m^2) and 4.3% of patients had a BMI of ≥ 40 kg/m^2. The distribution of BMI of patients in the APEX cohort of patients with THR is shown in *Figure 9*.

Our searches of MEDLINE and EMBASE considered long-term patient-reported outcomes after THR. Searches identified eight studies that specifically focused on the relationship between BMI and patient-reported outcomes at ≥ 12 months after THR. Three studies included patients from multiple centres,[127–129] and five studies were conducted at a single centre.[103,104,132,133,135] Study details are summarised in *Table 4*. In studies with data that allowed estimation, rates of follow-up ranged from 6% to 38%.

Jones and colleagues followed up approximately 167 patients (72% eligible) from a Canadian health region 3 years after a THR.[127] The authors used WHO criteria to classify patients into groups of BMI (< 25 kg/m^2, 25–29.9 kg/m^2, 30–34.9 kg/m^2, ≥ 35 kg/m^2). In the cohort, 13.9% of patients had a BMI of ≥ 35 kg/m^2. In an analysis with adjustment for age, sex, diabetes and cardiac disease, the authors reported that similar long-term WOMAC pain and function scores were achieved in patients with different levels of BMI. Considering data collected at 6 months, the authors noted that recovery of function and reduction of pain was slower in patients with a high BMI (≥ 35 kg/m^2) than groups with lower BMI.

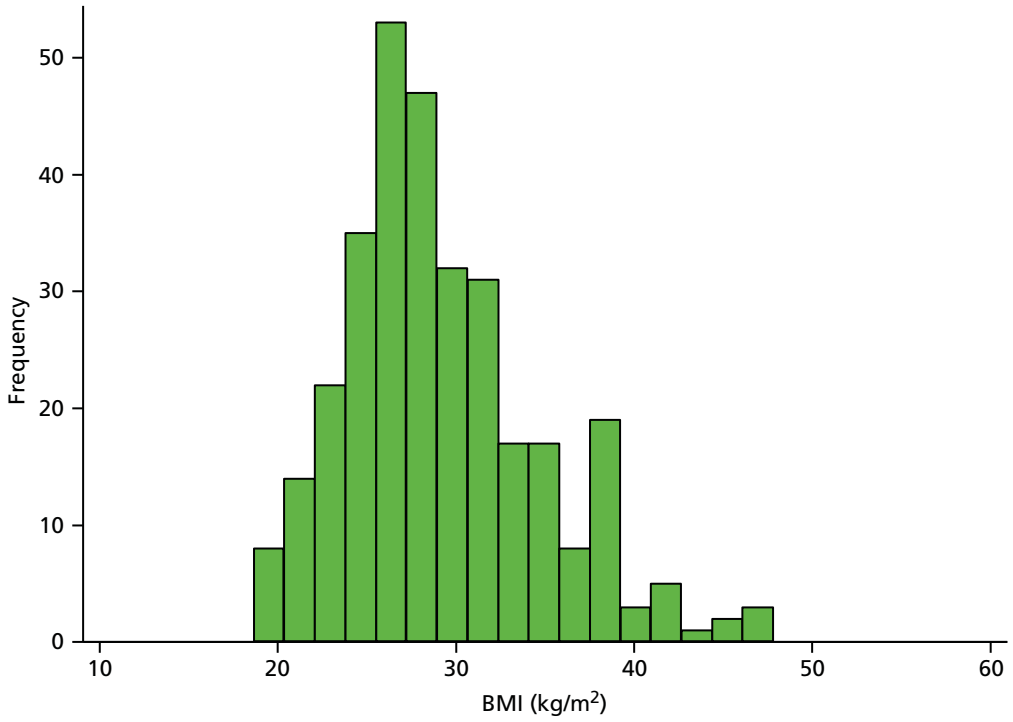


FIGURE 9 Distribution of BMI in the APEX THR cohort.

Judge and colleagues[128] followed up 1375 patients (64% eligible) who had received a specific design of THR prosthesis at seven UK centres 5 years after surgery. The mean BMI of patients in the cohort followed up was 27.6 kg/m^2 (SD 4.8 kg/m^2) and it was treated as a continuous variable. In multivariable analyses including age, sex, primary diagnosis, occupation, comorbidities, health-related quality of life (HRQoL), hip ROM, surgical variables and Oxford Hip Score (OHS), there was a relationship between increasing BMI and poorer long-term function and pain as measured by the OHS. The authors considered the differences in function and pain associated with BMI to be small.

In a study at three orthopaedic centres in the Netherlands, Stevens and colleagues[129] followed up 653 patients (77% eligible) 12 months after receiving a THR. The mean BMI was 27.0 kg/m^2 (SD 4.1 kg/m^2) and the authors defined three groups (< 25 kg/m^2, 25–30 kg/m^2, > 30 kg/m^2). After adjusting analyses for age, sex, comorbidities and complications, increased BMI was associated with worse long-term function but the size of the effect was low, particularly in comparison to that of presence of comorbidities and complications.

Moran and colleagues[135] followed up 687 patients (86% eligible) with THR at a single UK centre. The mean BMI in this cohort was 27.8 kg/m^2 (SD 5 kg/m^2) and the authors reported that only 9 out of 687 patients (1.3%) had a BMI of > 40 kg/m^2 and that no conclusions could be drawn for these patients. After adjusting for sex, comorbidities, OHS and SF-36, BMI treated as a continuous variable was not a significant predictor for any SF-36 domains.

Nilsdotter and colleagues[103] reported the follow-up of 198 patients (94% eligible) with THR from a single centre in Sweden at a mean of 3.6 years. The authors analysed BMI as a continuous variable but did not report mean or categorical values. Increasing BMI was associated with poorer long-term WOMAC function in univariate analysis. After adjustment for sex, comorbidities, WOMAC, SF-36 (including mental health), employment, marital status, contralateral osteoarthritis, need of walking assistance, walking distance, analgesic use and regional or widespread pain, BMI was not associated with long-term WOMAC function.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Davis and colleagues[132] followed up 1095 patients (68% eligible) from a single UK centre 60 months after THR. The mean BMI in the cohort was 28 kg/m^2 at baseline and 9.2% of patients had a BMI of $\geq$ 35 kg/m^2. Patients were divided into groups according to their BMI (< 25 kg/m^2, 25–29.9 kg/m^2, 30–34.9 kg/m^2, $\geq$ 35 kg/m^2). In multivariable analysis with age, sex, pre-operative hip score, SF-36, comorbidities and consultant, increasing BMI predicted poorer long-term SF-36 physical function and bodily pain. However, the authors acknowledged that although absolute levels of long-term pain and function were poorer than in patients with low BMI, there were dramatic improvements in patient outcomes in those with high BMI.

Singh and Lewallen[104] reported a 2-year follow-up of 5707 patients with THR (62% eligible) at a single US centre. Four per cent of patients had a BMI of $\geq$ 40 kg/m^2 or greater. The authors divided patients into five groups according to their BMI (< 25 mg/m^2, 25–29.9 mg/m^2, 30–34.9 kg/m^2, 35–39.9 kg/m^2, $\geq$ 40 kg/m^2). In an analysis adjusted for age, sex, comorbidities, depression, anxiety, operative diagnosis, distance from centre and implant design, patients with BMI of $\geq$ 35 kg/m^2 reported significantly greater long-term moderate or severe pain than the lowest BMI group.

In a study from a single centre in Canada, Gandhi and colleagues[133] followed up 636 patients (per cent eligible not reported) for an average of 3.3 years. The mean BMI in this cohort was 27.6 kg/m^2 (SD 4.9 kg/m^2) and was treated as a continuous variable in analyses. After adjusting for age, sex, comorbidities, WOMAC and SF-36 scores there was a non-significant trend for less improvement in WOMAC score with increasing BMI.

With the increasing levels of BMI in developed countries, it is important that patients and health-care providers are aware of any factors that influence the long-term outcome of THR. We identified eight studies that reported the association between BMI and a long-term patient-reported outcome in multivariable analysis.[103,104,127–129,132,133,135] If reported in the studies we identified, patients had broadly similar average BMIs to those reported in the National Joint Registry for England and Wales[3] and the APEX cohort described in *Chapters 6* and *7*.

In three studies, the absolute long-term OHS,[128] WOMAC function[129] and a simple measure of pain severity[104] were more favourable in lower BMI groups. In another study this was observed for WOMAC function in univariate but not multivariate analysis.[103] In two studies there were no long-term differences in WOMAC pain or function,[127] WOMAC score or SF-36.[135] Further to the selection of studies according to specific quality criteria, studies had either one or no additional marker of quality based on centres studied and losses to follow-up. Differences in results of studies were not explained by issues relating to these additional markers of study quality.

In the four studies for which BMI was treated as a continuous variable in multivariable analysis, authors reported no strong association between BMI and long-term function,[103,128,133,135] or pain.[128,135] Two studies reported changes in function which may be a more appropriate method of analysis as patients with higher BMI generally have poorer function before surgery. There were greater improvements in OHS[128] and WOMAC[133] in patients with lower BMI. Associations observed were not limited to studies according to additional markers of quality.

In four studies, authors focused on the relationship between categorical levels of BMI and patient-reported outcomes. There was some evidence that patients classified as obese ($\geq$ 30 kg/m^2) according to WHO classifications[139] had poorer function[129,132] or pain outcomes,[104] but only one study had an additional marker of good quality.[127] In a fourth study with one additional marker of good quality, no association was noted between pre-operative BMI and long-term function or pain, although the authors noted a slower recovery in patients with high BMI.[127]

Overall, the absolute levels of physical function and pain achieved after THR in patients with particularly high BMI may be somewhat lower than that achieved by other patients. However, there is a clear indication that many patients with high BMI benefit from THR with long-term improvements to physical function and reduction in long-term pain.

Pre-surgical mental health

The period between being placed on the waiting list and the day of surgery can be a time of distress for patients and is characterised by pain, poor physical function and uncertainty. Parsons and colleagues[140] identified six major themes describing patients' experiences of waiting for joint replacement: living and coping with pain; not being able to walk; coping with everyday activities; body image; help, advice and support; and the effect on family, friends and helpers.

Anxiety and depression are common in people with osteoarthritis.[141,142] In the APEX cohort of patients with osteoarthritis waiting for THR, pre-surgical anxiety and depression was identified using the Hospital Anxiety and Depression Scale (HADS) questionnaire. Definite or potential anxiety was reported by 33% of patients and definite or potential depression by 30% of patients.

One previous systematic review explored the relationship between pre-surgical anxiety and long-term patient outcomes in patients with THR.[143] Vissers and colleagues[143] searched MEDLINE and EMBASE to January 2011 and identified nine studies including 8823 patients receiving THR. The authors reported that there was limited and conflicting evidence on the relationship between psychological factors and postoperative function and pain.

Our literature searches identified seven studies with ≥ 100 patients with THR followed up for ≥ 12 months with pre-surgical mental health included in multivariable analyses. One study reported data from a joint registry,[125] one study included patients from multiple centres,[128] and five studies collected data from patients treated at a single centre.[103,104,130,131,133] Study details are summarised in *Table 4*. In studies that reported the number of patients eligible, between 6% and 38% of patients were not followed up.

In a 12-month follow-up study of 6158 patients (92% eligible) from the Swedish Hip Arthroplasty Register, Rolfson and colleagues[125] assessed the impact of the pre-operative European Quality of Life-5 Dimensions (EQ-5D) measure of anxiety and depression on long-term pain and satisfaction. In analysis of covariance adjusting for EQ-5D domains, comorbidities and age and sex, anxiety and depression were strong predictors of poor long-term pain relief and low patient satisfaction. Furthermore, in patients with persistent anxiety and depression, only 24% of patients showed improvement in the EQ-5D mobility dimension compared with 59% in those unaffected by high levels of anxiety or depression.

Judge and colleagues[128] followed up 70% of 1375 patients eligible from seven UK centres 5 years after they had received a specific THR prosthesis. The multivariable model included the SF-36 mental health score, age, sex, primary diagnosis, occupation, comorbidities, HRQoL and pre-surgical OHS. Poorer mental health measured by the SF-36 mental health score was associated with a less favourable long-term patient outcome as measured by the OHS.

Anakwe and colleagues[130] followed up 850 patients (94% eligible) 12 months after THR at a single UK centre. The Short Form questionnaire-12 items (SF-12) mental health component, diabetes, hypertension, history of depression, age, sex, SF-12 physical components, OHS, and musculoskeletal comorbidities were included in analyses. Although significant in univariate analyses, neither a history of depression nor the SF-12 mental health component predicted the level of long-term patient satisfaction in multivariable analysis.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Nilsdotter and colleagues[103] followed up 198 patients with THR (94% eligible) at a single centre in Sweden after a mean of 3.6 years. Multivariable analysis included sex, comorbidities, WOMAC, SF-36 (including mental health), employment, marital status, contralateral osteoarthritis, need of walking assistance, walking distance, analgesic use and regional or widespread pain. In preliminary univariate analysis, pre-operative SF-36 mental health status was not a significant predictor of long-term WOMAC function and was not entered into multivariable analysis.

In a single-centre UK study, Clement and colleagues[131] followed up 1312 patients with THR (per cent eligible not reported) at 12 months. In a multivariable analysis with age, deprivation, Charlson comorbidities, OHS, length of stay and SF-12 physical health, SF-12 mental health was a significant predictor of long-term change in OHS. Depression was the comorbidity with the strongest prediction of poor improvement in OHS.

Gandhi and colleagues[133] followed up 636 patients (per cent eligible not reported) from a single centre in Canada for an average of 3.3 years. In multivariable analysis with age, sex, comorbidities, BMI and fixation (cemented or uncemented), SF-36 mental health was not associated with long-term changes in WOMAC score or SF-36 physical function.

In a single-centre US study, Singh and Lewallen[104] followed up 5707 patients (62% eligible) 2 years after THR. Multivariable analyses included anxiety, depression, age, sex, comorbidities, operative diagnosis, distance from centre and implant design. Patients with depression but not anxiety [*International Classification of Diseases* (ICD) classifications] before surgery were more likely to report moderate to severe long-term pain at 2 years. A trend in a similar direction was not significant at 5 years.

All studies we included in the review reported multivariable analyses with inclusion of comorbidities and other factors in the statistical model. Authors examined outcomes in patients using generic measures of mental health (SF-12 mental health and SF-36 mental health), combined measures of anxiety and depression (EQ-5D anxiety/depression) and specific diagnoses of anxiety and depression (ICD code or clinical history).

In five studies in which generic mental health scores were measured before surgery using SF-36 or SF-12, results of multivariable analyses were inconsistent.[103,128,130,131,133] In two studies, patients with worse pre-surgical mental health scores had a poorer long-term outcome[128] or less improvement measured by the OHS.[131] However, in two studies, SF-36 mental health scores measured before surgery did not predict long-term WOMAC function[103] or change in overall WOMAC score.[133] Similarly pre-surgical SF-36 mental health did not predict long-term change in SF-36 physical function score.[133] In one study, the authors reported that long-term satisfaction was not predicted by pre-surgical SF-12 mental health score.[130] Inconsistencies between studies were not explained by differences in additional markers of quality.

Unlike the SF-36, which measures psychological distress and well-being, the mental health component of the EQ-5D relates specifically to anxiety and depression. In one study considered to be of good quality based on both additional markers, pre-operative anxiety/depression measured with the EQ-5D was associated with poorer long-term pain relief, satisfaction and mobility.[125] Three studies specifically reported outcomes in patients with anxiety or depression before surgery. In one study, patients with depression before surgery had poorer long-term pain outcomes but this was not the case for patients with anxiety.[104] In another study, depression before surgery was associated with poor improvement in OHS.[131] Both these studies were single centre and reported high losses to follow-up. In one study from a single centre but with low losses to follow-up, except in univariate analysis, patients with a history of depression did not report lower levels of long-term satisfaction after THR.[130]

Overall, there was some evidence that patients with depression before THR may have poorer long-term outcomes but evidence for pre-surgical anxiety was weaker. For general mental health measures evidence was equivocal.

Pre-surgical pain

Pain is the principal indication for THR[144] and the key patient expectations of surgery are good long-term functional and pain outcomes.[145,146] We identified two single-centre studies that had explored the relationship between pre-operative pain levels and long-term patient-reported outcomes after THR.[103,134] Details of studies are shown in *Table 4*.

In a study of 198 patients (94% eligible) from a single Swedish centre, Nilsdotter and colleagues[103] reported a multivariable analysis with follow-up at a mean of 43 months. Increased levels of SF-36 bodily pain domain measured before surgery were associated with poorer long-term WOMAC function outcomes in a statistical model including age, sex, comorbidities, BMI and SF-36 physical function and mental health components.

Garbuz and colleagues[134] followed up 147 patients (73% eligible) at a single Canadian centre 12 months after THR. Greater pre-operative pain measured with the WOMAC pain score was predictive of a poorer long-term WOMAC pain outcome in univariate analysis and after inclusion of age, sex and comorbidities in multivariable analysis.

Few studies have reported the relationship between pain levels before THR and long-term patient outcomes. In two studies with appropriate multivariable analyses, an increased level of pre-operative joint specific pain was associated with a greater risk of long-term pain and general pre-operative pain was predictive of poorer long-term functional outcome.

Pre-surgical physical function

As noted previously, the key expectations of patients undergoing total joint replacement are good long-term functional and pain outcomes.[145,146]

Searches identified six studies that had followed up patients at 12 months and conducted multivariable analysis with pre-operative physical function included in the statistical model. Three studies were conducted in multiple centres,[31,126,128] and three in single centres.[130,131,134] Characteristics of studies are summarised in *Table 4*.

In this classification we included four studies that reported overall WOMAC or OHS. As well as reflecting physical function these scores also include joint specific pain (OHS) or pain and stiffness (WOMAC).

Hajat and colleagues[126] followed up 3600 patients (77% eligible) 12 months after THR at multiple UK centres. In multivariable analysis with age, sex, waiting time, comorbidities, housing and surgical factors, a worse pre-operative OHS was predictive of a worse long-term OHS.

In a European multicentre study, Judge and colleagues[31] followed up 845 patients (64% eligible) with THR at 12 months. The authors included the WOMAC score, EQ-5D, age, sex, BMI, education, comorbidities and radiographic status in a multivariable model. A worse pre-operative WOMAC score was predictive of a poorer long-term outcome as judged by the Outcome Measures in Rheumatology-Osteoarthritis Research Society International (OMERACT-OARSI) rated good WOMAC response.

Judge and colleagues[128] reported the 5-year follow-up of 1375 patients (70% eligible) who had received a specific THR prosthesis at seven UK centres.[128] In multivariable analyses including age, sex, BMI, primary diagnosis, occupation, comorbidities and HRQoL, the pre-operative OHS was the strongest determinant of long-term OHS.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Anakwe and colleagues[130] reported a single UK centre study with 850 patients (94% eligible) followed up 12 months after THR. SF-12 physical and mental health components, diabetes, hypertension, history of depression, age, sex, OHS and musculoskeletal comorbidities were included in multivariable analysis. The SF-12 physical component score (PCS) measured before surgery did not predict long-term satisfaction. The pre-surgical OHS was associated with greater long-term dissatisfaction but only in univariate analysis.

In a study at a single Canadian centre, Garbuz and colleagues[134] followed up 147 patients (73% eligible) 12 months after THR. In univariate analysis a 10-out-of-100-point difference in pre-surgical WOMAC function was associated with a 35% increase in long-term WOMAC function. In multivariable analysis age, sex, and comorbidity did not change the association.

Clement and colleagues[131] reported 12-month follow-up of 1312 patients (per cent eligible not reported) with THR at a single UK centre. In a multivariable analysis with age, deprivation, comorbidities, length of stay and SF-12 physical and mental health, the pre-operative OHS was a strong predictor of long-term improvement in OHS.

The studies we identified suggested that better physical function before THR is associated with a better long-term functional outcome. This was apparent in one study with a specific functional measure[134] and in four studies with a more general patient-reported outcome.[31,126,128,131] This observation was supported when considering studies with an additional marker of good quality. In one study with a more general measure of pre-operative physical function, there was no association with long-term satisfaction.[130]

Total knee replacement

As shown in *Figure 8*, searches identified 33 studies reporting multivariable analyses including patients with TKR. In this section we summarise results from 22 studies of pre-operative BMI, mental health, pain and physical function as predictors of long-term patient-reported outcomes.[46,50,127,147–165] One study included important data in a second publication.[166] Details of studies are summarised in *Appendix 6* with brief details in *Table 5*.

Body mass index

There is a strong association between high BMI (≥ 30 kg/m^2) and the development of knee osteoarthritis.[137] People with high BMI are also more likely to require a TKR than those with lower BMI.[138,167] For example, in a cohort of 315,495 people in Norway, men and women in the top quartile of BMI (≥ 27.3 kg/m^2) had relative risks compared with the lowest quartile (< 21.6 kg/m^2) of undergoing a TKR of 6.16 (95% CI 4.23 to 8.95; $p < 0.0001$) and 11.06 (95% CI 7.83 to 15.62; $p < 0.0001$), respectively.[167]

Analyses of the National Joint Registry for England and Wales[3] show that 56% of patients undergoing TKR in 2012 had a BMI of 30 kg/m^2 or greater. In the RESTORE APEX RCT including 311 patients with TKR the mean BMI was 32.6 kg/m^2 (SD 6.5 kg/m^2, range 17.0–56.2 kg/m^2). The distribution is shown in *Figure 10*. Thirteen per cent of patients had a BMI of 40 kg/m^2 or greater.

Although clearly of potential importance as a treatment for severe knee pain, irrespective of a patient's BMI, concern has been expressed about the outcomes of TKR in patients considered to be obese.[137,168,169] Previous reviews have suggested that patients with a high BMI receiving TKR are at increased risk of deep infection,[170–172] complications[171–173] and need for revision surgery.[170,173] Long-term outcomes measured by surgeon assessed scores after TKR may be poorer in patients with a BMI of ≥ 40 kg/m^2 but not in patients with BMI of 30–40 kg/m^2.[173] No previous systematic review has considered the association of pre-operative BMI and long-term patient-reported outcomes.

Our systematic literature search identified 13 articles that met the inclusion criteria and were included in the review.[46,127,147,149,151–155,159–162] Details of these studies are summarised in *Table 5*. As a marker of generalisability, one study reported a registry analysis,[147] eight studies included multiple centres,[46,127,149,151–155] and four studies included patients from a single centre.[159–162]

TABLE 5 Systematic review of pre-operative predictors of patient-centred outcomes after TKR: included studies

Study	Number of patients; follow-up	Predictors	Outcome measures
Registry			
Baker and colleagues 2012[148]	22,691; minimum 6 months	Mental health	OKS, EQ-5D
Franklin and colleagues 2008[147]	8050; 12 months	BMI, mental health	SF-12 PCS
Multiple centres			
Alzahrani and colleagues 2011[149]	3177; 12 months	BMI	OKS, WOMAC
Cushnaghan and colleagues 2009[151]	259; mean 6 years	BMI	SF-36 PCS
Heck and colleagues 1998[157]	268; 24 months	Mental health, pain, physical function	SF-36 PCS
Jones and colleagues 2012[127]	Estimated 209; 3 years	BMI	WOMAC
Lingard and colleagues 2004[46]	741 at 1 year; 12 and 24 months	BMI, pain, physical function	WOMAC pain and function, SF-36 PCS
Lingard and colleagues 2007[150] and Lingard and colleagues 2004[46]	682; 12 and 24 months	Mental health	WOMAC pain and function
Merle-Vincent and colleagues 2011[158]	264; 24 months	Mental health	Satisfaction
Naylor and colleagues 2012[154]	146; 12 months	BMI	OKS
Papakostidou and colleagues 2012[155]	204; 12 months	BMI, mental health, pain	WOMAC
Perruccio and colleagues 2012[152]	435; mean 12.5 months	BMI	WOMAC
Singh and Lewallen 2013[156]	7139; 2 and 5 years	Mental health	Pain severity questionnaire
Sullivan and colleagues 2011[153]	120; 12 months	BMI, pain	WOMAC function and pain
Single centre			
Ayers and colleagues 2005[163]	165; 12 months	Mental health, physical function	WOMAC physical function, SF-36 PCS
Brander and colleagues 2003[50]	116 (149 TKRs); 12 months	Mental health	Pain VAS, McGill Pain Questionnaire
Clement and colleagues 2013[164]	966; 12 months	Mental health, physical function	OKS, Satisfaction
Deshmukh and colleagues 2002[161]	139; 12 months	BMI	NHP
Gandhi and colleagues 2010[160] and Gandhi and colleagues 2010[166]	551; mean 3 years	BMI, mental health	WOMAC, SF-36 Role Physical, SF-36 Physical Function
Núñez, and colleagues 2009[159]	112; 7 years	BMI	WOMAC function and pain
Rajgopal and colleagues 2008[162]	550; 1 year	BMI	WOMAC
Scott and colleagues 2010[165]	1141; 12 months	Mental health, pain, physical function	Satisfaction

NHP, Nottingham Health Profile.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

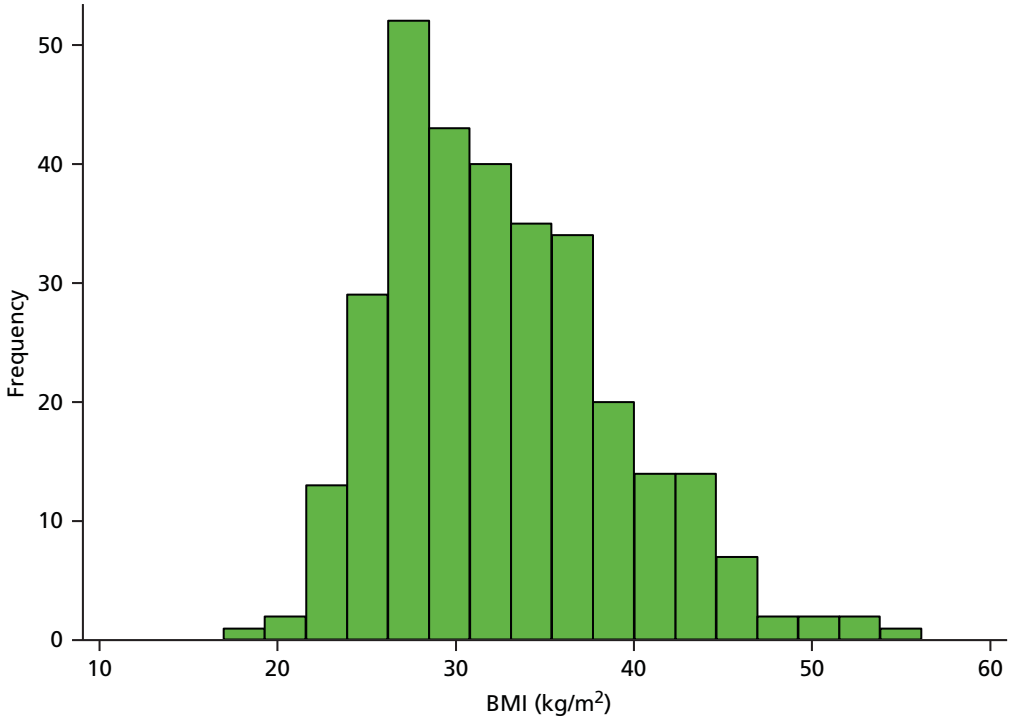


FIGURE 10 Distribution of BMI in the APEX TKR cohort.

Body mass index as a predictor of joint specific pain and function

Four studies assessed the impact of BMI on joint specific PROMs.[154,159,162,166] These provided a composite measure of pain and functional limitations, specifically the OKS and total WOMAC score.

In the multicentre Australian study reported by Naylor and colleagues,[154] 146 patients (90% eligible) were followed up at 12 months after TKR. The mean BMI in this cohort was 32.8 kg/m^2 (SD 5.7 kg/m^2). In multivariable analysis including age, sex and knee range of movement, but not comorbidities, patients with higher BMI reported worse long-term OKS.

Gandhi and colleagues[166] followed up a cohort of 677 patients with a total of 889 TKR operations (per cent eligible not reported) conducted by three surgeons in Canada 12 months after surgery.[166] The overall mean BMI in this cohort was not reported but the inclusion of patients with BMI of > 40 kg/m^2 is implied in the metabolic syndrome groupings shown. After adjustment for age, sex, comorbidities and baseline WOMAC scores, BMI of > 30 kg/m^2 was associated with poorer long-term WOMAC scores.

Patients in the Canadian study reported by Rajgopal and colleagues[162] were treated with TKR by four surgeons at a single centre. At 12 months, 550 patients (per cent eligible not reported) were assessed with the WOMAC score. In this cohort, 12.5% of patients had a BMI of ≥ 40 kg/m^2. BMI was analysed as a dichotomous variable < 40 or ≥ 40 kg/m^2. In multivariable analysis with adjustment for age, sex, mental health, prior contralateral knee replacement, pre-surgical WOMAC score and comorbidities affecting gait, patients with a BMI of 40 kg/m^2 had a poorer long-term WOMAC score.

In a single-centre Spanish study, Núñez and colleagues[159] followed up 112 patients (77% eligible) 7 years after TKR. A total of 12.5% of patients in this study had a BMI of > 35 kg/m^2. BMI was treated as a categorical variable with groups of < 35 kg/m^2 and ≥ 35 kg/m^2. In multivariable analyses with age, sex, comorbidities, sociodemographic and clinical characteristics, intraoperative variables, inpatient variables, postoperative clinical variables and pre-operative WOMAC scores, long-term WOMAC pain and function were poorest in patients with BMI of > 35 kg/m^2.

Evidence on the association between BMI and long-term joint specific pain and function is largely based on analyses where patients with particularly high BMI levels are compared with those with lower levels. There was evidence that those with high BMI did not achieve the levels of joint specific physical function and pain control seen in those with a lower BMI. This was supported by the one study with an additional marker of quality (multiple centres).[154] However, this study did not include comorbidities in multivariable analysis. Across all studies, there was insufficient information to consider the overall range of BMI in relation to joint specific patient outcomes.

Body mass index as a predictor of WOMAC function scores

Six studies explored the impact of BMI on WOMAC function scores.[46,127,152,153,155,159]

In a study including 860 patients (70% eligible at 2 years) from several countries, Lingard and colleagues[46] reported follow-up at 12 and 24 months after TKR. BMI was treated as a continuous variable and the overall mean was 29.4 kg/m^2 (SD 5.8 kg/m^2). In multivariable analysis with age, sex, WOMAC, SF-36 mental health, knee flexion, working status, education, income, comorbidities and country, increasing pre-operative BMI was associated with poorer WOMAC function at 12-month follow-up, but not 24-month follow-up. The size of the effect was small compared with that observed for pre-operative WOMAC function score and number of comorbidities.

In a study in multiple Canadian centres, Jones and colleagues[127] followed up an estimated 209 patients (72% eligible) at 3 years after TKR. A total of 19% of patients had a BMI of $\geq$ 35 kg/m^2 before surgery. In multivariable analysis with age, sex and comorbidities, BMI was treated as a binary variable ($<$ 35 kg/m^2 or $\geq$ 35 kg/m^2). Patients with BMI of $\geq$ 35 kg/m^2 had a poorer long-term WOMAC function outcome.

In a study in multiple centres in Greece, Papakostidou and colleagues[155] followed up 204 patients (90% eligible) 12 months after TKR. In this cohort, 52.9% of patients had BMI of $\geq$ 30 kg/m^2. BMI was analysed as a binary variable. In multivariable analysis with age, sex, education, social support, place of residence and baseline status of knee, long-term WOMAC function levels were similar in patients with BMI under or over 30 kg/m^2.

Perruccio and colleagues[152] followed up 435 patients (88% eligible) at multiple Canadian centres at a mean of 12.5 months after TKR. In this cohort, 45.3% of patients had a BMI of $\geq$ 30 kg/m^2. The authors included age, sex, education, comorbidities, other painful joints and WOMAC pain and function in multivariable analysis with BMI treated as a binary variable. Patients with BMI of $<$ 30 kg/m^2 and $\geq$ 30 kg/m^2 reported similar long-term WOMAC function.

Sullivan and colleagues[153] followed up 120 patients (per cent eligible not reported) from multiple Canadian centres 12 months after TKR.[153] Patients in this cohort had a mean BMI of 30.8 kg/m^2. In multivariable analysis with age, sex, comorbidities, pain, function, surgery, pain catastrophising, pain-related fear of movement and depression, BMI was treated as a continuous variable. BMI did not predict long-term WOMAC function.

Núñez and colleagues[159] followed up 112 patients (77% eligible) 7 years after TKR at a single centre in Spain. In multivariable analysis the authors included age, sex, comorbidities, sociodemographic and clinical characteristics, intraoperative variables, inpatient variables, postoperative clinical variables and pre-operative WOMAC scores. BMI was treated as a binary variable and those with BMI of $\geq$ 35 kg/m^2 had worse long-term WOMAC function.

Overall, there was some suggestion from two studies that patients with more extreme levels of pre-operative BMI ($\geq$ 35 kg/m^2) had poorer long-term physical function. Only one of these studies had an additional marker of good quality. In two studies for which the analyses applied a division of less than or greater than 30 kg/m^2, there was no apparent difference in functional outcome.[152,155] Both studies had two additional markers of study quality. In the two studies for which BMI was analysed as a continuous variable, there was

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

either no association[153] or a weak association[46] between increasing levels of BMI and long-term WOMAC function.

Body mass index as a predictor of WOMAC pain scores

Six studies looked at whether or not BMI was a predictor of WOMAC pain at ≥ 12 months after TKR.[46,127,152,153,155,159]

In a multicentre study from Canada, Jones and colleagues[127] followed up an estimated 209 patients (72% eligible) at 3 years after TKR. A total of 19% of patients had BMI of ≥ 35 kg/m^2. In multivariable analysis with adjustment for age, sex and comorbidities, BMI was treated as a binary variable (< 35 kg/m^2 or ≥ 35 kg/m^2). There was a borderline significant association between BMI and trajectory of pain recovery up to 3 years favouring patients with BMI of < 35 kg/m^2.

Lingard and colleagues[46] reported a multicentre study including 741 patients (86% eligible at 1 year) from the UK, USA and Australia with TKR followed up at 12 and 24 months.[46] The mean BMI was 29.4 kg/m^2 (SD 5.8 kg/m^2). In multivariable analysis, the authors included age, sex, WOMAC, SF-36 mental health, knee flexion, working status, education, income, comorbidities and country. With BMI treated as a continuous variable, there was no association between BMI and long-term WOMAC pain score at 12 months and 24 months.

Papakostidou and colleagues[155] followed up 204 patients (90% eligible) from multiple centres in Greece 12 months after TKR. A total of 52.9% of patients had BMI of ≥ 30 kg/m^2. In multivariable analysis with age, sex, education, social support, place of residence and baseline status of knee, BMI was treated as a binary variable. Long-term WOMAC pain levels were similar in patients with BMI under or over 30 kg/m^2.

Perruccio and colleagues[152] followed up 435 patients (88% eligible) at multiple Canadian centres at a mean of 12.5 months after TKR. A total of 45.3% of patients had a BMI of ≥ 30 kg/m^2. The authors included age, sex, education, comorbidities, other painful joints and WOMAC pain and function in multivariable analysis with BMI treated as a categorical variable. There was no association between BMI and long-term WOMAC pain.

In a study of patients with TKR at multiple centres in Canada, Sullivan and colleagues[153] followed up 120 patients (per cent eligible not reported) at 12 months after surgery. The mean BMI in this cohort was 30.8 kg/m^2. The authors reported a multivariable analysis with BMI analysed as continuous variable and adjustment for pain, function, age, sex, comorbidities, surgery duration, surgeon, pain catastrophising, pain-related fear of movement and depression. In this analysis BMI was not a predictor of long-term WOMAC pain.

In a single-centre study from Spain, Núñez and colleagues[159] followed up 112 patients (77% eligible) 7 years after TKR. The mean BMI in this cohort was 30.7 kg/m^2. In multivariable analysis with age, sex, comorbidities, sociodemographic and clinical characteristics, intraoperative variables, inpatient variables, postoperative clinical variables and pre-operative WOMAC scores, patients with BMI of ≥ 35 kg/m^2 had significantly worse WOMAC pain scores than patients with BMI of < 35 kg/m^2. However, the analysis in this study was limited by the small number of patients in the high BMI group ($n = 14$).

In the six studies with pain measured using the WOMAC score, there was little to suggest that pre-operative BMI was a determinant of long-term pain with the possible exception of high body mass index (≥ 35 kg/m^2). At these high levels of BMI, patients may be more likely to report long-term pain.

Body mass index as a predictor of general health outcomes

Three studies explored the influence of BMI on general health outcomes after TKR.[46,160,161] Outcomes reported were SF-36 domains or the Nottingham Health Profile (NHP).

Lingard and colleagues[46] reported an international study including 860 patients (70% eligible) receiving TKR at multiple centres. The mean BMI was 29.4 kg/m^2 (SD 5.8 kg/m^2). Higher BMI was a predictor of poorer SF-36 physical function scores at 24 months but not at 12 months after surgery. Other variables included in this multivariable analysis were age, sex, patient-reported outcomes, mental health, knee flexion, working status, education, income, comorbidities and country.

Deshmukh and colleagues[161] reported a UK study with 139 patients (77% eligible) treated by a single surgeon with follow-up at 12 months. In this study, the mean BMI was 28 kg/m^2 (SD 4.5 kg/m^2) and only two patients initially eligible had a BMI of $\geq$ 40 kg/m^2. In multivariable analysis including age, sex, side of arthritis, comorbidities, baseline NHP and knee scores, BMI accounted for only a small percentage of the variation in long-term NHP scores.

In a single-centre study from Canada, Gandhi and colleagues[160] followed up 551 patients (per cent eligible not reported) at a mean of 3 years after surgery. The mean BMI in patients in this study was 30.1 kg/m^2 (SD 6.3 kg/m^2). After adjustment for age, sex, ethnicity, education, comorbidities and SF-36 mental health status, BMI was not a predictor of long-term SF-36 role physical or physical function scores.

In summary, there is no clear evidence that BMI is a predictor of long-term general health outcomes after TKR. However, evidence is lacking at higher levels of BMI.

Body mass index as a predictor of change in patient-reported outcomes

Four studies examined the association between BMI and change in patient-reported outcomes from pre- to post TKR in multivariable statistical analysis.[147,149,151,162] In the two studies reporting eligibility, 53.4%[147] and 60.6%[151] of patients were not followed up. These high rates were largely explained by the study designs, a 1-year registry follow-up[147] and a follow-up of patients placed on the waiting list for TKR after a mean of 6 years.[151]

Franklin and colleagues[147] reported a 12-month follow-up of US registry data including 8050 patients (46% eligible). No information on mean levels of BMI was included. BMI was analysed as a categorical variable with groups of < 30 kg/m^2, 30–40 kg/m^2 and > 40 kg/m^2. In multivariable analysis with age, sex, mental health, physical health, diagnosis and quadriceps strength, patients with BMI of > 40 kg/m^2 had less long-term functional gain as measured by the SF-12 PCS.

In the study in 3177 patients (per cent eligible not reported) from multiple centres reported by Alzahrani and colleagues,[149] the mean BMI was 31 kg/m^2 and was analysed as a continuous variable.[149] In a statistical model included age, sex and comorbidities, BMI was not a significant predictor of achieving a minimal clinical improvement on the OKS or WOMAC score at 12 months after surgery.

The study reported by Cushnaghan and colleagues[151] included 259 patients (39% eligible) from three UK health districts followed up for a mean of 6 years after surgery. A total of 41.7% of patients followed up had BMI of $\geq$ 30 kg/m^2 before surgery. Multivariable analysis included age, sex, SF-36, smoking habits, comorbidities, Kellgren and Lawrence grade, previous knee injury, other painful joints and Heberden's nodes. The authors noted that patients with a BMI of $\geq$ 30 kg/m^2 had a similar improvement in SF-36 PCSs compared with patients with BMI of < 30 kg/m^2.

Rajgopal and colleagues[162] followed up 550 patients (per cent eligible not reported) at a single centre 1 year after TKR. A total of 12.5% of patients had a BMI of $\geq$40 kg/m^2. The authors included age, sex, mental health, prior contralateral surgery, WOMAC score and comorbidities in the multivariable model. There were no differences in long-term improvement in WOMAC function between patients with BMI of $\geq$40 kg/m^2 compared with those with BMI of $\leq$ 40 kg/m^2.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

In summary, the evidence suggests that greater BMI is not associated with less improvement in PROMs after TKR, although there is the possibility from one study with no additional markers of good quality that patients with more extreme levels of BMI have a poorer improvement in general functional health.[147]

Pre-surgical mental health

In their systematic review with searches of MEDLINE and EMBASE to January 2011, Vissers and colleagues[143] identified 19 studies including 6274 patients receiving TKR. There was strong evidence that pre-operative pain catastrophising was associated with increased pain in the first year after surgery and that poorer pre-operative mental health was associated with worse long-term physical function and pain. The authors identified no strong evidence that pre-operative depression influenced functioning in the year after TKR.

In our systematic review, we identified 12 studies with ≥ 100 patients with TKR followed up for ≥ 12 months with pre-surgical mental health included in multivariable analyses.[50,147,148,150,155–158,160,163–165] Two studies reported data from joint registries,[147,148] five studies included patients from multiple centres[150,155–158] and five studies collected data from patients treated at a single centre.[50,160,163–165] Study details are summarised in *Table 5*.

In an analysis of the National Joint Registry for England and Wales, Baker and colleagues[148] reported on 22,691 patients (55% eligible) with TKR followed up for at least 6 months and up to 12 months after surgery. The authors included age, OKS, EQ-5D, disability, general health, comorbidities, and surgical and hospital variables in a multivariable model. Pre-operative anxiety and depression measured using the EQ-5D were associated with poorer long-term improvement in OKS and EQ-5D.

Franklin and colleagues[147] followed up 8050 patients (47% eligible) from a US joint registry 12 months after TKR. In multivariable analysis, the authors included SF-12 PCS, sex, age, BMI, osteoarthritis diagnosis and poor quadriceps strength in the statistical model. The pre-operative SF-36 mental component score was an independent predictor of poor long-term physical function measured with the SF-36 PCS.

Heck and colleagues[157] followed up 268 patients (92% eligible) 24 months after TKR at multiple US centres. The authors conducted a multivariable analysis with age, ethnicity, sex, poverty, patient health status, WOMAC scales, SF-36 physical component, knee ROM, comorbidities, surgical factors and joint problems in the other knee. Poor pre-operative SF-36 mental health was associated with less improvement in the SF-36 PCS.

Lingard and Riddle[150] followed up 628 patients (70% eligible at 2 years) who had received a specific TKR prosthesis at 12 international centres.[150] In a multivariable model with age, sex and comorbidities, patients with psychological distress identified using the SF-36 mental health component had worse WOMAC pain at 12 and 24 months than non-distressed patients. There was no strong evidence to support such a relationship with long-term WOMAC function although there was a trend in a similar a direction. The authors reported that there were no strong associations between pre-operative psychological distress and changes in function and pain over either follow-up period.

In the study of Merle-Vincent and colleagues,[158] 264 patients (87% eligible) with TKR at multiple centres in France were followed up after 24 months. In a multivariable analysis with age, sex, BMI, Lequesne index and joint space narrowing, there was no strong evidence that patients with feelings of depression before surgery were more dissatisfied with their TKR.

Papakostidou and colleagues[155] followed up 204 patients (90% eligible) at two centres in Greece, 12 months after TKR. In a multivariable analysis with age, sex, BMI, education, social support, place of residence and baseline status of knee, the extent of pre-operative depressive symptoms, measured with the 10-Item Center for Epidemiologic Studies Short Depression Scale, were predictive of long-term VAS pain. The authors concluded that depressed mood had a strong positive correlation with long-term pain and functional limitation.

Singh and Lewallen[156] followed up 7139 patients (65% eligible at 2 years) with TKR at multiple US centres 2 years after surgery.[156] Pain outcome was measured using a standardised Mayo Clinic questionnaire. In a multivariable analysis with age, sex, BMI, operative diagnosis and comorbidities, anxiety identified in the comorbidity assessment was an independent predictor of moderate to severe pain at 2 years, whereas depression was marginally not. The authors also followed patients up at 5 years but losses to follow-up were greater than at 2 years. There was evidence for an association between both pre-operative anxiety and depression and moderate to severe pain at this longer follow-up.

In a study in 165 patients (per cent eligible not reported) with TKR at a single US centre, Ayers and colleagues[163] reported follow-up at 12 months. In multivariable analysis with age, sex, pre-operative function and comorbidities, poorer pre-operative SF-36 emotional health was associated with smaller improvements in SF-36 PCS and WOMAC physical function scores.

Brander and colleagues[50] followed up 116 patients (per cent eligible not reported) at a single US centre at 12 months after TKR. In multivariable analysis with age, sex, other demographics and physiological, psychometric and pain variables, pre-operative depression and anxiety were associated with greater long-term VAS pain.

In their study of 966 patients (per cent eligible not reported) with TKR followed up for 12 months at a single UK centre, Clement and colleagues[164] reported a multivariable analysis including age, sex, comorbidities, socioeconomic deprivation, OKS and the SF-12 components. Poorer pre-operative SF-36 mental health was associated with a poorer long-term improvement in OKS but was not related to satisfaction.

Gandhi and colleagues[160] reported the follow-up of 551 patients (per cent eligible not reported) with TKR at a single Canadian centre at a mean of 3 years. In multivariable analysis including age, sex, ethnicity, BMI, education and comorbidity, patients with poorer pre-operative mental health according to the SF-36 had worse long-term WOMAC and SF-36 functional outcomes.

Scott and colleagues[165] reported 12-month follow-up at a single UK centre of 1414 patients (87% eligible) who had received a specific TKR prosthesis.[165] In multivariable analysis with age, sex, SF-12 physical component, OKS and comorbidities, patients with depression or a poor SF-12 mental health status were more likely to be dissatisfied with their long-term outcome.

Studies investigating the relationship between pre-operative mental health and long-term patient outcomes used generic measures, specifically the SF-36 and SF-12 mental health components or more specific measures of anxiety or depression. For generic measures, poor mental health status before TKR was a predictor of long-term increased pain or poorer function in all seven studies that reported it.[147,150,157,160,163–165] There was a consistent suggestion in three studies that patients with anxiety had worse long-term pain or other patient outcomes.[50,148,156] In five studies, patients with depression or depressive symptoms had poorer long-term pain or functional outcomes.[50,148,155,156,158] Associations between aspects of pre-operative mental health and long-term patient outcomes were apparent in studies with one or two additional markers of good-study quality. For satisfaction as an outcome, the associations with pre-operative mental health measures were inconsistent.

Pre-surgical pain

We identified five studies with ≥ 100 patients with TKR followed up for ≥ 12 months with pre-surgical pain included in multivariable analyses. Four studies included patients from multiple centres,[46,153,155,157] and one study was based on analyses of patients from a single centre.[165] Study details are summarised in *Table 5*.

Heck and colleagues[157] followed up 268 patients (92% eligible) at multiple US centres 24 months after TKR. The authors conducted a multivariable analysis with the SF-36 mental health component, age, ethnicity, sex, poverty, patient health status, WOMAC scales, SF-36 physical component, knee ROM,

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

comorbidities, surgical factors and joint problems in the other knee. In this analysis pre-operative WOMAC pain was not a predictor of the long-term SF-36 physical component.

Lingard and colleagues[46] followed up 678 patients (79% eligible) from multiple international centres at 12 and 24 months after TKR. In multivariable analysis with age, sex, income, education, BMI, flexion, country, centre and comorbidities, one of the strongest determinants of long-term WOMAC pain was the pre-operative WOMAC pain score. The authors considered the difference in WOMAC pain scores to be clinically important.

In a study of 204 patients (90% eligible) from multiple centres in Greece, Papakostidou and colleagues[155] reported follow-up at 12 months after TKR. In multivariable analysis including depression, sex, BMI, education, social support, age, place of residence and baseline status of knee, pre-operative WOMAC pain predicted long-term WOMAC pain.

Sullivan and colleagues[153] followed up 120 patients (per cent eligible not reported) 12 months after TKR conducted at multiple Canadian centres. Greater pain catastrophising and pain-related fear of movement were predictors of poorer long-term WOMAC pain and function outcomes in multivariable analysis including age, sex, BMI, comorbidities, surgical factors, pain catastrophising, pain-related fear of movement and depression.

Scott and colleagues[165] followed up 1414 patients (87% eligible) at a single UK centre 12 months after receiving a specific TKR prosthesis. Although significantly associated with long-term dissatisfaction in univariate analysis, there was no association between pre-operative OKS pain and dissatisfaction in a multivariable mode including OKS function, SF-12 physical and mental components, age, sex and comorbidities.

Studies comparing pre- and postoperative pain measures consistently showed that patients receiving TKR with higher levels of pre-operative pain had worse long-term pain. All studies had one or two additional markers of good quality. Associations with long-term physical function and satisfaction were inconsistent.

Pre-surgical physical function

We identified five studies with ≥ 100 patients with TKR followed up for ≥ 12 months with pre-surgical physical function included in multivariable analyses.[46,157,163–165] Details of studies are summarised in *Table 5*. Two studies were conducted in multiple centres[46,157] and three studies in a single centre each.[163–165]

Heck and colleagues[157] followed up 268 patients (92% eligible) 24 months after TKR at multiple US centres. The authors included WOMAC function in a multivariable model with SF-36 mental health, age, ethnicity, sex, poverty, patient health status, SF-36, knee ROM, comorbidities, surgical factors and joint problems in the other knee. Patients with poorer WOMAC function had the greatest long-term improvement in SF-36 PCS. The authors noted that patients who were more likely to show improvement to general health had functional impairment at the time of surgery.

Lingard and colleagues[46] followed up 678 patients (86% at 1 year) from multiple international centres at 12 and 24 months after TKR. The authors included age, sex, income, education, BMI, flexion, country, centre and comorbidities in multivariable analysis. Poor pre-operative WOMAC function was an independent predictor of poor long-term WOMAC function outcome.

In a study including 165 patients (per cent eligible not reported) with TKR from a single US centre, Ayers and colleagues[163] reported follow-up at 12 months. The authors included pre-operative WOMAC physical function, age, sex and comorbidities in multivariable analysis. The model with increasing age and poorer physical function predicted a poorer SF-36 and WOMAC physical function outcome.

Clement and colleagues[164] followed up 966 patients (per cent eligible not reported) for 12 months after TKR at a single UK centre.[164] Patients with a better OKS score before surgery had better long-term OKS but were more likely to be dissatisfied with their operation in multivariable analyses with age, sex, comorbidities, socioeconomic deprivation, SF-12 physical component and back pain.

Scott and colleagues[165] reported a 12-month follow-up of 1414 patients (87% eligible) who had received a specific TKR prosthesis at a single UK centre. In multivariable analysis with SF-12 mental component, age, sex, depression and comorbidities, lower pre-operative OKS function was associated with greater satisfaction.

The relationship between pre-operative physical function and long-term patient outcomes after TKR was complex. In three studies there was a simple association between low pre-operative function before surgery and a poor long-term functional outcome. However, in another study patients with worse pre-operative function had a greater improvement in physical function. In two studies those with lower pre-operative function were more likely to be satisfied with their operation. Results of studies were consistent in those with one or two additional markers of good quality.

Discussion

Systematic review of cohort studies is a pragmatic exercise requiring specific inclusion criteria. In any population of people followed up before and after surgery the opportunity exists to carry out multivariable analyses. Inclusion of published analyses which may focus on the interests of researchers, editors, reviewers and readers is prone to bias.

For our reviews, we limited inclusion to studies with exclusively hip or knee replacement-based analyses. We included studies for which separate analyses were reported but not when data were combined as 'joint replacement'. Studies were excluded if they had < 100 patients and a long-term outcome was classified as ≥ 12 months. Again this represents a pragmatic approach owing to the large number of studies reported in the literature.

In the context of study quality, proportion not followed up probably relates more to generalisability as multivariable analyses include only patients with variables measured before and after surgery (or some estimate).

Our overview of studies reporting long-term patient outcomes according to pre-operative BMI suggests that many patients with high BMI benefit from total hip and knee replacement with long-term improvements to physical function and reduction in long-term pain. However, there was some suggestion that the absolute levels of physical function and pain achieved in patients with especially high BMI may be somewhat lower.

Patients with depression before surgery may have poorer long-term pain and functional outcomes after total hip and knee replacement. For patients with anxiety or poor general psychological health, there was evidence for a relationship with worse pain and functional outcomes in patients receiving TKR but evidence in THR was equivocal.

Patients with better physical function and lower pain before total hip and knee replacement generally achieved a better recovery in terms of joint specific pain and function. Patients with poor physical function before surgery may have greater absolute improvement.

Conclusion

Longitudinal studies reporting the associations between pre-surgical factors and long-term patient outcomes after total hip or knee replacement suggest that interventions before surgery to optimise a patient's physical function, pain levels and psychological health merit further study. In the context of advanced osteoarthritis for which conservative treatments have not controlled symptoms, an exercise and education intervention may aim to maintain functional levels or prevent further decline and facilitate recovery. Pain management and psychological counselling may also have a role in preparing patients for surgery and subsequent rehabilitation.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Systematic review of comorbid conditions and long-term patient-centred outcomes after total hip and knee replacement

Background

Multimorbidity is common in older people, with approximately 60% of people aged ≥ 65 years reporting two or more health conditions.[174] In a population aged ≥ 75 years, 60% reported one and 33.4% reported two or more health problems.[175] Among patients with advanced symptoms of osteoarthritis recruited into the APEX study, comorbid conditions were common; in patients receiving total hip and knee replacement, 64% and 71% of patients, respectively, reported at least one condition additional to osteoarthritis.

Details of prevalence of specific comorbid conditions in the APEX study are summarised in *Table 6*. In people receiving THR, commonly reported comorbid conditions were degenerative disc disease (24.7%), osteoporosis (15.0%), visual impairment (14.0%), upper gastrointestinal problems (14.7%), cardiovascular disease (12.0%), depression (13.7%), hearing impairment (8.3%), anxiety (11.7%) and diabetes (6.7%). In people receiving TKR, the commonly reported comorbid conditions were degenerative disc disease (22.9%), osteoporosis (18.5%), visual impairment (19.5%), upper gastrointestinal problems (18.2%), cardiovascular disease (20.2%), depression (10.8%), hearing impairment (15.2%), anxiety (9.4%) and diabetes (14.1%).

TABLE 6 Prevalence of comorbid conditions in the APEX cohorts

	THR			TKR		
Condition	Female	Male	All	Female	Male	All
Angina	3.9%	4.1%	4.0%	8.5%	11.8%	10.1%
Congestive heart failure	0.6%	1.6%	1.0%	1.3%	1.4%	1.3%
Heart attack	4.5%	4.9%	4.7%	4.6%	12.5%	8.4%
Stroke or transient ischaemic attack	2.8%	4.9%	3.7%	7.2%	9.7%	8.4%
Peripheral vascular disease	1.1%	3.3%	2.0%	2.0%	2.1%	2.0%
Any cardiovascular disease	8.4%	17.2%	12.0%	16.3%	24.3%	20.2%
Degenerative disc disease	28.1%	19.7%	24.7%	23.5%	22.2%	22.9%
Asthma	14.6%	5.7%	11.0%	17.0%	8.3%	12.8%
Chronic obstructive pulmonary disease	2.2%	2.5%	2.3%	7.8%	2.8%	5.4%
Diabetes type 1 and 2	6.2%	7.4%	6.7%	12.4%	16.0%	14.1%
Osteoporosis	15.2%	14.8%	15.0%	18.3%	18.8%	18.5%
Neurological diseases	1.1%	1.6%	1.3%	0.7%	2.8%	1.7%
Upper gastrointestinal disease	14.0%	15.6%	14.7%	23.5%	12.5%	18.2%
Depression	18.0%	7.4%	13.7%	13.7%	7.6%	10.8%
Anxiety or panic disorders	12.9%	9.8%	11.7%	12.4%	6.3%	9.4%
Visual impairment	15.7%	11.5%	14.0%	20.3%	18.8%	19.5%
Hearing impairment	6.7%	10.7%	8.3%	11.1%	19.4%	15.2%
Total number of patients	178	122	300	153	144	297

Research on pre-surgical comorbidities has often focused on associations with adverse events. In a US study including > 950,000 patients with joint replacement, the in-hospital rate of serious postoperative adverse events including infection, non-healing wounds, pulmonary embolism and vascular complications was 2.6%.[36] In 260 patients with knee replacement, Kirschner and colleagues[176] reported that 6% of patients had serious adverse events within 3 months of knee replacement. More general adverse events occurred in a further 26% of patients.

Adverse events are associated with lower patient satisfaction and poorer long-term HRQoL. In a study of 264 patients followed up 2 years after TKR, patients were more likely to be satisfied if they had no complications after surgery [odds ratio (OR) 6.6, 95% CI 1.8 to 24.7; $p = 0.004$].[158] In another study of 112 patients followed up 7 years after TKR, the number of post-discharge complications was associated with poorer WOMAC pain ($p < 0.001$), stiffness ($p = 0.018$) and function ($p = 0.042$).[159] Furthermore, in a study of 1703 patients with TKR, 19% were dissatisfied with their outcome.[177] In a multivariable model, the OR for a patient being dissatisfied was 1.86 in the presence of a complication requiring hospital admission.

The majority of adverse events, after appropriate treatment, mobilisation and rehabilitation, have no serious effect on long-term recovery. For some patients the adverse events are more serious and the consequences severe. For example, patients with surgical site infections describe extreme pain, prolonged immobilisation, isolation and insecurity, and feelings of hopelessness.[178] If untreated with revision surgery, infection can result in severe pain, persistent dislocation and death.[179] Similarly, the consequences of pulmonary embolism are extremely serious, with a 3-month mortality rate of about 17.4%.[180] Deep-vein thrombosis is more common and, although treated effectively in most people with anticoagulant therapy, associated costs are substantial. In a Canadian study, average medical costs were CA$2503 [approximately £1615 (cost correct as of 2010)] with a further CA$2677 [approximately £1727 (cost correct as of 2010)] attributable to non-medical costs including loss of earnings, assistance and transport.[181] Khan and colleagues[182] estimated that complications after non-cardiac surgery may lead to increases in hospital stays of 114%, with significant associated hospital costs.

Solomon and colleagues[183] explored the predictors of adverse events (death, infection, pulmonary embolism, pneumonia, and myocardial infarction) within 3 months of knee replacement in a cohort of 9073 patients from 276 US hospitals. The 37% of patients with one or more comorbid health conditions had a 50% greater risk of an adverse event.

It is important to be aware of the increased risk of adverse events and poorer long-term patient outcomes in patients with additional comorbid conditions. Scores reflecting the extent of comorbidity are widely used to assess risk of death and adverse events in patients requiring joint replacement surgery. However, to guide care of patients receiving joint replacement it is also important to know if patients with specific comorbidities have different long-term patient-reported outcomes from those who are unaffected. Appropriate pre-surgical interventions with assessment and management of clinical conditions may help to reduce the incidence of adverse events and improve long-term patient outcomes after total hip and knee replacement.

Our aim was to review the evidence on the associations between comorbid conditions and long-term patient outcomes. When good-quality evidence was available on associations between comorbid conditions and post-surgical adverse events, we summarise this briefly.

Particular comorbid conditions prevalent in populations of patients receiving total hip or knee replacement and with potential for treatment were considered, specifically diabetes, cardiovascular disease, hypertension, thyroid disease and anaemia.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Methods

General methods	As described in *Systematic review methods*
Databases and dates	MEDLINE and EMBASE from inception to 16 October 2013
Search strategy	Joint replacement/specified patient centred outcomes. MEDLINE search strategy based on terms in *Appendix 3*. In addition, a series of specific searches linking total hip or knee replacement with specific comorbidities: diabetes, cardiovascular disease, hypertension, anaemia, thyroid disease
Study design	Cohort studies
Patients	Total hip or knee replacement
Follow-up	≥ 12 months
Data extraction	Date of publication, hip or knee, country, baseline dates of study, follow-up duration, pre-surgical measures
Outcomes	Patient-reported outcomes
Quality assessment	Quality assessment related to generalisability as described in the systematic review of pre-operative predictors of patient-centred outcomes after total hip and knee replacement

Results

Total hip replacement

The review flow diagram is shown in *Figure 7*. Searches identified five studies reporting analyses of specific comorbid conditions identified before surgery and long-term patient-reported outcomes.[127,130,166,184,185] Two of these studies reported separate analyses of different comorbidities in the same cohort.[184,185]

Study characteristics are summarised in *Appendix 7* with brief details in *Table 7*.

Diabetes

In the APEX study, 6.7% of patients receiving a THR reported that they had type 1 or type 2 diabetes.

Searches identified four studies reporting long-term patient-reported outcomes in patients according to their pre-surgical diabetic status. Two studies each included patients from multiple centres,[127,185] or a single centre.[130,166] The proportion of patients followed up varied from 6.3% to 49.9%, which was largely explained by lower follow-up rates in studies of longer duration.

TABLE 7 Systematic review of comorbid conditions and long-term patient-centred outcomes after THR: included studies

Study	Number of patients; follow-up	Comorbidity	Outcome measures
Multiple centres			
Cushnaghan and colleagues 2007[184] Judge and colleagues 2012[185]	249; mean approximately 96 months	Hypertension	SF-36 PCS
Jones and colleagues 2012[127]	Approximately 167 (231 eligible); 3 years	Cardiovascular disease, diabetes	WOMAC function and pain
Judge and colleagues 2012[185] Cushnaghan and colleagues 2007[184]	249; mean approximately 96 months	Diabetes, thyroid disease	SF-36
Single centre			
Anakwe and colleagues 2011[130]	850; 12 months	Diabetes, hypertension	Satisfaction
Gandhi and colleagues 2010[166]	707; 12 months	Diabetes, hypertension	WOMAC

In a study in two Canadian hospitals, Jones and colleagues[127] followed up an estimated 167 patients (72% eligible) after THR. Diabetes mellitus was not a significant independent factor predicting recovery measured by WOMAC function or pain scores in a multivariable analysis including cardiac disease, age, sex, BMI, education, principal diagnosis, living arrangements, type of living accommodation, previous joint surgery, ambulatory status and number of comorbid conditions.

Judge and colleagues[127] followed up 249 patients (50% eligible) from two UK health districts at a mean of 96 months.[185] In multivariable analysis with diabetes, hypertension, thyroid disease, age, sex, BMI, smoking habit, previous knee injury, Heberden's nodes, number of painful joints and radiographic grade, the OR for no improvement in SF-36 physical function was 5.45 (95% CI 0.99 to 29.89) in patients with diabetes compared with non-diabetics. This was close to statistical significance. In another analysis of this cohort, the MD in change in SF-36 physical function was 25.8 points (95% CI 6.8 to 44.9 points) favouring patients with no diabetes.[184] However, both analyses were based on only eight patients with diabetes.

In a study at a single UK centre, Anakwe and colleagues[130] followed up 850 patients (84% eligible) with THR for 12 months. Diabetes was not associated with long-term patient satisfaction in multivariable analyses including other comorbidities, age, sex, OHS, SF-12 physical and mental components and musculoskeletal comorbidities ($p = 0.227$).

Gandhi and colleagues[166] followed up 707 patients (83% eligible) after a THR at a single Canadian centre. In a multivariable analysis with BMI, hypertension, hypercholesterolaemia, age, sex, WOMAC score, and cumulative illness rating scale, self-reported diabetic status did not predict the extent of WOMAC function improvement 12 months after THR ($p = 0.46$). However, in analyses considering the combination of medical conditions relating to metabolic syndrome (hypertension, obesity, hypercholesterolaemia and diabetes), presence of all four conditions was associated with a poorer long-term WOMAC score ($p = 0.04$).

The four studies we identified did not provide any conclusive evidence on the impact of diabetic status on long-term patient-reported outcomes.[127,130,166,185] This may be explained by good glycaemic management in patients with diabetes receiving THR in the cohorts we identified.

Patients with diabetes may be more likely to have complications after their THR. During the hospital stay, patients with diabetes may be at greater risk of stroke, pneumonia and requirement for a blood transfusion but not prosthetic joint infection.[186] In a literature search relating to infection including all studies reporting outcomes in patients according to diabetic status we identified 10 longitudinal studies with 376,138 patients in which 2487 deep infections were recorded.[186–195] As shown in *Figure 11*, the relative risk of developing a deep infection was 2.14 (95% CI 1.44 to 3.18) in patients with diabetes compared with non diabetics. We used a random-effects model owing to the high extent of heterogeneity ($I^2 = 74\%$). This was largely explained by one large study with follow-up only to hospital discharge.[186]

In an analysis of the US National hospital discharge survey including 43,215 patients receiving any orthopaedic surgery, diabetes was associated with an increased risk of inpatient mortality in univariate analysis but this was not statistically significant in multivariable analysis (OR 1.23; $p = 0.18$).[196]

In a study of 16,317 patients with total hip or knee replacement, there was an increased risk of myocardial infarction and venous thromboembolism after joint replacement in patients with diabetes or hypertension.[197] Considering the cluster of hypertension, diabetes, obesity and dyslipidaemia that constitute metabolic syndrome, the risk of myocardial infarction was increased by 128% and the risk of venous thromboembolism more than tripled.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Study or subgroup	Diabetes Events	Total	No diabetes Events	Total	Weight	Risk ratio M–H, random, 95% CI
Hip						
Bolognesi 2008[186]	113	17,385	1712	263,385	18.4%	1.00 (0.83 to 1.21)
Chan 2005[187]	2	82	12	1247	5.2%	2.53 (0.58 to 11.14)
Choong 2007[188]	4	87	10	732	7.4%	3.37 (1.08 to 10.50)
Cordero-Ampuero 2010[189]	6	24	11	100	9.8%	2.27 (0.93 to 5.53)
Dowsey 2008[190]	5	133	17	1074	8.8%	2.38 (0.89 to 6.33)
Iorio 2012[191]	3	126	3	1400	4.7%	11.11 (2.27 to 54.48)
Namba 2005[192]	1	100	4	970	2.8%	2.42 (0.27 to 21.49)
Namba 2012[193]	44	5591	111	24,900	16.7%	1.77 (1.25 to 2.50)
Pedersen 2010[194]	34	3278	367	54,297	16.7%	1.53 (1.08 to 2.18)
Vannini 1984[195]	5	47	23	1180	9.4%	5.46 (2.17 to 13.72)
Subtotal (95% CI)		**26,853**		**349,285**	**100.0%**	**2.14 (1.44 to 3.18)**
Total events	217		2270			

Heterogeneity: $\tau^2=0.21$; $\chi^2=34.52$, df=9 ($p<0.0001$); $I^2=74\%$

Test for overall effect: $z=3.76$ ($p=0.0002$)

Test for subgroup differences: not applicable

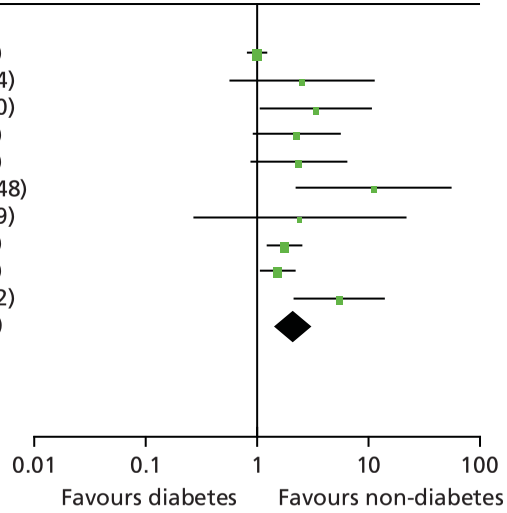


FIGURE 11 Summary plot of deep infection complications after THR by diabetic status. df, degrees of freedom; M–H, Mantel–Haenszel.

In a US cohort of 1,030,013 patients receiving total hip or knee replacement, patients with diabetes were compared by the level of glycaemic control.[198] In those patients with uncontrolled diabetes, the risk of surgical and systemic complications was significantly higher and mortality greater than in those with controlled diabetes. Danish hip registry data from 3278 patients also suggests increased risk of revision due to deep infection in patients with diabetes, particularly in those with short diabetes duration or diabetic complications probably reflecting poor blood glucose control.[194]

Cardiovascular disease

In the APEX study, 12.0% of patients receiving THR reported a cardiovascular-related condition.

Our searches identified one study in multiple centres with multivariable analysis assessing patient-reported outcomes according to presence of cardiovascular disease.[127]

In the study of Jones and colleagues[127] at two Canadian centres, an estimated 167 patients (72% eligible) with THR were followed up at 3 years. In an analysis adjusted for age, sex, BMI, education, principal diagnosis, living arrangements, type of living accommodation, previous joint surgery, ambulatory status and number of comorbid conditions, patients with cardiac disease had worse long-term WOMAC pain ($p = 0.014$) and function ($p = 0.012$), and a slower recovery.

The mortality rate within 90 days after THR is about 1%[199] and cardiovascular disease is generally the leading cause of death.[43] Research in patients receiving a THR with comorbid cardiovascular disease has mainly focused on adverse events after surgery.

Ackland and colleagues[200] developed a risk index based on patient history of ischaemic heart disease, heart failure and cardiac risk factors. This method was able to stratify patients with elective orthopaedic surgery by risk of in-hospital adverse events. However, with an area under the receiver operating characteristic curve of 0.62 (95% CI 0.57 to 0.67), the predictive ability was modest.

Bozic and colleagues[201] developed a risk calculator for 90-day mortality and prosthetic joint infection in patients with THR. The risk model included age, sex, ethnicity and socioeconomic status and 29 pre-operative comorbidities including cardiopulmonary conditions. The authors concluded that levels of risk could be used to counsel patients with heart disease before surgery. Sanders and colleagues[202] explored the effect of time since a vascular event (stroke, myocardial infarction and unstable angina) on outcomes of total hip and knee replacement in 414,985 patients. The authors concluded that patients with a vascular event in the year before surgery were at greatest risk of death within 30 days of surgery.

In an analysis considering long-term outcomes, Singh and Lewallen[203] noted a greater risk of periprosthetic fractures in patients with heart disease identified before THR.

Hypertension

In a US study including 53,252 Medicare patients with THR, 66% of patients had hypertension before surgery.[201]

Our searches identified three studies that included hypertension before surgery in multivariable analysis for the prediction of long-term patient-reported outcomes.[130,166,185]

Cushnaghan and colleagues[151] reported a multivariable analysis in 249 patients (50% eligible) from two UK health districts followed up for 96 months after THR. Hypertension was not a significant predictor of change in SF-36 physical function score, MD in change 0.5 points (95% CI –6.5 to 7.6 points).

In a single-centre UK study with 850 patients (94% eligible) followed up for 12 months, Anakwe and colleagues[130] compared levels of satisfaction with THR in patients with and without hypertension. A total of 8.7% of hypertensive patients were dissatisfied with their THR compared with 6.4% of those

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

without hypertension. This did not reach the specified level of statistical significance ($p < 0.10$) for inclusion in multivariable analysis.

In their study of metabolic syndrome, Gandhi and colleagues[166] followed up 707 patients (83% eligible) 12 months after THR at a single Canadian centre. In multivariable analysis with BMI, self-reported diabetic status, hypercholesterolaemia, age, sex, WOMAC and comorbidity score, hypertension was a significant predictor of lower overall WOMAC improvement at 1 year ($p = 0.006$).

Overall, there was limited evidence that patients with hypertension identified before surgery have poorer long-term patient outcomes. As described previously, its importance may be as part of the cluster of cardiovascular risk factors that constitute metabolic syndrome.

Considering adverse outcomes after THR, Bozic and colleagues[201] reported that patients with hypertension had an increased risk of mortality and joint infection. In a multivariable analysis, hypertension was an independent variable included in a risk equation to identify patients at risk of joint infection and mortality.

Anaemia

We did not identify any studies reporting the association between pre-surgical anaemia and long-term patient-reported outcomes after THR. Searches identified one systematic review by Spahn[204] looking at studies of perioperative anaemia and clinical outcomes. The author concluded that pre-operative anaemia in patients with hip and knee surgery was associated with increased need for blood transfusion, infection and death, poorer physical functioning and recovery, and longer hospital stay.

More recent analyses of registries and large cohort studies support this review. Jämsen and colleagues[205] reported a multivariable analysis comparing mortality rates in 1998 patients with hip and knee replacement. After extensive adjustment for patient and clinical characteristics including other comorbidities, the hazard ratio for death was 1.47 (95% CI 1.08 to 1.99) in patients with pre-operative anaemia compared with those without. In another multivariable analysis including 15,722 patients reported by Greenky and colleagues,[206] pre-operative anaemia was associated with a greater risk of prosthetic joint infection but not mortality. In a multivariable analysis including 40,919 patients with THR followed up for 90 days, Bozic and colleagues[207] reported that patients with pre-operative anaemia had a greater risk of prosthetic joint infection (hazard ratio 1.36, 95% CI 1.15 to 1.62). Pre-operative anaemia was not associated with mortality within 90 days in multivariable analysis in this cohort.

O'Malley and colleagues[208] identified factors associated with major complications after THR leading to delays in hospital discharge. In multivariable analysis including BMI, pre-operative bleeding disorder, comorbidities and surgical factors, pre-operative anaemia was associated with increased risk of major complications before discharge. Major complications resulted in a mean increase in hospital stay of 62 days.

In a prospective analysis of data from patients with THR at a single centre, Myers and colleagues[209] noted a higher infection rate and need for transfusion in patients with pre-clinical anaemia on admission. Inpatient stay was, on average, 18 days in patients with anaemia compared with 11 days in patients with no pre-clinical anaemia.

Research on anaemia and THR has focused on early adverse events and death. Patients with anaemia may be at greater risk of infection and other major complications, are more likely to require blood transfusion and may have a substantially increased length of hospital stay.

Thyroid disease

In the Whickham survey of men with a median age of 58 years and women with a median age of 59 years, the prevalence of hypothyroidism was 1.3% and 9.3%, respectively.[210] This compares with the prevalence of treatment for hypothyroidism in people with severe osteoarthritis of 7.0% and 14.0% in men and women, respectively, in the APEX cohort.

Our searches identified one study with long-term patient outcomes after THR according to whether or not patients had thyroid disease.[185] Details of the study are summarised in *Table 7*.

In the study of Judge and colleagues,[185] 249 patients (50% eligible) with THR in two UK health districts were followed up for a mean of approximately 96 months. In univariate analysis, there was no suggestion of a difference in long-term SF-36 physical function in patients with thyroid disease compared with people without thyroid disease (OR for no improvement or worse SF-36 physical function 0.96, 95% CI 0.36 to 2.53). The OR for a meaningful improvement in SF-36 physical function score (at least 30 points) was 0.33 (95% CI 0.07 to 1.49), a non-significant trend favouring patients with no thyroid disease.

Total knee replacement

The review flow diagram is shown in *Figure 8*. Searches identified six studies that reported analyses of specific comorbid conditions identified before surgery and long-term patient-reported outcomes.[127,151,163–166] Study characteristics are summarised in *Appendix 8* with brief details in *Table 8*.

Diabetes

Diabetes is a common comorbid condition in patients receiving TKR. In an Australian cohort of 1214 patients with knee replacement, the prevalence of diabetes was 17.0%.[211] Of 3,672,247 patients discharged from US hospitals after unilateral TKR, about 13% were diabetic.[212] In the APEX study, 14.1% of patients with TKR recruited into a UK RCT had type 1 or type 2 diabetes.

Six studies reported long-term patient outcomes according to pre-operative diabetic status. Of these, two were from multiple centres[127,151] and four included patients from a single centre.[163–166]

Cushnaghan and colleagues[151] followed up 259 patients (39% eligible) from three UK health districts at a mean of 72 months after TKR. In multivariable analysis, a trend for greater improvement in SF-36 physical function in diabetic patients was not statistically significant (mean relative change 3.8, 95% CI –8.5 to 16.2). The analysis included only 16 patients with diabetes.

TABLE 8 Systematic review of comorbid conditions and long-term patient-centred outcomes after TKR: included studies

Study	Number of patients; follow-up	Comorbidity	Outcome measures
Multiple centres			
Cushnaghan and colleagues 2009[151]	259; mean 6 years	Diabetes, hypertension, thyroid disease	SF-36 physical function
Jones and colleagues 2012[127]	Estimated 209; 3 years	Cardiovascular disease, diabetes	WOMAC
Single centre			
Ayers and colleagues 2005[163]	165; 12 months	Cardiovascular disease, diabetes	WOMAC function, SF-36 physical component
Clement and colleagues 2013[164]	966 (number eligible not specified) 12-month follow-up, losses to follow-up not described	Diabetes, cardiovascular disease, hypertension, anaemia	OKS, satisfaction
Gandhi and colleagues 2010[166]	889 (approximately 1067 eligible); 12 months, 16.7% not followed up	Diabetes, hypertension	WOMAC
Scott and colleagues 2010[165]	1141 (1290 eligible); 12 months, 13.1% not followed up	Diabetes, cardiovascular disease, hypertension	Satisfaction

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Jones and colleagues[127] followed up an estimated 209 patients (72% eligible) after TKR at two Canadian centres. At 3 years, there was little to suggest that WOMAC pain and function differed according to diabetic status; however, the authors observed that pain and function scores worsened slightly after 6 months among diabetic patients but not in non-diabetics.

Ayers and colleagues[163] followed up 165 patients (per cent eligible not reported) from a single US centre at 12 months after TKR. In multivariable analysis there was no association between diabetic status and long-term physical function measured by WOMAC and SF-36 scales.

In a study from a single UK centre with 1141 patients (87% eligible) followed up at 12 months, Scott and colleagues[165] found no association between diabetic status and long-term satisfaction after TKR.

In a study from a single Canadian centre, Gandhi and colleagues[166] followed up 889 patients (83% eligible) after TKR. Self-reported diabetic status showed a trend for poorer WOMAC score at 12 months but this was not statistically significant ($p = 0.07$). In analyses considering the combination of medical conditions relating to metabolic syndrome (hypertension, obesity, hypercholesterolaemia and diabetes), in the presence of all four conditions there was a trend for poorer long-term WOMAC score but this was not statistically significant ($p = 0.08$).

Clement and colleagues[164] followed up 966 patients (per cent eligible not reported) at a single UK centre 12 months after TKR. In multivariable analysis, diabetes was not associated with a poorer long-term patient outcome ($p = 0.47$).

There is no strong evidence to suggest that long-term patient outcomes after TKR differ according to diabetic status; however, much research has focused on the risk of adverse events. In our literature search on the incidence of infection by diabetic status, we obtained data from 14 studies including 633,813 patients in which 3988 deep infections were recorded.[186,191,192,207,211,213–221] In a random-effects meta-analysis shown in *Figure 12*, the relative risk for infection in patients with diabetes compared with non-diabetics was 2.03 (95% CI 1.54 to 2.67).

In studies with more general orthopaedic inclusion criteria, patients with diabetes had an increased risk of myocardial infarction and venous thromboembolism. This was particularly evident in patients with the metabolic syndrome cluster of risk factors.[197] There was also a suggestion of an increased risk of inpatient mortality for patients with diabetes, but this was not statistically significant.[196]

Cardiovascular disease

In the APEX study, 20.2% of patients receiving TKR reported a cardiovascular-related condition.

Our literature searches identified four studies reporting multivariable analysis of patient-reported outcomes according to presence of cardiovascular disease. One study was conducted in multiple centres[127] while three studies included patients from a single centre.[163–165]

Jones and colleagues[127] followed up an estimated 209 patients (72% eligible) at 3 years after TKR at two centres. Cardiac disease before surgery was not a predictor of long-term WOMAC pain or function.

In the study of Ayers and colleagues,[163] 165 patients (per cent eligible not reported) with TKR at a single centre were followed up at 1 year. Only univariate analyses were reported for individual comorbid conditions. There was a lower improvement in the SF-36 physical component in patients with cardiovascular comorbidity than those without but the relationship was not strong. For WOMAC physical function, there was a suggestion that patients with cardiovascular comorbidity had a lesser improvement in physical function than those without.

Study or subgroup	Diabetes Events	Total	No diabetes Events	Total	Weight	Risk ratio M–H, random, 95% CI
Knee						
Adams 2013[213]	71	7567	216	32,924	13.2%	1.43 (1.10 to 1.87)
Asensio 2010[214]	10	36	13	106	7.3%	2.26 (1.09 to 4.71)
Bolognesi 2008[186]	115	46,000	900	409,091	14.0%	1.14 (0.94 to 1.38)
Bozic 2012[207]	606	18,262	1683	64,749	14.8%	1.28 (1.17 to 1.40)
Chesney 2008[215]	1	53	15	1279	1.7%	1.61 (0.22 to 11.95)
Dowsey 2009[211]	11	206	7	1008	5.5%	7.69 (3.02 to 19.60)
Fan 2008[216]	5	82	9	390	4.6%	2.64 (0.91 to 7.68)
Galat 2009[217]	16	955	43	16,829	9.2%	6.56 (3.71 to 11.60)
Iorio 2012[191]	4	199	13	2248	4.4%	3.48 (1.14 to 10.56)
Jämsen 2010[218]	11	655	4	910	4.2%	3.82 (1.22 to 11.95)
Meding 2003[219]	4	329	35	4891	4.9%	1.70 (0.61 to 4.75)
Moon 2008[220]	3	171	2	171	2.1%	1.50 (0.25 to 8.86)
Namba 2005[192]	3	255	6	1558	3.2%	3.05 (0.77 to 12.14)
Namba 2009[221]	24	2449	158	20,440	11.0%	1.27 (0.83 to 1.94)
Subtotal (95% CI)		**77,219**		**556,594**	**100.0%**	**2.03 (1.54 to 2.67)**
Total events	884		3104			

Heterogeneity: τ^2=0.13; χ^2=58.67, df=13 (p<0.00001); I^2=78%
Test for overall effect: z=5.00 (p<0.00001)

Test for subgroup differences: not applicable

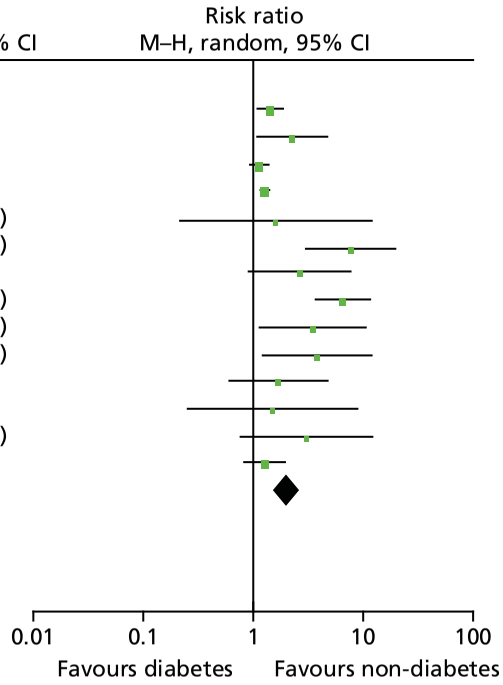


FIGURE 12 Summary plot of deep infection complication after TKR by diabetic status. df, degrees of freedom; M–H, Mantel–Haenszel.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Scott and colleagues[165] followed up 1141 patients (87% eligible) with TKR at a single centre 12 months after surgery. In univariate analysis, there was little difference in long-term satisfaction in those with heart disease compared with those with no heart disease.

In the study of Clement and colleagues,[164] 966 patients (per cent eligible not reported) with TKR at a single centre were followed up for 12 months. Patients with a history of heart disease had a poorer improvement in OKS compared with those with no history of heart disease.

Overall, there was a suggestion that people with heart disease had somewhat poorer long-term improvement in pain and function, but this was only evident in two studies with no additional markers of good quality. Further research has studied the association between comorbid cardiac disease and adverse events.

Variables in the risk calculator for in-hospital adverse events described by Ackland and colleagues[200] included specific cardiac diseases and risk factors but the discriminatory ability of the model was modest. Gill and colleagues[222] looked at factors predicting mortality within 90 days of TKR in a cohort of 3048 patients, of whom 14 died. Patients with any major cardiovascular disease before surgery had a greater risk of death within 90 days of surgery. In the study of Sanders and colleagues,[202] a greater risk of death within 30 days of surgery was observed in patients with a vascular event in the year preceding total hip and knee replacement.

Hypertension

Searches identified four studies reporting long-term patient outcomes according to whether or not patients had hypertension before surgery. Studies were in multiple[151] or single centres.[164–166]

In a study in three UK health districts, Cushnaghan and colleagues[151] followed up 259 patients (39% eligible) from three centres at a mean of 72 months after TKR. In multivariable analysis, hypertension was not a significant predictor of change in SF-36 physical function score.

Gandhi and colleagues[166] followed up 889 patients (83% eligible) after a TKR at a single Canadian centre. Similar WOMAC function improvement was observed at 1 year, irrespective of presence of hypertension. The authors noted a trend for poorer long-term WOMAC score in patients with the four conditions relating to metabolic syndrome but this was not statistically significant.

Scott and colleagues[165] followed up 1141 patients (87% eligible) from a single UK centre 12 months after TKR. In univariate analysis, more patients with hypertension were dissatisfied with their outcome than those with no hypertension.

In a study at a single UK centre, Clement and colleagues[164] followed up 966 patients (per cent eligible not reported) 12 months after TKR. There was no difference in change in OKS in patients with hypertension compared with those with no hypertension.

Considering adverse events, Bozic and colleagues[223] followed up 83,011 patients with TKR 90 days after surgery. In multivariable analysis, hypertension identified pre-operatively was not associated with infection or mortality.

There was no clear evidence that patients with hypertension had worse long-term pain and function outcomes after TKR. As observed with diabetes, management of blood pressure may affect studies of the association between pre-operative hypertension and post-surgical outcomes. Most people with a diagnosis of hypertension will be treated before surgery; indeed management of undiagnosed hypertension may be required in the preparation for elective surgery.

Anaemia

We identified one study with patients from a single centre that reported long-term patient outcomes after TKR according to pre-operative anaemia status.[164]

Clement and colleagues[164] followed up 966 patients (per cent eligible not reported) 12 months after TKR at a single UK centre. There was a small difference in improvement in OKS between patients favouring those with no anaemia but the relationship was not strong.

The systematic review of Spahn[204] considered clinical outcomes of patients with hip and knee surgery. Pre-operative anaemia was associated with post-surgical mortality and infection, increased need for blood transfusion, poorer physical functioning and recovery, and longer hospital stay.

More recently, Bozic and colleagues[223] followed up 83,011 patients with TKR for 90 days after surgery. In multivariable analysis, pre-operative anaemia was associated with an increased risk of infection but not mortality.

Jämsen and colleagues[205] reported an increased risk of death in 1998 patients receiving knee or hip replacement with pre-operative anaemia compared with those without. In a multivariable analysis including patients with total hip or knee replacement, Greenky and colleagues[206] reported a greater risk of infection but not mortality.

In summary, there was no strong evidence relating pre-operative anaemia to long-term patient outcomes. However, by reducing adverse events and limiting hospital stay, strategies to manage anaemia before surgery may have substantial benefits for both patients and health-care providers.

Thyroid disease

Searches identified one study conducted in multiple centres reporting patient-reported outcomes in patients with or without thyroid disease who received a TKR. Cushnaghan and colleagues[151] followed up 259 patients (39% eligible) in three English health districts at a mean of 72 months after TKR. In multivariable analysis, thyroid disease was not a significant predictor of change in the SF-36 physical component.

Discussion

Approximately 60–70% of patients receiving total hip and knee replacement report one or more comorbid condition and are at risk of an adverse event after surgery. Although this is valuable information in itself with the possibility of extra monitoring and care, preparatory strategies with treatment of individual conditions may prevent adverse events and improve long-term patient outcomes. Our systematic review of large prospective cohort studies investigating the relationship between pre-operative comorbidities and long-term patient outcomes highlighted some possible areas for intervention.

We did not confirm a relationship between diabetic status and long-term patient outcomes after total hip or knee replacement; however, patients with diabetes are at greater risk of early adverse events and are over twice as likely to have a deep infection after their total hip or knee replacement with potentially devastating consequences for patients and substantial health-care implications. Supported by the observation that patients with uncontrolled diabetes have poorer outcomes than those with better glycaemic control, optimisation of diabetes control before surgery may be of long-term benefit to patients receiving total hip or knee replacement and merits appropriate evaluation.

Although not consistently so, there was some suggestion that patients with cardiovascular disease had poorer patient outcomes after total hip and knee replacement. As with diabetes the impact of cardiovascular disease on patients may be an increased rate of adverse events, possibly limited to those patients with more recent occurrence of acute coronary syndromes.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Evidence on the importance of hypertension on long-term outcomes in patients with hip or knee replacement was equivocal. As a widely treated condition in older people, it is unlikely that the patients receiving joint replacement would have uncontrolled hypertension. No studies were found looking at outcomes by level of blood pressure control.

There was evidence from one study that diabetes and hypertension, in combination with other conditions (high BMI and hypercholesterolaemia) that make up metabolic syndrome may be associated with poorer long-term patient outcomes.[166] However, this was only statistically significant in patients with THR.

We identified no studies reporting long-term patient outcomes in patients according to presence of pre-operative anaemia. Patients with anaemia had increased need for perioperative blood transfusion and increased risk of early adverse events, which probably explains a substantially longer average hospital stay.

Further evidence is now required from intervention studies on whether or not improved management of conditions before surgery can improve long-term patient outcomes, possibly mediated through a reduction in adverse events. Encouragement for this approach in diabetes comes from two large studies.[194,198] In the US Nationwide Inpatient Sample of nearly 1 million patients with joint replacement, the risk of postoperative complications was increased in patients with uncontrolled diabetes.[198] This was supported by data from the Danish Hip Arthroplasty Registry suggesting that those with complications due to diabetes had a greater risk of revision, owing to deep infection.[194] However, an analysis of data from a US integrated health-care system did not report a poorer outcome in patients with HbA_{1c} (glycated haemoglobin) $\geq 7\%$, a marker of poor diabetes control.[213]

In this review, we focused on five specific comorbidities. Further studies are required to explore the associations between other conditions and long-term patient outcomes. For example, in the APEX cohort of patients receiving TKR, 19.5% of patients reported visual impairment and 15.2% reported hearing impairment. If there is evidence linking these to poor outcomes, this would indicate the potential value of appropriate screening and treatment.

In the UK, the Royal College of Anaesthetists and Association of Anaesthetists of Great Britain and Ireland provides patient guidance on preparation for surgery.[224] Recommendations include giving up or quitting smoking, reducing weight, dental check-up and GP check-up for long-standing medical problems. Numerous blood tests are routinely performed before surgery but their value in predicting adverse events[225] and management of health conditions[226,227] is uncertain. The best evidence on clinical effectiveness and cost-effectiveness of interventions and prognostic models comes from their evaluation in randomised trials and, ultimately, in systematic review and meta-analysis.

Conclusion

In specific clinical conditions, we found little research on patient-reported outcomes. In studies looking at long-term patient outcomes according to diabetic status, research was inconclusive. However, studies show that patients with diabetes, previous heart disease and anaemia are at greater risk of post-surgical adverse events and study of appropriate interventions through systematic review and RCTs is indicated.

Chapter 3 Patient and public involvement in the RESTORE programme

There has been ongoing PPI throughout the programme as follows.

Collaboration with Arthritis Care, a national charity supporting people with arthritis

The previous regional director (Pippa English-Penfold) and, subsequently, the Director of Service Development (Phil Baker) have taken part in programme meetings to determine the direction of work packages and the programme as a whole. We also held a mid-programme event at which Arthritis Care was represented and contributed. Within the SPIRAL study there has been active collaboration with Arthritis Care through the design and delivery of the 'Challenging Pain' and 'Keep Challenging Pain' interventions, pre- and post joint replacement. We have also attended Arthritis Care's AGM in 2011 and presented an introduction to randomised trials and discussed SPIRAL with members of Arthritis Care.

Engagement with the Patient Experience Partnership in Research

In 2010 a patient group, the PEP-R group, was established to provide a forum through which patients could provide who contribute to the design and delivery of research in the University of Bristol's Musculoskeletal Research Unit (MRU). This group currently comprises eight people who have musculoskeletal conditions, many of whom also have had joint replacements. Group members totalled 18 (nine women and nine men, aged 25–85 years), with a maximum of 11 members at any one time. The group meets for 2 hours every 6–8 weeks. In keeping with guidance from INVOLVE – the national advisory group that supports greater public involvement in NHS, public health and social care research[228] – group members were reimbursed for their time and travel expenses.

Support and training for the patient partners was provided by a dedicated PPI co-ordinator who is a trained researcher with several years' experience supporting patient partners in research. Support included structured training sessions and one-to-one meetings with patient partners. Training and learning is incorporated into PEP-R meetings. Researchers have described and discussed study design (e.g. randomised trials) in the context of studies. In response to group members' feedback, sessions have also included discussion of epidemiology, statistics and qualitative methods. PEP-R members have also visited the MRU.

The co-ordinator liaised between research staff and patient partners. Researchers from the MRU work closely with the new 'People and Research West of England' partnership promoting and supporting service user involvement in research, and patient partners had access to events and the service user network. PEP-R group members are regularly provided with information about how their input has influenced the implementation of studies so that they can see their impact on the research, including verbal feedback on previously discussed projects at the start of every meeting and written feedback in the form of leaflets every few months.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Patient Experience Partnership in Research inputs into many studies within the unit and one of them was RESTORE. Researchers from RESTORE have attended eight meetings of the PEP-R group. The format of these sessions includes group discussion, presentations, card-sorting tasks and written answer sheets. It was important for researchers to have a written record of the session, so discussions are recorded on a flip chart or written sheets completed by group members. Material is sent out to group members in advance so that they have the chance to read it beforehand. They had the choice of providing their input verbally during a session, or by telephone or e-mail afterwards.

All of the work packages have been discussed and developed in collaboration with patient representatives and PEP-R. Patient representatives have provided input into patient recruitment and information literature, research processes, identifying outcomes of importance to patients, questionnaire design and dissemination and helped ensure that outputs of packages informed one another.

The work of the PEP-R group, including work on the RESTORE project and other projects was recognised in a University of Bristol's engagement award 2014.

APEX

Patient representatives inputted into the refinement of patient information materials to ensure that they were clear. One issue with early recruitment materials in APEX was the inclusion of information about spinal anaesthesia. Through discussions with patients it became clear that this was confusing and potentially worrying. Therefore, this information was removed from the recruitment packs. PEP-R has learned about randomised trials through discussion of the APEX trial and of trials in general with researchers facilitating PEP-R sessions. Issues of blinding and sharing results with participants have been discussed with patient representatives and these discussions helped to inform the decision to tell participants in APEX about their allocation to intervention or control groups. Patient representatives advised on the appropriate terminology and the level and amount of information provided to participants when contacted to arrange their 12-month research follow-up visits. They confirmed that the proposed explanation of the visit made the need to undress for an examination explicit and favoured the less clinical term 'surgical site' as opposed to 'wound' or 'scar' with regard to the examination of the replaced joint. As a result, the research nurses were able to incorporate these changes into their subsequent interaction with the participants.

ADAPT

Patient representatives provided suggestions about how to frame the requirements of study participation to participants and in relation to questionnaires. In ADAPT, questionnaires were long and data were collected at three time points. This meant that data collection would involve patients visiting the hospital on three occasions each and also completing long questionnaires. Patient input helped in the presentation of the questionnaires to make them easier to read and complete; however, as these were validated instruments, changes could not be made to the questions or response options. Since study completion, patient representatives provided suggestions for feedback in leaflet form to study participants as well as suggestions of other ways of disseminating findings to the public. Their suggestions included providing a brief summary of the project as participants might have forgotten, using visual representations, signposting to other ways the information will be used and where participants could read about the study in greater detail, for example, giving links to journal articles.

SPIRAL

Patient representatives discussed the study in detail and provided their input into the intervention and study recruitment material, which led to refinements to all these aspects of the study. These discussions resulted in a change in the name of the study to SPIRAL and improving the formatting of the patient information sheet. They also discussed issues around non-participation in the study and made suggestions about how it could be made easier for patients to take part, including providing help with transport and holding the groups in local venues rather than hospitals. These suggestions will be used to guide the

design of future research protocols. Since study completion, patient representatives provided suggestions for feedback in leaflet form to study participants.

ARENA

Patient representatives were asked to feedback on the development of this study. They provided input into the development of the exercise class in terms of patients' requirements during the class and opinions of the exercises proposed. For example, they highlighted the importance of providing assistance with travel arrangements for those with transport difficulties, the inclusion of refreshment breaks and music during the class, and the additional of an exercise aimed to improve patients' ability to get in and out of bed. They also emphasised the importance of study participants having details of person whom they could contact between classes. In response to this, a contact name and telephone number was available to all participants throughout the study. In addition, they provided the research team with reassurance that the introduction of an exercise class after knee replacement was a positive approach and they supported the concept of providing function-based exercises within a group setting. Following completion of the ARENA study, the patient representatives have supported further proposals to pursue a larger trial comparing the exercise class with usual care. They felt that providing further individualised treatment within the exercise class would be beneficial to patients. This has been included the design of a grant proposal to explore the exercise class in a future study.

PROOF-THR

Patient representatives discussed the protocol and study materials, leading to refinements in these. As a direct result of these discussions, the design of the main study compared with the pilot was changed by adding in a follow-up visit to check progress by the same occupational therapist (OT) who had visited them before surgery if the patient requested one. In addition, as a compromise for the patient input regarding follow-up, the OTs were given a pre-paid mobile phone each and the patients were given the number to call for verbal advice. This was actually used quite a lot and proved very popular with the patients. It was also suggested that the visiting OT give advice on benefits, but this is not standard OT practice as it is a complex area that requires specialist advice. Instead, helpful phone numbers were given to participants if requested.

Systematic reviews

The importance and value of systematic reviews has been discussed with the patient representatives. This has been particularly helpful in developing new projects with extensive discussions on how to follow-up results of reviews relating to comorbidities and rehabilitation.

Patient experience study

Patient representatives discussed this study in detail, leading to the addition of questions in the interview topic guide such as questions around when and why problems first developed with the joint. Other suggestions taken on board include adding an e-mail address to the back of the patient information booklet to enable potential participants to contact the research team via e-mail and the positive implications of including the Hip Disability and Osteoarthritis Outcome Score (HOOS) or KOOS questionnaires in the 12-month follow-up interview in addition to the pre-operation interview. Since study completion, the patient representatives have provided suggestions for feedback in leaflet form to study participants.

In addition, in January 2013 we held a dissemination event with members of PEP-R. Arranged as a 'science café', the event provided opportunity for discussion about all work carried out on the RESTORE programme.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Patient and public representation on steering groups

The overarching study group includes representation from a patient with experience of bilateral hip replacement. She has attended programme and work package meetings providing input into the development of questionnaires, suggestions for improvements to the studies and ensuring that the programme is relevant to patients (see *Patient involvement in Patient Experience Partnership in Research: a personal view*). In addition, the steering groups in the individual work packages APEX and the Patient Experience Study included patient and public representatives. Their role differed from those on the patient forum. Oversight groups monitored progress and conduct of the work package. These patient and public representatives discussed the study design, delivery and identifying avenues for dissemination and to ensure that study findings will be presented to a range of stakeholders. They were supported by the PPI co-ordinator.

Evaluation of patient and public involvement

We assessed patient involvement in the programme by collecting regular, systematic feedback from patient partners and researchers. This helped us refine our involvement processes as the programme progresses, as well as to provide advice on PPI activity to others within NHS and University sectors.

Eight patients, who were members of PEP-R at the time of the evaluation (November 2011), and 14 researchers completed a questionnaire examining the impact of the activity on themselves and the research. Group members described their interest and learning about the topics and research in general. They particularly valued feedback about how PEP-R's input had shaped studies. Researchers identified the benefits of obtaining patients' views on the importance, relevance and feasibility of their projects. They welcomed the opportunity to speak to an interested and knowledgeable group and stressed the importance of early involvement. A selection of comments are shown in *Table 9*.

TABLE 9 Example comments on PEP-R by group members and researchers

Group member	Comments
Group member E	*We have been asked and listened to about our opinions, which has led to improved layout of information leaflets and questionnaires. Also the content and language used in leaflets and questionnaires*
Group member A	*Where funding has been granted, I am sure that PEP-R has contributed – our combined experience as patients has made a big contribution to the process. We know the research team listen carefully to our input*
Group member C	*Feedback from researchers also indicates that modifications to documentation, etc. have also been made*
Researcher V	*As a researcher you can have many ideas for research projects, but without consultation with patients, it can be difficult to know whether these issues are actually of importance to patients. I wanted to engage with PEP-R as it provided an opportunity to ensure that the research was of interest and relevance to patients*
Researcher U	*The ethics committee asked me about patient involvement . . . I picked up a feeling that my contact with the group more than satisfied this requirement. I also found many of the suggestions that were made by the group helped me to improve my study design*

Dissemination of research findings

Working with Arthritis Care and patient representatives, we have developed a dissemination strategy that addresses the needs of policy-makers, health professionals and service users. We envisage that this will be achieved by dissemination in reports, end of project feedback leaflets for research participants, peer-reviewed articles, conference presentations, lay summaries of findings in magazines and websites. Engagement with PEP-R will continue, particularly focusing on identification of dissemination strategies and working in partnership with researchers to develop plain English summaries of research.

Patient involvement in Patient Experience Partnership in Research: a personal view

Victoria Wells has been a patient-partner in RESTORE throughout its duration. She previously underwent joint replacement. This section outlines her experience of patient involvement in the programme and her views about the research.

I came from the operating table to sitting around the research table. I remember the first research meeting where everyone was introducing themselves and talking about RESTORE. Being part of that from a lay perspective gave the research extra grounding in experiences. It's been good having nurses, patients, physios and surgeons working alongside researchers as they all bring different views, painting the whole picture. It's very easy to have research that misses the patient and it's good to have the patient there.

In RESTORE I've had individual conversations with the study leads, and researchers were able to approach me so that I could answer their questions. There were no barriers there and the researchers seemed not to be worried about asking me questions. They were able to ask me questions and were sensitive to the patient journey that I had had. As result of personal experience I'm able to put in real life experience into the research or make suggestions to approach other patient partners. I could also break down academic text into more readable forms, for example for patient leaflets. I was able to bring in some influence from 'outside the box' and it was also like being able to turn a box inside out.

With APEX my input was in how the study would be described to patients at the sensitive stage before surgery when people needed to know about their pain relief. My thoughts were listened at that early stage. I really remember coming to my second research meeting as we talked about information in the APEX trial and about the information that would eventually be disclosed to patients in the trial. Blinding was important, and so was the information about the treatment that patients got.

With ADAPT the questionnaires needed a lot of input before they went to patients, and that was important. With ARENA there were quite a few informal conversations for my input, although SPIRAL and ARENA the studies were patient-centred anyway. In the patient experience study I had quite a few conversations looking at the patient experience in the long-term, beyond the ward, and making the most of your joint replacement. I've had interesting conversations around the systematic review work, and there were informal discussions and I do feel like that work has taken my views onboard. With the health economics my engagement has also been informal and the cost-effectiveness side of the work is hugely important. With the informality it's less like being interviewed and it's more of a discussion and the team members are more relaxed and feel able to ask me questions, which is what you'd get in qualitative research because it would be a conversation and no pressure for a particular outcome because you can just explore the study and think about things in different ways. With the health economics and systematic reviews it's been explained in ways that I can understand and made me think in a different way, and this is kind of hidden and useful.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Having contact with researchers hasn't always been about having a specific outcome in mind, it's about exploring a study that enables involvement, so that the thought processes are clear. Patient and public involvement doesn't always need to be prescriptive, but this can only happen if you've built up a relationship over time and the involvement I have had I have built this up with the RESTORE team.

As a result of early involvement in RESTORE and my understanding of patient and public involvement I was able to advise on the creation of PEP-R (the Unit's patient forum), which gave richer information from a collective of patients rather than an individual. I feel like it's creating a minibus of people and we are passengers because no two experiences are the same. I've been involved in PEP-R but have also been able to hand over that baton to others, I was on the planning and steering group and was able to hand that over and that felt good.

Victoria Wells, University of Bristol, 2014, personal communication, reproduced with permission

Chapter 4 Understanding patient's experiences of total hip and knee replacement: a qualitative study

Parts of this chapter have been reproduced with permission from Johnson EC, Horwood J, Gooberman-Hill R. Patients' journeys through total joint replacement: patterns of medication use. *Musculoskeletal Care* 2014;**12**:92–102[229] © 2013 John Wiley & Sons, Ltd; and reproduced with permission from Johnson and colleagues.[230]

Abstract

Background

We aimed to characterise and explore the patient pathway through total hip or knee replacement surgery in current routine NHS care.

Methods

In a qualitative study, 34 patients receiving joint replacement were interviewed before surgery, 2–4 weeks, 6 and 12 months after surgery. Interviews elicited patients' experiences of preparing for, undergoing and recovering from surgery. Analyses used a thematic approach or interpretive phenomenological analysis.

Results

Patients noted that delays to joint replacement in the NHS are common, which has implications for well-being. Patients' experiences of time differ from the linear conceptualisation of time required to plan NHS services.

Undergoing surgery can increase feelings of vulnerability and alter a patient's trust in their own body, the influence of interactions with others on confidence levels, and fears concerning the potential for causing harm to their new prosthesis. Patients rely extensively on, and value, both informal and formal support networks over the perioperative period. Transformation from a person living with osteoarthritis to a person recovering from a surgical intervention can lead to alterations in the assistance people receive from others.

When patients are not offered the support of health and social professionals, patients may feel distress and abandonment. Patient expectations for joint replacement surgery are complex and can be driven by previous personal experience, experiences of others and information provided by the hospital.

Conclusions

Our findings suggest important ways in which the provision and delivery of care and education for people undergoing joint replacement in routine NHS care can be refined and improved.

Background

Qualitative work has provided insight into the experience and impact of living with osteoarthritis including treatment options and surgery.[5,24–27] In relation to surgery, studies have explored pathways to surgery;[4,29] decision-making about joint replacement;[231] and patient satisfaction and outcome.[28,30] However, little research has explored how patients experience their journeys through joint replacement from pre-operative care to postoperative recovery. Our qualitative research addresses this gap in evidence by focusing on experiences of pre-operative circumstances and preparation, views about the hospital stay and the operation, as well as exploring longer-term recovery, rehabilitation and outcome in the year after surgery.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

The research aimed to provide robust patient-centred evidence that could inform future design and delivery of health care for people undergoing joint replacement. We used an inductive approach to the work and the areas of literature that we draw on are those that became most relevant as data collection and analysis progressed. These were related to the wait for surgery, the experience of delay, confidence and expectations as well as the experience of time in the lead up to surgery.

Understanding the patient experience: total hip replacement

Waiting for hip replacement surgery

Within the NHS, waiting times for medical interventions are a recognised element of current health care,[232] as patients passing through the system are provided with appointment dates for consultations and treatments by a system increasingly predicated on a discourse of patient choice.[233–235] A continual drive to reduce waiting times for intervention, to monitor and measure the passage of time, highlights the salience and relevance of a consideration of the temporal landscape within current health-care processes. The issue of waiting times is important given that a growing body of research highlights the detrimental impact that waiting for elective surgery can have. For example, patients awaiting hip surgery have previously reported experiencing significant increases in pain and physical disability,[236] high levels of psychological distress[237] and an overall deterioration in HRQoL.[238] Our exploration of patients' experience of time aimed to provide in-depth understanding of the impact and implications of waiting for surgery in current NHS care.

The role of confidence during the journey through hip replacement

Confidence, which is concerned with a person's judgement about their own, or others', abilities and vulnerability,[239] which can be defined as capable of being physically or emotionally wounded (www.merriam-webster.com/dictionary/vulnerable)[240] are both concepts evident in the literature concerning the experience of older age. For example falls, which are common in this population,[241,242] can result in reduced confidence and an enduring fear of falling. This can lead to people choosing to disengage from usual activities.[243] As osteoarthritis is associated with ageing, affecting 10% of people > 5 years of age in the UK,[1] confidence and vulnerability may have particular relevance to the experiences of patients undergoing joint replacement. A subtheme 'building confidence' arose in a recent study,[32] involving interviews with patients after they had undergone THR. This encompassed patients' experiences of feeling fearful of falling and damaging their new hip and also related to confidence and use of walking aids after surgery. This builds on earlier work by Grant and colleagues[244] which reported that with increasing confidence, patients who had undergone THR 4–6 months previously talked of slowly relinquishing their reliance on mobility aids. A metasynthesis of older adults' lived experiences of discharge from hospital after undergoing orthopaedic intervention reports that patients' confidence can be influenced by their perception of the expertise of staff and consistency of information received around the perioperative period.[245] This small body of work provides some initial understanding regarding the influence and relationship of elements of the orthopaedic surgical experience on patients' confidence level and vulnerability. Our exploration of patients' experiences aimed to build on and extend these insights by providing an in-depth understanding of the ways in which their confidence was affected by, and affected, their journey through hip replacement surgery.

The experience of support during the journey through knee replacement

Living with osteoarthritis and undergoing surgery brings about pain and functional limitations. We know from existing literature that at times of disability, informal care has a large part to play[246] and recent work highlights the importance of informal support for people living with osteoarthritis. This shows that assistance from family and friends with everyday activities (such as help around the home) is valued[140] and has positive implications for mental and physical health.[247,248] People with osteoarthritis also engage with more formal support, including contact with health professionals and social services.[249] However, patients may have little contact with health-care professionals after discharge from surgery, at which time family are particularly important in provision of support, including personal care.[32,250] The value of this support is well documented[32,244] but can cause mixed reactions including gratitude and frustration towards family and

concern about placing burden on others.[245,250,251] Importantly, previous research has not considered how patients' relationships with others may change as they move from living with pain and limitations associated with osteoarthritis, through to postoperative recovery and to functional independence. Therefore, we conducted research to explore how undergoing and recovering from knee replacement surgery affects patients' experiences and use of support networks.

An exploration of patients' hopes and expectations for hip and knee replacement surgery

A large body of quantitative work has investigated patients' expectations for recovery from elective orthopaedic surgery.[32,145,165,252–254] This evidence has highlighted the importance of considering the role and function of expectations around the perioperative period. For example, we have learned that patients' pre-operative expectations for joint replacement are both important in their decision to have surgery[252] and can help to predict outcomes.[253] We also know that realisation of patients' pre-operative expectations after hip and knee replacement surgery are significant in influencing their reported outcomes and satisfaction.[145,165,254] This body of work has not provided detailed understanding of expectations for recovery from joint replacement from the patient perspective. A recent qualitative study,[32] attempted to address this gap through an examination of the experiences of patients undergoing THR. The authors report that participants held high expectations of what having surgery 'would do for them' and suggest the value of patients having the opportunity to discuss their expectations of joint replacement in order to limit 'false optimism'. This work illustrates the importance of using qualitative methods in order to gain novel insights into expectations of joint replacement surgery. However, McHugh and Luker[32] report only on the expectations of hip replacement patients and interviews were undertaken 6–8 months after surgery, a time-point when participants' recovery may have still been incomplete. Therefore, we were interested in gaining an in-depth understanding of patients' expectations for recovery from both hip and knee replacement surgery, with a focus on the fulfilment of these expectations 12 months after surgery. We hoped to gain insight both into the processes by which patients' expectations were formed and the reasons why their expectations were, or were not, met.

Methods for qualitative studies

Sampling and recruitment

Patients who were listed to undergo either total hip or knee replacement surgery in the Avon Orthopaedic Centre (AOC) were eligible to take part in the qualitative study. Between February 2011 and August 2012, study invitation packs were posted to 179 patients (111 hips and 68 knees). Of those who returned a reply slip to the research team expressing their agreement to be contacted about the study ($n = 52$), we purposively identified a sample of men and women who were a range of ages. These comprised 29 patients undergoing hip replacement and 10 undergoing knee replacement. The programme's qualitative researcher contacted individuals in this sample to discuss the study in more detail and for any concerns to be addressed.

Of the 29 hip patients contacted, 24 agreed to meet with the researcher to take part in an initial interview. The remaining five were no longer eligible to take part (e.g. they had been recruited into an alternative study that precluded their inclusion, their operation date had been brought forward). All knee patients who were contacted agreed to meet with the researcher. These sample sizes ensured that data from the hip sample was at saturation point, such that no new themes were emerging from analysis by the end of data collection at the first data collection point.[255] The sample size for the knee cohort was determined as appropriate for the conduct of fine-grained interpretive phenomenological analysis.[256]

Data collection

In-depth semistructured interviews were conducted with all participants after they had been placed on the surgical list for joint replacement surgery. We also aimed to interview participants 2–4 weeks, 6 and 12 months post surgery. All participants provided their written, informed consent to take part immediately prior to the initial interview. As the study was longitudinal, the researcher also sought participants' verbal agreement to ongoing participation before each follow-up interview.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Initial interviews, which lasted between 65 and 135 minutes, took place at participants' preferred location: either in their own homes ($n = 29$) or on University premises ($n = 5$). Follow-up interviews, which lasted from 20 to 90 minutes, largely took place over the telephone, other than when a participant requested a face-to-face interview in their own home ($n = 6$) or on University premises ($n = 1$). In addition, participants whose surgery was delayed by > 3 months from their original admission date ($n = 3$) were asked if they were willing to take part in an additional interview focusing specifically on their experience of delay. Two participants (one hip patient and one knee patient) agreed to this additional contact.

Interviews were carried out with 21 of the 24 hip patients and 8 of the 10 knee patients at the three follow-up points. Five participants did not take part in postoperative interviews: three because they chose not to have surgery, one because their medical circumstances precluded a follow-up interview, and one because the date of the surgery moved beyond the time constraints of this study.

The data collection time points and numbers of participants for hip and knee patients are shown in *Tables 10* and *11*.

TABLE 10 Understanding the patient experience: data collection time points for hip patients

Time point number	Approximate time of interview in relation to surgery	Number of participants and interviews
Time point 1	When on the waiting list for surgery	24 participants
Time point 2	2–4 weeks after surgery	21 participants (one had no operation and was not followed up, one had a delayed surgery date and was not contactable, one was interviewed about their delayed operation)
Time point 3	6 months after surgery	21 participants
Time point 4	12 months after surgery	21 participants
Additional time point	When a patient had a delayed surgery date	One participant
Total number of interviews		88 interviews, with 24 participants

TABLE 11 Understanding the patient experience: data collection time points for knee patients

Time point number	Approximate time of interview in relation to surgery	Number of participants and interviews
Time point 1	When on the waiting list for surgery	10 participants
Time point 2	2–4 weeks after surgery	Eight participants (one did not have an operation and was not followed up, one had delayed operation)
Time point 3	6 months after surgery	Eight participants
Time point 4	12 months after surgery	Eight participants
Additional time point	When a patient had a delayed surgery date	One participant
Total number of interviews		35 interviews, with 10 participants

Interview procedure

Interview questions were framed by topic guides specific to each time point. They were informed by existing literature and developed through discussion with patient representatives. Core questions aimed to elicit participants' experiences of preparing for, undergoing and recovering from surgery and additional probes were used to facilitate elaboration and to achieve depth. Pre-surgery interviews addressed pain and functional limitations, expectations, existing knowledge about surgery and its outcomes, and preferences for pre-operative management. Post-surgery interviews addressed pain, function, views on the care that patients have received as well as their future plans and hopes for/of rehabilitation and recovery. At the 6- and 12-month interviews, participants were asked to talk about their experiences of long-term recovery and adaptation. These interviews also revisited topics that arose from earlier interviews, including ongoing and missing support needs. Interviews exploring delay to surgery addressed participants' views about delay and their experiences of support. Interviews were conducted by qualitative methodologists with social and behavioural science backgrounds and it was made clear to participants that the researchers were not clinical staff.

Interviews were audio-recorded, transcribed and anonymised, with the exception of two interviews which were recorded in note form owing to audio-recording equipment failure. Ethical approval was provided by NHS South West 1 REC (10/H0203/44).

Data analysis

Initially, we analysed data from all time points of patients undergoing hip replacement separately from the data from patients undergoing knee replacement. We used different analytic approaches with each data set. Once the analysis of the two data sets was completed, we brought the hip and knee data together and conducted analysis on the pre-operative and 12-month data together.

Hips: inductive thematic analysis

We used inductive thematic analysis for the data set of interviews with patients undergoing hip replacement. This was chosen as a means of exploring change over time as well as comparing and contrasting experiences in a relatively large data set which comprised 88 interviews by the time of completion. Analysis was iterative with data collection, with use of software to enable data organisation. Anonymised transcripts of audio-recordings and notes from interviews with patients undergoing hip replacement were imported into the qualitative data management software package ATLAS.ti® 6 (ATLAS.ti software; ATLAS.ti, Berlin, Germany). Initial analysis of transcripts began shortly after data collection started and was ongoing and iterative. Analysis informed further data collection such that early findings were used to refine the topic guides and identify questions to ask in future interviews. Transcripts from each participant were combined and treated as one single data set and were analysed using inductive thematic analysis.[257] A member of the research team first identified thematic codes which were grounded in the data. Next, through identifying connections between the codes, the research team clustered them into superordinate themes. To enhance analysis and enable team discussion and interpretation, double coding was conducted on a sample of four interview transcripts at each time point (total double coding on 16 interview transcripts). The double coding was conducted independently by members of the team who also had social and behavioural science backgrounds. The double-coding process was used as a means to stimulate close reading of the transcripts by the qualitative research team, who met regularly to discuss the codes and who worked to achieve a consensus about coding. Consensus, as agreement, was arrived at through discussion. To improve understanding of the whole data set, those aspects of data that appeared to contradict general experiences were identified and explored. The data from all patients, including those who did not have THR, were included in the analysis because their experiences of preparing for and waiting for surgery provide valuable insights.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Knees: interpretative phenomenological analysis

We used interpretative phenomenological analysis (IPA) to analyse data from knee replacement patients. This was chosen as a way to explore participants' personal lived experiences and how they make sense of them in detail and depth with an emphasis on the detail of cases in a group of participants likely to be undergoing similar experiences.[256,258] IPA is an idiographic approach, focusing on the particular rather than the universal and starts with the detailed examination of case studies, which then tentatively progresses to more general statements about groups of individuals.[259] Taking this approach we were able to describe patients' lived experiences and their process of preparing for, undergoing and recovering from surgery (i.e. how their experiences unfolded). The process of analysis was guided by a series of principles gleaned from the reflections of Smith and colleagues within research methods publications, e.g. Smith and Eatough[258] and Smith and Osborn.[260]

Hips and knees: inductive thematic analysis

After identifying salient themes relating to expectations in the hip replacement data and having conducted IPA with the knee replacement patient data, we were interested in also exploring these issues for knee patients. Therefore, we imported knee transcripts into ATLAS.ti and undertook thematic analysis on this data set, employing the procedures previously described to investigate these issues further. This enabled us to explore patients' hopes and expectations of surgery across the longitudinal qualitative data set as a whole.

Results

As described in *Methods for qualitative studies*, 24 hip replacement patients and 10 knee replacement patients took part in the longitudinal qualitative study. Of the hip patients, 13 were men and 11 were women, with ages ranging from 52 to 82 years (*Table 12*). Of the knee replacement patients, six were men and four were women, with ages ranging from 61 to 78 years (*Table 13*).

Waiting for hip replacement surgery

Within the hip data set we explored each participant's journey from his or her initial referral to secondary care through to his or her final surgery date. As shown in *Table 14*, accounts revealed that participants took one of five main routes from referral to surgery.

The experience of waiting for surgery after entering secondary care and impact of delay and cancellation emerged from our analysis as salient issues for participants. We present a summary of experiences from two angles: (1) the psychosocial impact of waiting and (2) the conceptualisation and experience of 'time' during this period.

The psychosocial impact of waiting to undergo hip replacement

Two overarching themes relating to the psychosocial impact of waiting for THR were identified: emotional reactions and impact, and wider impact on social support networks (*Box 1*). The impact of waiting was influenced by the time that patients had spent waiting for surgery and their journeys through health care before surgery. These aspects of waiting for hip replacement are described in turn.

Psychological impact

Whether or not they experienced delay, participants all described emotional reactions to the experience of waiting.

TABLE 12 Understanding the patient experience: participant demographics for hip patients

Pseudonym	Age (years)	Sex
Mr Bedford	73	Male
Mrs Burton	70	Female
Mr Day	74	Male
Mr Everett	66	Male
Mr Foreman	61	Male
Mr Golding	62	Male
Mr Grant[a]	82	Male
Mrs Hardcastle	71	Female
Mr Higgs	71	Male
Mr Horton	73	Male
Mrs Kade	73	Female
Mrs King	53	Female
Mrs Lovell	69	Female
Mr McKenzie	66	Male
Mrs Noble	74	Female
Mrs O'Brian	65	Female
Mrs Quinn	69	Female
Mr Rayner[b]	79	Male
Mr Smith	75	Male
Mr Thomas	58	Male
Mr Upton	52	Male
Mrs Vickers	80	Female
Mrs Warburton[c]	77	Female
Mrs Young	72	Female

a Did not have surgery – felt 'too old' to undergo major surgery.
b Medical circumstances precluded follow-up interviews.
c Did not have surgery – reasons unknown.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 13 Understanding the patient experience: participant demographics for knee patients

Pseudonym	Age (years)	Sex
Mr Armstrong	70	Male
Mr Cook	64	Male
Mr Ostafew[a]	78	Male
Mrs French	76	Female
Mr Ings	64	Male
Mr Jackson	68	Male
Mrs Parker[b]	67	Female
Mr Clark	65	Male
Mrs Evans	74	Female
Mrs Biggs	61	Female

a Did not have surgery – reasons unknown.
b Date of surgery moved beyond time of study.

TABLE 14 Understanding the patient experience: pathways to surgery

Pathway	Route from referral to surgery
Pathway A	No delay experienced ($n = 12$) in their secondary care pathway
Pathway B	Journey affected/delayed by hospital factors ($n = 4$). For example, earlier operations in the day over-running; unforeseen circumstances; administrator error and equipment failure
Pathway C	Journey affected/delayed by underlying health conditions ($n = 5$). These encompass both pre-existing conditions and those that were only diagnosed during pre-operative health screening. Appropriate pre- and perioperative management of a participant's health result in both short- and long-term postponement of their operation
Pathway D	Journey affected/delayed by others health ($n = 1$). A patient chooses to postpone their surgery because of caring responsibilities/duties
Pathway E	Mixed pathways ($n = 2$). Participants experience more than one influence on their pathway. For example, initial postponement of their operation because of health issues and further cancellation owing to hospital factors

BOX 1 Quotations to illustrate the psychosocial impact of waiting to undergo hip replacement

Psychological impact

Interviewer: *Yes, and can you recall how you felt on that morning, when you got that phone call saying, where are you?*

Mr Foreman: *To some extent I was taken a little bit in disbelief and quite devastated, to be perfectly honest. I've had operations before, but psychologically you build yourself up and think right, this is the day, it's going to happen today, fine. But getting that phone call at . . . And yes, psychologically it knocked me for six. Probably for a couple of days I was obviously not very happy at all.*

It's frustrating for me because I can't do anything.

Mr Rayner

Wider impact on social support networks

Because he definitely got it arranged for, he could come down when I was going in on the, this week, on the 25th. But it's rearranging his work shifts, its rearranging things, whether he could get the time off to come down the next time.

Mrs Vickers

Mr Foreman: *Yes, it was [a difficult time], not only for me, for the rest of my family as well, because they'd obviously geared everything up for everything to happen on that particular day.*

Interviewer: *What sort of alterations did they then have to make to their plans?*

Mr Foreman: *Transportation wise, my wife does some part time work, and she had to reorganise things so that we could make the trip on the Monday as well. It was probably more the fact that a phone call at that time, saying where are you, was a bit of a blow, to be perfectly honest.*

Consequences of preceding pathway on current experience

I feel I wasted nearly a year of my life. Uh, not happy about it but uh, a certain amount of responsibility was mine, I went in and said I got sciatica. Um, I, most patients diagnose themselves in the first place but nobody questioned it. Nobody said 'ah, hang on a minute it might be something else'. You know. Course it was not bad to start with, be fair it was not bad, but you know, it did not start full force, it's gradually got more and more painful as time's gone on.

Mr Horton

It's been long enough now so. . . . Well we said we are ruling out most of this year. This year's a non-entity.

Mr Smith

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Participants on pathways B, C and E who experienced postponement of their surgery date experienced a range of emotional reactions. Frustration and disappointment were frequently reported; however, some participants expressed understanding and acceptance of postponement. They tried to rationalise the news and described their gratitude when delay was a matter of weeks rather than months. The wait for surgery can also have more detrimental emotional consequences, for instance leading to a feeling of helplessness and utter desperation. Participants talked of feeling as if they were 'left to linger' in the secondary care system and forced to 'live in limbo'.

Participants on pathway A without any delay or changes to their surgery date also described some disappointment at the length of time that they had had to wait for their operation. They recalled their dissatisfaction that their operations were not scheduled as soon as they had hoped and the disruption to their lives caused by this. The impact of delay on physical well-being and functioning also had some psychological effects. Mr Rayner's experience provides a useful example. He experienced recurrent postponement of his operation owing to investigative but inconclusive tests for additional health problems. While waiting for THR he then experienced a rapid deterioration in his general health and functional well-being, and expressed 'frustration' at the situation.

Wider impact

Accounts illustrated how cancellation of operations could have wider impact, particularly affecting support networks. Participants explained how their friends and family also had to cope with and manage the participants' own deteriorating health as well as share in their disappointment about a delay to the surgery date. Participants described how family and friends put their lives on hold and had to cope with the detrimental impact of 'living in limbo'. Cancellation and delay also had a more practical impact as friends and family had to renegotiate their own plans to remain supportive during the perioperative period.

Consequences of preceding pathway on current experience

Participants' views of their wait for surgery and the detrimental impact of the waiting period were influenced by their experience of time already spent living with pain and discomfort. Many participants described complex and sometimes slow journeys through health care from initial onset of their problems through to eventual referral to secondary care.

Two key factors were central in accounts of patients' journeys through care. First, participants reported that they had initially delayed seeking advice and support from primary care practitioners. Reasons cited for this included a fear of the undesirable inevitable (i.e. surgery); other priorities (e.g. caring for a sick spouse); and choosing to 'put up' with pain and discomfort. Second, many participants reported the sense that referral from primary to secondary care had been delayed. Explanations provided for this delay included receiving an incorrect diagnosis; that their GP saw them as 'too young' to undergo THR; and that their GP strongly advocated alternative strategies (e.g. weight loss, use of pain relief). Participants' accounts highlighted the interaction between frustration with management in primary care and subsequent impatience with the time spent waiting in secondary care.

Conceptualisation of time

Two overarching themes relating to conceptualisation of time were identified: unavoidable changes to use and passage of time in the lead-up to surgery, and time in the context of health care.

Unavoidable changes to use and passage of time in the lead-up to surgery

The progression of time from onset of osteoarthritis towards THR was marked by the experience of pain and patients made unavoidable changes to their use of time (*Box 2*).

BOX 2 Unavoidable changes to use and passage of time in the lead up to surgery

The left hip, um the pain has been there for years, but not severe. I've felt it for years. Then when the right hip was done, yeah, it was definitely there then, that was in the end of 2004. Since then it's progressed slowly, and then in the last year it's got a lot worse.

Mrs Quinn

It's made me feel very isolated because of not being able to get out and go and see people and do things . . . it does restrict your life really to the sofa. The more, the longer it goes on before the operation the more I'm sitting on the sofa.

Mrs Burton

It was um, anywhere from you know January 2010 to October 2011 or something like that you know. Uh, uh, we were working on the wrong lines . . . I feel I wasted nearly a year of my life.

Mr Horton

Well I can't do anything for anybody really at the moment. Just stuck. I managed to get to my daughter's wedding in April and my friends funeral in May. But apart from that I just don't go anywhere. I just can't do it. . . . I like going on coach trips and things but I haven't been able to do anything you know.

Mrs Kade

Well I'm constantly aware, constantly aware of it. Well um, when you say totally, I suppose it's, it governs your life, let's put it like that.

Mr Bedford

The other night it was bad and I had to get up and move about, just to try and relieve it. I take paracetamol and sort of get back into bed and read . . . in the night-time everything is worse because it's so quiet and dark and there's nobody awake . . . it's a long night. I get up and turn the television on . . . but I've been forcing myself not to do that, because then I'll go and make a cup of coffee and then it sort of rolls in . . . I was waking up at three o'clock and not having any sleep until I went to bed the next night.

Mrs Young

Participants' accounts highlighted how they had been living with pain for long periods of time and many had experienced deterioration and acceleration of their problems in the lead-up to surgery. As well as describing the long periods for which they had lived with pain, participants also described the experience of pain in terms of time. They described fleeting spasms (a 'horrible twang') that lasted seconds as well as constant, unrelenting pain or 'throbbing ache'. Living a life in continuous pain with no respite appeared to provide the sense that time was drawn out during the lead-up to, and wait for, surgery.

Participants described making unavoidable and considerable changes to the way in which they spent their time because of pain and functional difficulties. When waiting for their operation, participants described withdrawal from their everyday activities and no longer actively engaging with life. For example, participants talked of inability to walk or stand for long because doing so resulted in 'unbearable pain'. Many talked of giving up pastimes that had previously provided much pleasure, such as golf and gardening. Most of those who had been working had stopped doing so. Participants found themselves progressively unable to fill and enjoy their time as they once had done and, instead, described how they often found themselves 'sitting down and doing nothing' in their homes rather than actively engaging with life and 'doing'. They talked about feelings of 'lost time' and a sense that time had slowed. The sense was in part due to the long process before diagnosis and then referral to secondary care. For some, such as Mr Horton, this was seen as a failure to diagnose the problem and working 'along the wrong lines'.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

In addition, the accounts of some participants indicated that day and night became conflated in the lead-up to surgery. While they would have previously been awake in the daytime, some reported resting and sleeping during the day to seek relief from the exhaustion of living in pain and due to side effects of pain medication. Participants also described pain onset or increasing intensity at night, which regularly woke them up or kept them awake. Unable to sleep well at night and sleeping during the day, participants experienced time slowing down as they waited for surgery and expressed distress, isolation and upset.

Time in the context of health care

Participants reported that their journeys through health care to arrive at surgery were lengthy, partly because they did not necessarily seek help for joint problems, but also because of slow processes of referral from primary to secondary care (*Box 3*). Such delays earlier in their journey through health care could influence the experience and impact of the wait for surgery once within the secondary care system.

BOX 3 Time in the context of health care

I think the doctors [GPs] could have assessed the problem quicker no doubt . . . initially the first doctor I saw didn't think I needed a hip operation. Four months after another doctor decided that maybe I should get checked out in [Hospital name] . . . That was a long wait. It would have been nice to have gone in maybe March or so and get an assessment and said this needs doing then. I'd have had it done by now . . . It's been long enough now so . . . we're ruling out most of this year. This year's a non-entity.

Mr Smith

Anyway, psychologically preparing, yes it's really thinking about um the actual day of going in, I guess. And there's a lot of things to do in preparation for going in, reorganising things that you normally do every day, and that sort of thing . . . warning people that you cannot do this and you cannot do that, and yeah there's a lot of that, takes up quite a lot of time.

Mrs Quinn

They give me exercises to do at home and I've been doing them religiously. Well they told us to do it twice a day. So I've been doing it twice a day . . . I would have been working today but I thought I'd take the day off. Give me a chance to get the shopping done, get myself packed, get myself in the right frame of mind to go.

Mr Golding

I wish it had happened a bit quicker but I suppose everybody wishes that. There seems to have been an awful long time from when he [anaesthetist] said to me it should be about six to eight weeks. It's been a lot longer than that.

Mrs Noble

Mr Golding: *Well this actually you see, what happened was I was originally planned to go in this Saturday, then they said we want to call you forward to the Saturday before.*

Interviewer *Did they explain the reasons for that?*

Mr Golding: *No. No I think they had somebody who had dropped out. For some reason but I do not know. Um so yes I said ok but I had this funny feeling it would not happen. Um, I said to my wife I do not think it will happen . . . And I was right but um, yeah so they have had what they call a desktop conference i.e. I suppose across computers with the Consultant anaesthetist and they must decide on a plan and they'll follow that plan through on Saturday.*

Once in the secondary care system and before admission to hospital for surgery, participants' time was also increasingly filled with activities relating to surgery. These included trips to hospital for pre-operative education, assessments and consultations, and tasks relating to psychological and physical preparation. These activities focused participants' attention on, and heightened their awareness of, the upcoming date in their calendar and also meant that they had to arrange their other commitments and activities.

Participants also described how time in the lead-up to surgery did not always pass at a regular, steady pace. They felt that the date of their planned admission to hospital could appear closer or further away. Some participants felt that the date was approaching too quickly and this evoked anxiety and nervousness. Others were eager and impatient to have surgery and expectations about how long their wait would be were influenced by discussions with health-care professionals in secondary care. However, some were also unsure about how long they would have to wait and thought that the timing of their operation was not static, but would be changed. Participants described uncertainty and, in relation to their experience of time, how they had to put their lives on hold when waiting for surgery.

Participants also experienced changes to their admission date and this could be due to hospital factors, ill health or the option of a date change by choosing to change surgeon. However, the impact of these factors was sometimes complicated; for instance, one participant accepted the offer to change her surgeon because it would mean that she did not have as long to wait for her operation. The new date for her operation was then postponed because her glycaemic control for type 2 diabetes was not deemed adequate for surgery. A referral 'back' to primary care aimed to ensure support to achieve better glycaemic control, which was then followed by a wait to re-enter the secondary care system and to learn her surgery date.

The role of confidence during the journey through hip replacement

Within the longitudinal hip data set, we also explored how participants experienced confidence and vulnerability during their journeys through joint replacement surgery. Six themes were identified: participants' changing trust in their bodies; feelings of vulnerability in relation to a surgical procedure; use and function of aids to be better safe than sorry; damage limitation and obeying the rules; awareness and fear of dislocation; and the influence of interactions with others on confidence.

Participants' changing trust in their bodies

Participants' accounts highlighted how their faith and trust in their body changed over the perioperative period (*Box 4*). During pre-operative interviews, participants described lack of confidence in their hip joints, describing their hips as 'worn', 'damaged' and no longer 'strong'. Many had experienced the sense of their leg giving way beneath them, which meant that they felt that their bodies were letting them down and, as a result, participants spoke of feeling fearful of falling, 'unsteady' and 'unsafe'; all of which impacted their daily lives. Before surgery, participants also spoke of feeling 'frightened' when using stairs without a rail and avoided certain movements to avoid putting too much pressure on their affected joint. Some participants also spoke of a sense of vulnerability in public areas, believing that they were unable to react quickly or effectively to situations (such as a physical attack).

After surgery, many participants described how they had quickly attained new or increased confidence in their body and prosthesis. They talked of feeling more physically capable and of how their leg no longer threatened to give way. Freedom from this, together with ability to engage in physical tasks that were previously difficult, enhanced trust and confidence in their bodies' capabilities. Some participants spoke of their absolute confidence in their new hip joint and a belief that it would outlast them. However, at 12 months after their surgery, some participants said that they remained troubled by lack of confidence and faith in their body and the prosthesis. These participants described becoming more nervous of slipping over and falling since having surgery. They also spoke of a sense that the leg for which the hip joint was replaced felt weaker after surgery and uncertainty about the ability of their bodies. This had detrimental impact on their QoL.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

BOX 4 Participants' changing trust in their bodies

Pre-operative experience: lacking confidence

I can still walk about which I'm glad that I can walk but as for sort of relying on it to uh, for movement, no I haven't got a lot of confidence in it.

Mr Day (time point 1)

It gives me um, the stabbing pain and feels like it's going to collapse.

Mr Smith (time point 1)

You know, you can't go down and step into the garden and just dead head a few plants you know. Um. Try to use the walking sticks. Um I'm scared of using them because I don't feel safe. I know I've got to practice with them but I'm scared of falling. I know with my luck if I fell it would be the other hip that went you know and then where would I be. So I sort of try and do what I can but think to myself no that's really not safe. Don't do that.

Mrs Kade (time point 1)

. . . and I think also just you know, you don't feel so confident about doing things. You go out now and with all the crap you got going on out there, you know, you never know out there. I never worried about that, um, 2 years ago there was a big fight outside the house and I went out and broke it up and stopped half a dozen lads trying to kill a couple of others you know. Uh, went to court, did all my bit, you know, I wouldn't do that now. I would feel vulnerable if I did that now, I would get hurt. Uh, because I don't feel physically capable enough . . . I'm not able to move, I can't run. Um, I certainly can't change direction.

Mr Thomas (time point 1)

Postoperative experience: increased or changed confidence

I think things have worked out excellently. I believe – I feel um more confident in what I can do physically. Er, you know, doing jobs around and about. I feel er, in activity terms, I feel fitter, and I feel more capable of doing things er than I did before. So to me, you know, personally I think it's exceeded what I probably expected.

Mr Thomas (time point 3)

Yeah I'm very confident. When you're on two sticks, then you go down to – down to one stick, then you can have the confidence to – to walk without a stick initially. But then once you get that initial confidence over and say, 'Oh I can do it with – do it without', and then it just grows and grows and grows and it just happens, you just think of – of another hip, without the pain.

Mr McKenzie (time point 4)

Well I haven't . . . I haven't got the confidence in my leg I've had done. It's because like seeing an X-ray to what they've done, I just fear that I don't wanna damage it. D'you know what I mean . . . But I just haven't got that confidence after this 12 months, I always fear that I don't wanna fall down . . . I think it does take a bit of the quality of life away because you . . . for the moment you're not . . . you'd like to do a lot more, and yet I haven't got the confidence really with it. D'you know what I mean? Thinking about it, then will I be doing myself harm.

Mr Higgs (time point 4)

BOX 4 Participants' changing trust in their bodies (*continued*)

Um I'm um trying obviously to get myself sort of mentally and physically, you know, back to um how I was. Um but I'm um sort of struggling with the mental side of things at the moment . . . I do not know perhaps what my capabilities are now. Um so every now and again I sort of like push myself to um doing something, and I think, yes, I can do that, um and would have to go on to the next stage. Um I suppose where you have been physically impaired um in some respects, that you're not quite sure what you can achieve now. Um so I'm having to do it in sort of small stages. And to say to myself, right, yes, you can do that, carry on to the – to the next thing.

Mr Foreman (time point 3)

Feelings of vulnerability in relation to a surgical procedure

Participants also articulated feelings of vulnerability in relation to the operation itself (*Box 5*). These feelings included concern about the body's ability to withstand surgery and apprehension about the potential for surgery to go wrong (e.g. in relation to potential detrimental side effects of anaesthetic). Participants described concern about leaving hospital to return home, seeing hospital as a safe environment. Feelings

BOX 5 Feelings of vulnerability in relation to a surgical procedure

Pre-operative concerns

I shouldn't say this, but it worried me, I got myself in a – because they say that, you know, you've got to be in pretty good nick for operations, and it did worry me a bit, you know, whether my body'll stick up to it.

Mr Higgs (time point 1)

Mr Smith (time point 1): *Getting a bit scared now day by day. Yeah a little more scared.*

Interviewer: *What is it specifically that you feel a bit scared of or apprehensive about?*

Mr Smith (time point 1): *Having the operation . . . Just thinking what if it's going to go wrong.*

Um, but as to the operation yeah I am nervous. I hate hospitals anyway and I seem to be in and out in the last few years with various things being done so, you know, but previously there's always been somebody in the house to look after me when I get home and there isn't going to be anybody now. So I am a bit worried about that.

Mrs Burton (time point 1)

Postoperative concerns

I did, I felt quite sort of vulnerable and I didn't want to be out of this sort of safe environment at that point . . . . I didn't want anyone to think I was malingering and didn't want to get on because that wasn't true but there's, it's quite daunting when you leave that safe place.

Mrs Lovell (time point 2)

I always wonder if the joint will come out again. Because they do fail occasionally. There's also been a bit of a scandal about um, wrong materials being used.

Mr Horton (time point 4)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

of vulnerability were heighted for those participants who were concerned about returning home if they felt that there would be no one there to look after or support them. Some participants were also concerned about the potential for the failure of the prosthesis and the presence in their bodies of the materials from which the prosthesis was made.

Use and function of aids: better safe than sorry

Participants spoke about their use of, and the benefits of, walking aids over the perioperative period (*Box 6*). Before surgery, many used walking aids on a regular basis. They were used to maintain and boost confidence, offer reassurance, prevent falls and offer support in situations that evoked vulnerability. Use of aids peaked in the early weeks after surgery. At the 2- to 4-week postoperative interview, many participants continued to use walking aids, saying that this reduced the risk of harm to their new joint; this was in spite of feeling that they should be able to manage now without this 'safety net'.

At the time of the 6-month interview, most participants were no longer using walking aids; however, this was not universal. Some spoke of occasional use, for instance, when extra security was needed but others continued to use a walking stick regularly when outside, saying that aids were 'just like a comfort blanket' that provided reassurance.

BOX 6 Use and function of aids: better safe than sorry

Use and function of aids before surgery

. . . but sometimes when I've been out walking; it feels as though the joint is going to give way . . . And of course you get excruciating pain when that happens and I suppose the stick has just helped as a little bit of a confidence booster, the fact that you've got something else that you're not going to fall over with.

Mr Foreman (time point 1)

Use and function of aids after surgery

I can almost walk without a stick now but er, just to be on the safe side, I stay on it.

Mr Bedford (time point 2)

I have not used one [a stick] for months and months. Except when I'm on a rough walk, then I do because if you're trudging through mud, the last walk I went on it was very, very muddy. Yes, I use one of those special walking sticks.

Mrs Quinn (time point 4)

Damage limitation and obeying the rules

After surgery, participants avoided and restricted movements and activities that could cause potential damage to their new joint (*Box 7*). They spoke of not wanting to 'push their luck' or to 'push the joint to the limit, you know, before it's settled'. They were nervous and described a need to remain respectful of their prosthesis and of the need to follow the postoperative restrictions and 'rule book'. They talked of their 'fear' of 'overdoing it' and were careful and aware of their movements (e.g. standing for too long, twisting). Accounts suggested that these concerns and behaviours were driven both by a fear of harming their new joint and of not wanting to 'undo any good that's been done'. Some participants explained that after the initial postoperative weeks had passed they became more adventurous in the activities and movements that they engaged in. However, others remained apprehensive of particular activities (e.g. lifting, higher impact sports, dancing and gardening) and were careful when performing certain movements (e.g. bending to put tights on). This was related to a concern of not wanting to damage their new joint by placing strain on it.

BOX 7 Damage limitation and obeying the rules

Postoperative concerns

I was dead scared to disobey any of the rules, I followed them religiously.

Mr Horton (time point 3)

I'm taking it really strictly and I follow the rules, I do not bend at the moment and I don't lift anything, well nothing that might be heavy. Um so following all their rules, um move carefully, so at the moment I can't say that anything is causing me any pain . . . I'm not allowed to bend or lift anything for 6 weeks. So I will go for 6 weeks before I try doing anything like bending or sort of going back to normal. Like sleeping, I don't normally sleep on my back, but um I've been told that I have to stay on my back for 6 weeks, so I've been doing that . . . But I will follow exactly what they say until the 6 weeks are up.

Mr Golding (time point 2)

I don't really want to get down on my hands and knees yet. I feel a little bit tremulous. But um that's just me . . . I suppose once you've got something inside you that's artificial and could go possibly wrong, it sort of er stops you. I don't want to get down on hands and knees.

Mrs Hardcastle (time point 3)

I am always aware of it [new hip] because, as I say, I am, I um limit what I do because I don't want, I won't push myself. You know, I won't [deep breath] run, jump and bend and I worry that I might do something to my hip. So I am aware all the time really.

Mrs King (time point 4)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Awareness and fear of dislocation

Before surgery, participants were mindful of the need to 'look after' their new joint to avoid dislocation. Concerns about dislocation peaked in the weeks after surgery (*Box 8*). At this time participants experienced occasions when they felt that their hip was about to dislocate and spoke of their apprehension. Awareness of the potential for dislocation was informed by the verbal information and written literature provided by the hospital. This was heightened by knowledge of other people's experiences and previous personal experience. For some participants, concerns about potential dislocation became an enduring fear, continuing to influence their behaviour and activities in the long term.

The influence of interactions with others on confidence

Although interactions with others and knowledge about dislocation could reduce confidence, participants also described how their confidence could be increased through encounters (*Box 9*). For instance, some described how conversations with surgeons before surgery boosted their confidence in care and treatment that they would receive. Some spoke of the importance of education and information in order to feel informed about the operation and recovery. Health professionals also continued to bolster participants' confidence in the weeks and months after surgery. In addition, observing the experiences of others who had had positive experiences of joint replacement enhanced confidence.

BOX 8 Awareness and fear of dislocation

Concerns before surgery

This is the only thing I'm having trouble with getting used to, is that I know, once I've had it done, I mustn't do that . . . Once they've done it, um I don't want to – I'll make damn sure I don't dislocate it.

Mr Upton (time point 1)

Concerns after surgery

I think it was a couple of days after I came home, I was standing up and I was getting ready for bed, and I felt the head of the femur move. And I thought, 'Oh my God, it's going to dislocate.' But it didn't, it couldn't have been in properly . . . I was a bit frightened.

Mrs O'Brian (time point 2)

I think what done me was I was talking to a gentleman who – who said um this friend he worked with had a new hip, and um he went back to work after three months, and like a silly fool, he lifted something heavy, and his joint come out. And it kind of done something to me, 'cos I don't want mine to do that.

Mr Higgs (time point 3)

Interviewer: *And what sort of things have you been doing, or what have you done to get to that?*

Mr Upton (time point 3): *Well I think, if anything, it's probably a question of what I haven't been doing, I think, rather than what I have been doing. Um I haven't been doing the sort of um – the wrong movements, um sort of crossing my legs and sort of twisting myself and doing whatever. Um by sticking to the rules, really the sort of not dislocating it bit, um that I came out with in my head, by sticking to that and not doing what I shouldn't do, I think it's helped it cure itself . . . I suppose, in a way, I was frightened to stop them, because I still felt that, you know, we were given this 12 weeks sort of time slot um about the fear of dislocation. But I think perhaps I was um so worried that I could still dislocate it, I made damn sure I wasn't going to. Um and so even this time when I went in again, I was sort of pre-programmed, I didn't have to be told what I had to do this time because I was still doing it with the other one.*

BOX 9 The influence of interactions with others on confidence

So actually going into the place, um again [name of Surgeon] said, 'I'm going to come round to see you before I – you get wheeled off', or whatever. And so, you know, I've got every confidence he's going to come round and check I'm ready for it, and if I tell him, 'I've got last minute thoughts and I don't want you chopping my leg off', um fine . . . well we had a joke when he first saw me, he said um, 'I'll try and make sure they're both the same length when you come out'. Um to me, the human side of things is – is great.

Mr Upton (time point 1)

Mr Higgs (time point 4): *Um [clears throat] well prior to the operation there was a booklet. And there was a meeting, and er it was um – it was informative and comprehensive, and um I think that sort of everything that was mentioned fell into place. So as far as the information, there was plenty of information.*

Interviewer: *OK and did that information influence your recovery, do you think?*

Mr Higgs (time point 4): *Yes it gave me a little bit more confidence. It's er – it's not knowing is which er chips away at the confidence, doesn't it?*

Um at first it felt a bit sort of um different. And er I sort of – I was afraid to sort of move my leg and, you know, you're anticipating er – the anticipation of having the surgery, and you think, 'Well what can I do? What am I able to do?' But the physiotherapist, she sort of put me at ease and she um just told me what I can do gently to start with, and she helped me like move me leg, showed me which way I've got to move me legs and things, and what I've got to do.

Mr Day (time point 2)

I know several people. I actually work at a golf centre and, of course, a lot of the senior people have had hips and knees done. And yeah, they tell me how good the operations are. I know several people, actually . . . Well, they did say that one person didn't feel any pain at all after he'd had . . . his knee, it was. They gave me a lot of confidence. Everybody I spoke to, they seemed to have had a good result . . . It does boost your confidence.

Mr Everett (time point 1)

Understanding the patient experience: total knee replacement

The experience of support during the journey through knee replacement

We were also interested in exploring how undergoing and recovering from knee replacement surgery alters patients' experiences and use of their support networks. Using IPA[259] we examined patients' experience of knee replacement at all time points and identified three superordinate themes relating to the experience of support: (1) relationships with health professionals over the knee replacement journey; (2) implications for informal relationships and support networks; and (3) providing support to others.

Relationships with health professionals over the knee replacement journey

'I've got faith in him': trust and confidence in the surgical team

Participants who were undergoing knee replacement expressed considerable 'trust' and 'faith' in surgical teams. This seemed to relate to their experience of living with osteoarthritis, in which participants dealt with increasing pain and impaired mobility. By the time that they had reached secondary care, many felt

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

that they had no choice but to rely on medical opinion and expertise, and that surgery was inevitable. This was rooted in previous positive encounters in consultations as well as experiences (their own and others) of successful outcomes after other types of surgery.

Contact with secondary care team

After having their operation, participants' contact with secondary care health professionals shifted from the surgical team to a team of nurses, physiotherapists and auxiliaries. Relationships with health professionals also changed; participants wanted to receive support and guidance rather than the total control that they had wanted from surgical teams. After returning home, all participants had some contact, although often infrequent, with secondary care professionals – predominantly consultants and sometimes physiotherapists. They were 'keen' to receive follow-up appointments and 'eager' to obtain clinical opinion about aspects of the recovery process, for instance when they should stop using walking aids or return to leisure activities. These interactions bolstered confidence and offered reassurance.

'You were sort of cut adrift': unmet support needs during the recovery process

Participants also spoke of unmet support needs during the recovery process. For example, many felt that input from physiotherapists was received too late in the recovery process and that earlier involvement would have helped to reduce feelings of abandonment, enhanced motivation to exercise and facilitated earlier recovery. Postoperative aftercare in the community was also described as lacking. After discharge from hospital one participant, a widow, was not offered the support of a district nurse. Instead she described struggling with her own care, such as changing her surgical stockings, and had to implement her own support by paying for help. This participant felt that more formal support would have provided reassurance and reduced her feelings of isolation.

Differing perceptions of expertise: primary versus secondary care health professionals

Although confidence in secondary care health professionals was consistently high, participants trust in and willingness to seek support from primary health-care professionals was more mixed. Perceptions of support on offer and that received from primary care during the postoperative period was influenced by experience of care received before surgery. For example, some participants expressed dissatisfaction with primary care before surgery, describing their sense that care and advice had been inconsistent. When patients felt that primary care had not been helpful before their surgery, they were less likely to seek support actively from primary care on return home from hospital (*Box 10*).

Implications for informal relationships and support networks

Changes in level and type of assistance

There were changes in level and type of assistance provided and received at different points in the journey through knee replacement. Before surgery, participants described the importance of help provided by family and friends for everyday activities (such as fetching groceries and household chores). Immediately after surgery, the need for this kind of support sharply increased, with support needed for many more daily tasks, such as carrying a drink. Undergoing surgery also led to changes in participants' roles in their relationships and family units. For example, one participant described how, when recovering from surgery, he was looked after by his children who were 'running errands and things' and felt that his wife treated him 'like a baby'. These changes sometimes evoked negative emotions, including despondency and helplessness. However, as recovery from surgery progressed, the need for support and associated sense of helplessness reduced.

'She's always there you know when I want her': the assumption that family will help

For participants who were married, help often came from spouses. Married participants ($n = 7$) who all lived with their spouses initially turned to their spouses for assistance during the journey through knee replacement. After surgery, in addition to spouses taking on increased responsibility for tasks relating to everyday living and functioning, they also assumed additional caring responsibilities, including help with personal care (e.g. helping to bathe). Some also played a role in medical aspects of the recovery process.

BOX 10 Quotations to illustrate relationships with health professionals over the knee replacement journey

'I've got faith in him': trust and confidence in the surgical team

He [has] done my brother's leg, both legs, about 6 years before me, and he's had – you know, brilliant. I asked for him. And he's been there for a long time as well, he's not a new chap.

Mr Jackson (time point 3)

Contact with secondary care team

They were caring . . . they'd be available any time um . . . the only trouble was then I wasn't allowed to walk at all for that intervening more or less a week like, 4 days, 5 days . . . if I wanted to go to the loo I had to call for a nurse to come with a wheelchair to take me there.

Mr Armstrong (time point 2)

'You were sort of cut adrift': unmet support needs during the recovery process

I rang them week before last . . . he [physiotherapist] said 'Of course we are very busy at the moment, but I will be in touch with you again, but there is a two to three week wait' . . . But I was quite annoyed . . . I felt like saying to him well don't bother. I mean they say I can drive within six to seven weeks . . . I wouldn't even of had any physio by then . . . I know everybody is very busy and you're only one of a number really aren't you, but this physio thing really that did annoy me, because they stress about you having physio and making sure you bend your knee and all this and then nobody comes . . . it don't make sense to me.

Mrs French (time point 2)

Differing perceptions of expertise: primary versus secondary care health professionals

I'm afraid my doctors are very poor at the moment . . . we've had the same doctor for about 40 years and he retired and at this practice we got now we get a different doctor every week, they seem to be coming and going. If you go to see anybody, they don't know nothing about you . . . I had an experience with them, one doctor give me these tablets for pain killers, something I'd never tried before and then when I went back a couple of . . . I don't know 3 or 4 weeks later I said 'Oh your colleague gave me these' and she said 'He shouldn't of never give you them' and chucked them in the waste bin. I thought blimey they can't even trust each other . . . So that's put me off a bit.

Mr Jackson (time point 2)

For example, Mr Armstrong's wife administered postoperative anticlotting injections and Mr Clark's wife, a retired nurse, removed his stiches. Although many participants appeared comfortable in accepting that their spouse was occupying this novel role, others felt 'awkward' and embarrassed at asking spouses to undertake duties that they felt should be provided by paid professionals.

Use of extended informal support networks

Participants looked outside their immediate household to other family members (e.g. children, grandchildren, siblings) and friends to meet their postoperative support needs when they could not be fulfilled by a spouse. For example, several participants were the only driver in a household and this meant that friends and family were asked to drive on their behalf while postoperative restrictions were still in place (patients are currently told not to drive for 6–8 weeks after knee replacement). Participants who did not live with spouses asked friends and family for help, particularly in the early postoperative period.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

'I'm lucky': willingness to accept help

Participants expressed mixed emotions about the help they received from their friends and family around the time of surgery. Several viewed such support as 'helpful' and 'invaluable' and felt fortunate to be 'spoilt' by friends and family who 'rallied' around them. Although surgery was often seen as a way of maintaining independence the time around surgery was a period when help and support from others was a necessity. Many participants craved their return to self-sufficiency and most participants did eventually regain the independence that they had sought (*Box 11*).

BOX 11 Quotations to illustrate implications for informal relationships and support networks

Changes in level and type of assistance

Well my wife has been working like a trooper you know [since discharged from hospital]. I mean, trouble is she won't let me do stuff. . . . going to the shop. Um, you know getting a magazine, treating me like a baby. Um, I mean just doing extra. . . . I mean I cannot drive a car so, you know, I used to do virtually all the driving. Now my wife is doing all the driving.

Mr Cook (time point 2)

'She's always there you know when I want her': the assumption that family will help

Interviewer: *And where did you have that done, having the staples out?*

Mr Clark (time point 3): *Er now um [laughs] um my wife, [name], is a nurse. And um well she retired about a year ago. And um we thought rather than, you know, um – she knew the people in um – in the hospital, and they gave her a thing for taking them out, um she's ever so good and ever so careful, rather than go into hospital. Um she took them out at home for me.*

Use of extended informal support networks

Interviewer: *What sort of things have they [friends and extended family members] been doing?*

Mr Jackson (time point 2): *Lifts everywhere, my wife can't drive . . . so to and from hospital for any appointments or to do the shopping, anything.*

'I'm lucky': willingness to accept help

Interviewer: *what sort of support have you had?*

Mr Ings (time point 4): *Well I've been lucky like that; the wife and the kids are pretty good, you know, I've had the support of them around me. I suppose if it was somebody living on their own it might be a bit different.*

Interviewer: *Yeah, what in particular are you thinking of?*

Mr Ings (time point 4): *Oh loneliness and getting to do things.*

Providing support to others

Although not a shared experience, a striking feature in the accounts of some participants was the impact that knee replacement had on the support they provided to others and how caring responsibilities influenced their journey through joint replacement (*Box 12*). For example, Mrs Biggs, a widow and sole provider of support for her mother and brother-in-law, was particularly articulate about the reliance of others on her and the impact of surgery on this. Owing to her caring responsibilities, and despite limitations and pain imposed on her by osteoarthritis, she strived to maintain her role and not let others down. Undergoing surgery meant that Mrs Biggs temporarily passed her normal caring responsibilities onto her sister. Keenness and determination to decrease 'burden on others' as soon as possible and to return to her original role supporting others served to drive and motivate Mrs Biggs in her recovery from the operation. Successful knee replacement also meant that some participants felt able to assume a new role offering support to others, which they felt would have been impossible before their surgery.

Combined hip and knee data sets

An exploration of patients' hopes and expectations for hip and knee replacement surgery

We were interested in learning more about participants' expectations for recovery from hip and knee replacement surgery and how their expectations were met. We present here the findings of our analysis from the pre-operative and 12-month data sets.

Hopes and expectations relating to long-term pain after joint replacement

All participants hoped that hip or knee replacement would reduce their pain (*Box 13*). For most, this was a key motivating factor for their decision to have the operation. Some participants described awareness that long-term pain was a potential issue after surgery. However, some thought this might be mild while many hoped to achieve complete freedom from pain in their operated joint in the year after surgery. Expectations relating to pain were based on previous personal experience of undergoing joint replacement surgery, knowledge of others' experiences – both successful and unsuccessful – and information resources provided by the hospital. Most participants also described a hope that they would be able to stop use of pain relief and anti-inflammatory medication in the year after surgery. However, some also thought that they would

BOX 12 Quotations to illustrate providing support to others

Interviewer: *are you where you thought you'd be six months ago in terms of recovery?*

Mrs Biggs (time point 4): *Um, yes I think I, because things moved so well after. Yeah, yeah. But I was determined any way that I wouldn't be a burden to anyone.*

Interviewer: *No and does that make a difference do you think?*

Mrs Biggs (time point 4): *Yes, oh yeah . . . Well for me mentally it does because of course uh, you know I feel I got a lot of responsibility here to keep the home running and I don't want uh, to feel any one else has to come in and um, you know take over from me . . . it certainly encouraged me to get going, yes, yes.*

Yesterday, we got a little local, uh, pamphlet or whatever you'd like to call it down [town name] it was looking for volunteers actually to help families that might be in, were going through different kinds of troubles . . . so I'm going to ring them. And I wouldn't have done that, well I would, you know – I'd, I'd, I couldn't really move efficiently, you know. . . . I wouldn't have done it 12 months ago. I wouldn't have been physically able to just go out and be confident enough to walk.

Mrs Evans (time point 4)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

BOX 13 Hopes and expectations relating to long-term pain after joint replacement

Having the hip replacement, the motivation is to get rid of the pain.

Mrs Quinn (time point 1)

Interviewer: *What about the pain, what are you hoping for?*

Mr Bedford (time point 1): *Zero actually. I nearly, because I said that's what happened with this. If it's the same before when I had that one done it's unbelievable.*

Mr Thomas (time point 1): *I was telling him [a friend] about having mine done. He said 'the one thing you'll do when you wake up, he said you won't have that friend with you', and that's why I call it a friend. Yeah, he said 'you won't have that annoying, nagging little thing that's you know, grinding away quietly there', he said. 'It just won't be there' and he said that's what he liked about it the most. He said 'that sort of' he said it was gone. He said it was completely not there. And [another friend] actually said the same as well. He said his pain just disappeared . . . He just said 'my pain had gone away'. He said it was absolutely gorgeous.*

Interviewer: *Is that what you're expecting or?*

Mr Thomas (time point 1): *That's what I would hope yes. You know, I won't have that grumbling irritation, yeah.*

Interviewer: *So how else do you think your life will be different 6 months after your operation?*

Mr Thomas (time point 1): *Well if I haven't got pain I won't be such a grumpy old git . . . because I'm sure I'm grumpy because I'm, I'm not, yeah I'm in pain. I'm not noticing it because you, yeah I'm saying I do affectively show it. But yeah I'm hope I'm not such a grumpy old sod. [Wife] will be able to tell you that probably better than me.*

I read it in one of the leaflets that they [the hospital] gave me . . . you may still be in some pain. That's one of the down, downsides of having a hip replacement, you may have one leg longer than the other, infection, still pain. It's one of those risks. But hopefully that won't be me.

Mrs King (time point 1)

Interviewer: *After you've had the operation, would you expect to reduce or change the pain relief you have?*

Mrs Parker (time point 1): *I expect to be reducing but I don't expect to do without, because I have quite a bad neck . . . obviously the Co-codamol helps that as well, so I don't expect to give up pain killers but I hope it will go down a bit.*

have to continue using medication to manage pain in other parts of their body. Participants also described their hopes for the positive benefits of reduced pain in the longer term after surgery, for instance improved mood and enhanced sleep quality.

Expectations relating to postoperative function

Before surgery participants described living with restrictions on movement and mobility, reliance on walking aids and inability to 'do a lot physically nowadays' (*Box 14*). They anticipated that joint replacement would confer better function and bring about a future in which they would be able to 'get around easier', walk further and with a 'normal stride', navigate stairs and steps with more confidence and ease, and achieve independence from walking aids. They also spoke of hoping to once again be able to kneel down, bend down and reach their toes and have the capability to return to riding a bike again.

As a result of these changed functional abilities, participants anticipated that they would, in the year following surgery, be able to become more active and enhance their general level of health and fitness. However, several participants also acknowledged that there would continue to be some restrictions on their physical capabilities. For example, they spoke of how they would have to continue to avoid lifting heavy objects even in the long term and would also be unable to return to playing high-impact sports. They also believed that although walks to the local shops would become a future reality, hill trekking and climbing mountains would not. In addition, expectations relating to postoperative function were tempered by a sense that they may not achieve the level of function that they had before the onset of the problems with their hip or knee joint. This was informed by the sense that they continued to age and that some lived with problems in other parts of their body.

Like their expectations for pain, hopes for postoperative function were informed and shaped by their own and others' experiences of undergoing similar medical interventions, in addition to information received around the time of surgery.

Expectations for changed engagement in social, work and life activities

Participants described expectations for participation in social and work activities after hip or knee replacement (*Box 15*). These expectations were related to anticipation of reduced pain and increased function and were particularly driven by observations of how well others had recovered from similar operations. For example, participants hoped to return to work and looked forward to attending social clubs again, meeting friends for lunch and other valued activities including golf, bowls, bell ringing and ballroom dancing. They also hoped to be able to take holidays once more, have day trips out and travel to see friends and family, both within the UK and abroad. Participants had to stop or limit these kinds of activities before surgery because of difficulties relating to their osteoarthritis.

Participants' accounts also showed how they hoped that joint replacement would provide them with the chance to engage with life once again: 'to be able to get out again', to 'go out and enjoy themselves', 'get on with their life' and to 'get back their quality of life'. For some, this also meant taking up new hobbies and interests such as joining a walking club and starting voluntary work. Many participants talked of their hope to be able to participate in these activities by certain points in time, for instance Christmas or their birthday. However, a few participants did not put time markers on when, and if, their goals would be achieved, talking of 'just having to wait and see' and 'just depending on how I get on'.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

BOX 14 Expectations relating to postoperative function

Interviewer: *And if we did speak in a year's time, how do you think that life will have changed?*

Mr Everett (time point 1): *Well, I just hope that I can walk normally. And it would be nice to think I'd be pain free. This is the hip. And what more can you ask for? Hopefully to be able to do more or less what you did before, other than lifting.*

Interviewer: *Are you hoping to be doing some things in six months time, twelve months time that you are not now?*

Mr Ings (time point 1): *Well yeah I hoping to get out on the garden, kneeling down doing planting seeds, or weeding. At the moment I got to do it all standing up . . . Sit in the bath and have a bath. Kneeling in the bath, that's a problem at the moment. I cannot kneel in the bath . . . I hope to be able to get up and down the stairs. At the moment I'm going up the stairs a stair at a time, not like the normal [banging on the table]. I go up one, rest up, one.*

Well I'm hoping I can just walk out the door, I will be grateful just for that. I do not have big inspirations of climbing Mount Everest.

Mrs Young (time point 1)

I know I won't be out Olympic sprinting but I accept that, I will hope that I will be um, far more capable than I am and that's what I'm looking forward to.

Mr Thomas (time point 1)

Well everybody that I've spoken to has been very satisfied and uh, they've gone on well. As I say they're walking again and walking with the group. So they can do what four or five miles I suppose, which is pretty good for anybody really. Um, and yes they've been very pleased . . . you think well if they can do it, I can do it as well.

Mrs Noble (time point 1)

Also a friend of mine, a lady up the road there, she's had both of hers done and she's walking now without sticks or anything.

Mr Bedford (time point 1)

Interviewer: *Would you anticipate that you would be using any walking aids in the future?*

Mr Upton (time point 1): *I would always, unfortunately, have to use walking aids. It would be nice to think that I didn't have to use them in the house. I always have to outside because I could have a fit at any time, and outside if you have a fit there tends to be things like concrete pavements and – and buses and things like that, that you might fall in front of.*

Um, the surgeon when I saw him he said that its um its, what he was saying there was we'll probably get your knee working like it did 10 years or 15 years ago. Don't expect to go any better than that. And um he did tend to, so well that's not too bad if I can get back to that.

Mr Armstrong (time point 1)

BOX 15 Expectations for changed engagement in social, work and life activities

Well when it started I thought that uh, it would be an advantage for me playing golf. Because as I say my mate who I play golf with for a long time, uh, he had both his knees done and he was getting bad. He had to pack up golf and he had his both done and he came back and he was playing all right. When I say playing all right he had no trouble with his knees. I thought this is fantastic you know.

Mr Ostafew (time point 1)

Interviewer: *What are your motivations for having the operation?*

Mr Higgs TP1: *Well to enjoy life I suppose like and, you know, not to sit back and think, 'Well I'm finished for now.' Because er the only time I'll be finished for is when I'm underground, gone. Yeah that's how I'm built inside. You know, I like get out and do something. And I might even do like little jobs again, because people – [I'm] in big demand.*

I'll go over and see my daughter and my, I've got three grandchildren over there [name of country] and then my life over there which I enjoy. I enjoy that over there . . . we'll see how it works out. But that's going too far ahead for me. I can only go so far at one time. I'm only gonna do one step at a time and see how I'll, go into hospital first get that over and done with. Get up out of hospital, get up and going.

Mr McKenzie (time point 1)

I can't get down to pick the ball up. My son's got to come with me and pick the balls up for me so I can throw them down like you know [when playing the bowls]. I know it might sound a silly little thing but its, it's an embarrassing sort of thing . . . it's you know another little thing that I hope, in about 6 months time, when the season starts next year, I shall be able to go up and pick the balls up no problem.

Mr Day (time point 1)

Mrs Quinn (time point 1): *I think um er you get – you do feel quite tired with the pain. And I think – I'm hoping that you get more energy so, you know, enthusiasm for things. I can't say it's completely gone or anything like that, but I think that you will – you will have more enthusiasm to do things. I haven't actually stopped doing things much, but I realise that um some – some social things have gone down. I mean I still do all the activities um basically but um maybe with less enthusiasm. And so that will come back, and so quality of life.*

Interviewer: *What's quality of life for you?*

Mrs Quinn (time point 1): *Well yes it's, it's feeling um enthusiasm for doing the things that you do. And being able to do things like babysitting grandchildren, like going visiting exhibitions like, you know, all the sort of things that would be nice to do, that maybe have been cut back.*

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Fulfilment of expectations relating to pain

Twelve months after surgery, 15 participants described complete relief from pain in their operated joint (*Box 16*). This group talked of being 'absolutely over the moon' with this outcome and of how they now 'felt a hundred times better'. The operation had surpassed their expectations and they revealed how it was a 'wonderful' relief to be free of long-term pain. They described how it was 'lovely' to 'move around without pain'; for example, how they were now able to bend down and walk without experiencing a 'terrible pain'. As a result, as hoped, those in this group who were not living with pain in other parts of their body had halted their use of pain relief. However, 12 participants said that although they were free from the pre-operative intensity of pain arising from the grating of 'bone on bone', they continued to experience discomfort, soreness, tenderness, a dull ache or twinges in the area of their operated joint. They attributed this pain to a variety of causes. For example, some said that the discomfort was caused by their muscles tightening, while others thought that their recovery from surgery was not yet complete. Participants with ongoing problems were also able to identify triggers that intensified these sensations,

BOX 16 Fulfilment of expectations relating to pain

No pain at all . . . no painkillers . . . I was on eight paracetamol a day I think it was, on the maximum and you couldn't sleep at night because you could be comfortable in bed, so everything just hard work and just more complicated where I've got nothing like that now.

Mrs Noble (time point 4)

I don't even think about it [the knee replacement] . . . I mean the only huge difference is, I'm not in any pain at all.

Mrs Evans (time point 4)

I'm very happy with it. I didn't realise how good it would be to be free of pain, you know, as I am now like, you know. But um, yeah, I've been very happy with it.

Mr Day (time point 4)

I don't normally think of it until it actually hurts . . . it's when I'm in bed normally. Um not right away but in the middle of the night sort of thing you know . . . I put it down to me muscles, tightening up and you know, you can't have things happen to your body and nothing you know, no come back on it.

Mrs Young (time point 4)

Mrs King (time point 4): *It's uncomfortable then when I move. I sort of have – I'm like a little old lady again getting up, you know, I have to sort of push down on my arms to [deep breath] you know, like struggle to get – get up. But, you know, but I'd still rather be like that than have the pain I had before, definitely . . . before I had it done, yeah, that was – that was like a constant grinding, you know, when I walked it felt like it was – it was horrible. But this is like – I'm sure it's muscles now.*

Interviewer: *Is this what you were expecting at this point to be sort of feeling?*

Mrs King (time point 4): *I wasn't expecting anything, to be honest . . . But I'm – I'm – I'm pleased if I'm not in that horrible pain. I can put up with the discomfort. Be nice not to wake up in the night like that but then, you know, suppose it'll go in time . . . it's more dull to what it was . . . like I say, it's not pain, it's not er, 'Oh my God, you know, I've gotta go and take some tablets'. . . . And it's not enough to warrant taking tablets.*

such as exercise, 'stretching themselves too much', moving from sitting to standing, or standing in the same position for too long. Although living with ongoing discomfort, most members still said that they were 'grateful' for the treatment that they had. In keeping with attitudes to pain relief medication before surgery, participants in this group did not see pain to be 'bad enough' to warrant taking pain relief medication; however, two knee replacement participants described continued experience of a more 'severe pain' and they expressed frustration and unhappiness with this outcome. Again, as they did during the pre-operative interview, participants reflected on how previous experiences of joint replacement – their own and others', in addition to information received around the time of surgery, played an important role in their expectations relating to pain after surgery.

Fulfilment of expectations relating to postoperative function

Participants spoke of how a reduction in the pain experience meant that at 12 months post operation they were able to move their body around with less difficulty and to walk further than they could before having joint replacement surgery (*Box 17*). They were also able to ride a bicycle, more confidently navigate steps and stairs and had experienced the anticipated independence from walking aids. However, this was not a universal outcome, with walking aids still used by some participants when they walked for any distance as they continued to offer reassurance, as they had done before surgery. Participants also talked of ways in which they continued to experience a lack of freedom and restrictions on the way in which they were able to move their body. For example, some highlighted how they were unable to run or experienced difficulties when bending down to the floor to, for example, pick up objects. Accounts also showed how participants continued to experience difficulties in walking up hills, how their walking pace had slowed and that they were unable to cope with longer walks, as they had hoped. Many of those who had undergone knee replacement surgery spoke of how they were now unable to kneel down. Nonetheless, these restrictions on movement, for most, did not seem to interfere with satisfaction with recovery and were perceived as 'no major hindrance'. A perception among participants that general ageing also played a significant role in limiting the overall potential for movement and mobility can perhaps help to explain this view.

Fulfilment of expectations relating to engagement in social, work and life activities: 'I've got my life back'

Participants talked of the ways in which their lives had positively changed since undergoing joint replacement surgery (*Box 18*). They described how they were now 'more active' and how life had become 'more enjoyable' as a result of having the operation. They spoke of having 'a new lease of life', of 'making up for lost time' and of how they were able to actively engage with more activities in each day now. As hoped, they had returned to many of the activities that they undertook prior to the onset of the difficulties with their hip or knee joint – a return to employment, social clubs, gardening, playing skittles, improved intimate relationships with partners and had already enjoyed holidays and trips to see family and friends. Planning for, and engaging in, these activities provided them with a psychological 'lift' and they talked of feeling 'more positive' and 'optimistic' about the future. However, for some participants, their pre-operative expectations to engage in particular social activities (e.g. taking holidays and games of golf) once they had recovered from their joint replacement surgery, were tempered, or had to be put on hold, because of other health conditions. In addition, a few participants who did not talk of additional health conditions also revealed that they continued to hold themselves back from undertaking the hobbies and activities that they had previously enjoyed and had hoped to return to (e.g. ballroom dancing). This was attributed to a lack of confidence in their new joint and concerns relating to falling.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

BOX 17 Fulfilment of expectations relating to postoperative function

Interviewer: *Are there any things you're doing now that you could not do before the operation?*

Mr Higgs (time point 4): *Um yeah I can – I can walk further . . . I've been up a ladder this week, and um there was no problem at all. Um so getting up and down stairs now, I can – I can do that naturally without sort of doing up one step at a time, if you know what I mean.*

I used to take big strides when I walk but you can't do that. Um but that's no bother . . . Well I do have trouble at walking up a slope since I've had my leg done . . . but it will improve.

Mrs Young (time point 4)

Interviewer: *And how are you finding the walking now?*

Mrs Kade (time point 4): *Slowly, I walk quite slowly to be honest but I don't know why I do, but I do but then my daughter said to me the other day 'but mum, you don't have to walk quickly, you've got all day to do it in, you don't have to rush to the shops, just walk at a nice even pace' . . . Looking at it logically she's right, and then, but the thing is, when you get older you still think you're 21 and you think your body should do what you did then and everything was at double speed wasn't it, and then logic kicks in and you think no, no, that's 50 years ago, just pace it a little bit . . . so I'm learning slowly.*

Mr Horton (time point 4): *So but um, walking any distance I'm better but I can't. I mean we've left the walking group. We can't. We tried it one day and we couldn't keep up by miles. So I said to [walking group leader] 'you'd better go on' I said 'we'll catch the bus home'.*

I am walking without sticks . . . I take the stick with me but very rarely do I need it and in actual fact I have found that walking with a stick makes my hip hurt so it is just an emergency thing really.

Mr Cook (time point 4)

Interviewer: *Are there other things that you're doing now that you couldn't do before the operation?*

Mr Clark (time point 4): *Um hmm not – I feel happier carrying things, weights and sort of moving, yeah, just normal sort of things which I was reluctant to do before. Um I do feel safer up steps and ladders, because I didn't realise how much you brace yourself through your legs, um I feel more confident with that . . . getting in and out of some cars and things, I find it easier, because I can bend my knee, you know.*

Interviewer: *Yeah and are there any things that you can't do now?*

Mr Clark (time point 4): *I don't kneel on it um at all. I haven't knelt on it.*

BOX 18 Fulfilment of expectations relating to engagement in social, work and life activities: 'I've got my life back'

I actually played nine holes um about a fortnight, three weeks ago, on a Sunday. We had a nice, sunny Sunday. Um, yeah, I got on with it all right. Um it's my back which is the biggest sort of problem there but um, no, I coped with sort of nine holes, you know, on quite a long course, um without any problems at all really.

Mr Clark (time point 4)

I've been on holiday twice and I'm going on holiday twice again next year and I didn't do anything like that for the last two year because I had too much pain to do it, and you know if we get a chance we go out for the day and so I really, I really have got a new lease of life completely.

Mrs Noble (time point 4)

Mrs Vickers (time point 4): *I do my hand bells and, you know, we go out, um do little concerts. And er I play bridge during the wintertime and odd times during the summertime, um that's Monday and Tuesday. Wednesday, if I don't play golf, I go up the golf club for lunch and then go out to the women's fellowship at church. So, you know, I'm out a lot.*

Interviewer: *Yeah and that's quite a change from this time last year, isn't it?*

Mrs Vickers (time point 4): *Yes um well I'm enjoying going out more, yes.*

My life's back, back to uh, normal. You know, huh, how can we put it. I suppose being an Englishman I'm always a bit sensitive about it. My sex life with my wife is now back to a much better position than it used to be. You know because sex became almost uh, impossible with my hip. But that is now, you know, back to a normal, sensible proportions. That has been a huge move forward.

Mr Thomas (time point 4)

Interviewer: *How is it going with the skittle playing, are you still doing that?*

Mr Day (time point 4): *Skittles, yeah, I played last night. [Laughs] Yeah, oh yeah, it's improved it a bit . . . you know, once I couldn't bend down and pick the balls up – um easy now.*

Interviewer: *And in terms of your recovery, how satisfied are you with it?*

Mrs Vickers (time point 4): *Oh satisfied 100%. I mean it's, I was so crippled really beforehand. I couldn't do things. I've got my life back again which, you know, is important to me . . . I do all the um – my activities at um – I go out quite a lot.*

Unfortunately because of my neck we won't be going on holiday abroad this year, I gave my holiday to my son that I'd booked because I can't, don't think I could cope with travelling by plane and that. We were going to the [name of county] but I don't think I can cope with the travel at the moment.

Mr Golding (time point 4)

I mean if I want to I could go back dancing again but I'm a bit, I'm a little bit nervous about that so . . . and you see you've got the slippery floor at the dance and also I will, I wear flat shoes around the house, whereas if I went dances I would have a small heel on my shoe and that makes you a bit more unstable. And you can't really go round the dance floor with a walking stick, so I'll probably give that a miss but I think I'm doing as much, if not more this year than I thought I ever would be able to.

Mrs Noble (time point 4)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Discussion

Through employing a qualitative, longitudinal design, we have achieved a detailed understanding of a range of issues concerning the experience and impact of hip and knee replacement. Specifically, we have gained a comprehensive understanding of patients' routes from referral to hip replacement surgery and have learned about the impact of waiting for surgery. This includes focus on patients' psychosocial well-being and their conceptualisation of time. We have gained an understanding of how confidence influences, and is influenced by, experiences of undergoing and recovering from hip replacement surgery. We have also generated novel perspectives on the trajectories of support used by patients over the journey through knee replacement. We have also achieved an in-depth understanding of the nature of patients expectations for hip and knee replacement surgery, how these expectations are formed and the ways in which they are accomplished (or not) 12 months after surgery. All of these insights have been made possible by the study designs, which is one of the first to explore patients' experiences of joint replacement in such detail from the pre- to 12-month postoperative period. Furthermore, a key strength of our work is the inductive nature of the approach, which ensured that the issues that we have addressed in this chapter are of particular salience and relevance to participants.

We have identified that delays to surgery are a common occurrence for patients in the NHS awaiting orthopaedic intervention. These changes to the date of surgery made by the system and patients' changing perceptions while waiting for health care both have implications for patients' well-being and this finding helps to explain views about health care. Our findings suggest that patients' experiences of time in the lead up to surgery are complex and multidimensional and clearly differ from the linear conceptualisation of time that is required to plan NHS services. We have gained detailed and useful insights into how undergoing surgery can increase feelings of vulnerability and alter a patient's trust in their own body, and the influence of interactions with others on confidence levels and the fears that patients have concerning the potential of causing harm to their new prosthesis. The research also highlights some of the strategies that patients engage in to limit this. We have learned that patients rely extensively on, and value, both informal and formal support networks over the perioperative period and that transformation from a person living with osteoarthritis to a person recovering from a surgical intervention can lead to alterations in the assistance participants received from others, including the source, type and level of assistance. However, when patients are not offered the support of health and social professionals over the perioperative period, for example to aid recovery, negative consequences can ensue (e.g. distress and feelings of abandonment). We have highlighted the complexity of patients' expectations for joint replacement surgery and how these expectations can be driven by previous personal experience of undergoing joint replacement surgery, knowledge of others' experiences – both successful and unsuccessful – and information resources provided by the hospital around the perioperative period. These insights will be useful in helping health-care professionals in educating, supporting and managing patients expectations to ensure that patients form realistic and achievable expectations for outcomes relating to pain, function and engagement with work, social and life activities.

Use of in-depth interviews facilitated a detailed exploration of participants' experience of undergoing and recovering from joint replacement surgery. Follow-up interviews allowed for clarification of any issues raised in earlier interviews. They also facilitated the development of a closer researcher–participant rapport, which encouraged the disclosure of personal accounts, helping to generate novel insights and richer data. The use of topic guides allowed consistent exploration of salient issues across participants but also the opportunity for additional probing and reflection in order to facilitate examination of prominent and unanticipated issues. To ensure analytic rigour, analysis was conducted by a team of experienced qualitative methodologists with backgrounds in social and behavioural sciences. The analysis process included double coding, discussion and agreement to arrive at the final list of themes. Furthermore, we engaged in several other validation strategies: discussion of findings with patient representatives, reflexivity and seeking out and paying attention to negative cases. We do not claim that the experiences of the participants were representative of everyone awaiting hip and knee replacement surgery; however, the rigour of analysis helps to improve the credibility of findings. In addition, although the research was carried

out with patients undergoing surgery at a single orthopaedic centre, men and women were included and the sample sizes were designed to accord with robust approaches. In the thematic approach used in the hips data set, we were confident that data saturation had been achieved. In the knees data set, use of IPA provided us with the opportunity to achieve depth in analysis and the data set size is within the norms of IPA methodology. The inclusion of patients from only one orthopaedic centre has the potential to affect transferability of findings, but the orthopaedic centre serves a diverse population in the region and it is likely that the results will resonate with the experiences of patients from other areas of the UK.

We took care in the design of the study to consider data collection approaches. Qualitative researchers have traditionally chosen to meet face to face with participants when carrying out in-depth interviews. However, research in the area now indicates that the mode of interview may have little impact on the number, character and depth of data generated during an interview.[261] However, we designed the study such that initial interviews took place in person to build rapport and consider it likely that this enabled the generation of even richer data during subsequent interviews that were conducted by telephone. The study had excellent retention; interviews were carried out with 21 out of the 24 hip patients and 8 out of the 10 knee patients at the three follow-up points.

Conclusion

Our findings suggest important ways in which the provision and delivery of care and education to people undergoing joint replacement in routine NHS care could be refined and improved. For example, patients can experience a range of emotional reactions if they experience delay and cancellation of their surgery date. Even without a delay, the wait for surgery alone can have detrimental physical and emotional consequences and cause wider psychosocial disruption. It is important that health professionals recognise these consequences, affirm patients' experiences, identify those at increased risk and work towards minimising delay and cancellation of operation dates when possible. In addition, findings demonstrate the value of recognising the fluid and dynamic nature of time and broader temporal issues embedded in the perceptions, interpretations and experiences of patients in the lead up to joint replacement. Findings also highlight how patients appear to value the offer of postoperative physiotherapy shortly after surgery as well as longer-term follow-up in secondary care. The latter may be of particular value for those patients who experience complications after surgery or who are particularly troubled by a lack of confidence and faith in their prosthesis.

The findings of our analysis suggest the importance of future directions for work that concerns patients' experiences of undergoing joint replacement surgery. For example, for some participants, concerns about potential dislocation became an enduring fear, something that influenced their behaviour and activities 1 year after surgery. This suggests the need to investigate the influence and impact of these concerns in the longer term and learn more about how best to support this group of patients. In addition, findings suggest the value of future work to address the specific impact of age, sex and cohabitation status on patients' use of support networks around the perioperative period.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Chapter 5 Measuring functional outcomes in patients having hip and knee replacement: a cohort study

Parts of this chapter have been reproduced from Wylde and colleagues.[262] © 2012 Wylde *et al.;* licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. Some parts have also been reproduced with permission from Wylde V, Lenguerrand E, Brunton L, Dieppe P, Gooberman-Hill R, Mann C, *et al.* Does measuring the range of motion of the hip and knee add to the assessment of disability in people undergoing joint replacement? *Orthop Traumatol Surg Res*, vol. 100, pp. 183–6.[263] Copyright © 2014 Elsevier Masson SAS. All rights reserved. Parts of this chapter have also reproduced from Lenguerrand and colleagues[264] © 2016 Lenguerrand *et al.* This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Background

In the ADAPT study we aimed to compare outcome measures over time in patients with hip or knee replacement and assess how well they measure impairment, activity limitation and participation.

Methods

Outcome measures were studied prospectively in 263 patients receiving joint replacement. Function was assessed prior to surgery and at 3 and 12 months using patient-completed questionnaires, clinician-administered tools and performance tests.

Results

A clinically significant improvement occurred in about 90% of patients with hip replacement and 70% of those with knee replacement. Patients with severe disease at the time of surgery were more likely to have substantial improvements in pain and functional ability.

Pain and function measures were highly correlated. People with anxiety or depression may assess themselves as being worse off than objective measures suggest. Measures of function may need adjustment for pain, psychological status, age and perhaps muscle strength to obtain a satisfactory picture of functional loss. Results suggested that physical function should be measured with both a PROM and a performance test. ROM is commonly assessed in clinical practice but did not correlate well with other measures of disease severity.

Conclusions

The ADAPT study highlighted the importance of different methods of assessing pain and function in patients receiving hip and knee replacement. Different pain characteristics predicted long-term pain in hip and knee replacement. Outcomes after joint replacement should be assessed with a patient-reported outcome and a functional test.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Background

In medical research it is conventional to use 'outcome measures' to assess change over time and the response to any intervention, such as a joint replacement.[265] Outcome measures are an artificial construct, as everyone's life and health changes continuously and well-being is influenced by many factors other than a specific illness or its treatment.[266] Nevertheless, we need outcome measures at appropriate time points when comparing the value of different approaches to health care. Research suggests that most of the benefit that can accrue from a successful joint replacement has occurred by 12 months after the operation.[48] In addition, we need to measure the long-term costs of providing treatments, which allows us to assess whether or not incremental health benefits are worth the incremental costs required to provide them.

It is essential that patient-reported outcomes after joint replacement are continuously reviewed and monitored to improve practice and optimise the results of surgery. However, the use of many different outcome measures can lead to difficulty in applying evidence to clinical practice and renders comparisons across studies and meta-analyses problematic.[267] One recent systematic review found extensive variation in the outcome measures used in RCTs of joint replacement.[119]

Measurement by clinician or patient report

The outcome after a hip or knee replacement can be assessed in different ways and can be classified according to who makes the judgement – a clinician, the patient alone, a 'significant other', or a mixture of two or more groups. In early studies, adverse events such as infection and prosthesis survival were the main issues of concern.[45] As prosthesis design and the control of adverse events improved, these issues become less important and attention turned towards clinician administered tools, such as the Harris Hip Score (HHS)[268] and AKSS[113] and more recently towards PROMs.[121] Clinician-administered tools have been widely criticised because of the recognised discordance between views of patients and clinicians.[269,270]

Research studies in joint replacement frequently use PROMs assessing different domains. Patients rate their pain, function, HR-QoL, social participation, mental health and satisfaction with the outcome of health-care interventions. In England, following the report of Lord Darzi,[121] PROMs are routinely collected after elective surgery.[271]

General or specific measures

Outcome measures may be general reflecting overall pain, function and well-being or specific relating to an arthritic hip or knee. 'Joint specific' measures are used to assess the effectiveness of an intervention targeting a joint (such as joint replacement); however, it is important to find out if a patient's general QoL has been affected.

It is generally agreed that we should assess pain and function when treating arthritis, as these are the two problems that bother people most. But it is not known what aspect of the pain (e.g. activity related pain, night pain or resting pain) and types of function (e.g. stair climbing, shopping, getting on a bus or playing golf) cause researchers endless problems. In addition, these often depend on issues such as culture and context.

There are many different outcome measures for use in assessment of health status and the response to interventions for people with arthritis and such instruments need to be validated before use. We need to be sure that they measure the outcome appropriately and that they are reproducible, responsive to change, consistent and acceptable to patients. Many researchers choose an instrument because it is widely used by others and this will help them to compare their results with those in the published literature.

Utilities

In health care, we attribute a measure of 'utility' to the time patients spend with a particular QoL profile. Utility is an economic term to describe the benefit that individuals derive from consuming goods or services. Because goods and services are scarce, individuals are faced with choices and their preferences are revealed by choosing to consume some goods and services over others. Individuals would rationally prefer goods and services that provide them with a higher utility level. In terms of health and health care, we consider that each patient has a given health profile that gives them a certain amount of health benefit or 'utility'. Better health profiles are those for which patients have a higher QoL and, therefore, higher utility scores as well. We measure each individual's health profile by asking patients to fill in generic HRQoL questionnaires. Such questionnaires can be filled in a myriad of ways, each corresponding to a different health profile. These are then sent for valuation to a random sample of individuals from the same population with a particular health profile. The weighted average of values for each health profile is the 'utility score' that a particular society has attributed to the specific health profiles.

Outcomes used in RESTORE

In *Table 15*, we summarise the key outcome measures used in the RESTORE programme.

The main issues of concern to patients undergoing total hip or knee joint replacement include pain and functional problems that are related to the joint disease, as well as general QoL and satisfaction with the surgery. In this chapter we consider joint specific pain and function. Pain is a purely subjective domain, so that we are dependent on patient self-report to assess it. In contrast, function can be assessed in many different ways, which include patient report, observation of specific or general activities, measurement of certain activities and third party observations and perceptions.

The WHO introduced the ICF,[80] which provides a theoretical framework on which to base the assessment of function. This framework splits function into three separate domains: impairment, activities limitations and participation restrictions. The value of this in the context of total hip or knee replacement can be illustrated by taking the example of climbing a step, a common problem for people considering a total hip or knee replacement. The impairments might include reduced joint movement, pain on movement and muscle weakness; the resulting activities limitations might be difficulty climbing stairs or difficulty getting onto a bus. Consequent participation restrictions might be inability to get to the shops or to go to stay with grandchildren because of the need to use stairs. Research has shown that the relationship between the impairment, activities limitations and participation restrictions domains of the ICF are not simple, with other factors such as self-efficacy and comorbidities acting as independent determinants of the relationships between these variables.[300]

It has been recommended that a combination of outcome measures should be used to assess function after total hip or knee replacement.[301,302] However, there are many reasons not to use a wide number of measures with every patient, whether in clinical practice or research. These include patient fatigue and burden, time constraints of clinic and research appointments, and time taken to process and analyse multiple information sources. Therefore, there is a need for guidance about which outcome measures are the most useful in assessing function before and after total hip or knee replacement.

The aims of the ADAPT study were to compare the properties and responsiveness of a selection of commonly used measures that are either self-assessment tools or functional tests, to examine how well they relate to the ICF concepts of impairment, activities limitations and participation restrictions, and to explore the changes in the measures and domains of outcome over time.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 15 Outcome measures used in the RESTORE programme

Name of measure	Mode of completion	General or joint specific	Health domain measured	Study used in
WOMAC[114]	Self-complete	Joint specific	Joint pain, function and stiffness	SPIRAL, APEX, ADAPT, PROOF-THR
HOOS[272]	Self-complete	Joint specific	Joint-related QoL, pain and function	Experience
KOOS[273]	Self-complete	Joint specific	Joint-related QoL, pain and function	Experience, ARENA
OHS[274]	Self-complete	Joint specific	Joint pain and function	PROOF-THR
OKS[117]	Self-complete	Joint specific	Joint pain and function	
Pain Self-Efficacy Questionnaire[275]	Self-complete	General	Self-efficacy for pain	SPIRAL, APEX
Brief COPE[276]	Self-complete	General	Coping strategies	SPIRAL, APEX
Beliefs and Medicines Questionnaire[277]	Self-complete	General	Beliefs about medicines	SPIRAL
EQ-5D[278]	Self-complete	General	HR-QoL and utilities	SPIRAL, APEX, ARENA, PROOF-THR
Functional Comorbidity Index[279]	Self-complete	General	Medical comorbidities	SPIRAL, APEX, ADAPT, ARENA
ICOAP[280]	Self-complete	Joint specific	Joint pain	APEX
HADS[281]	Self-complete	General	Depression and anxiety	APEX, ADAPT, PROOF-THR
Illness Perceptions Questionnaire-Revised[282]	Self-complete	General	Illness perceptions	APEX
painDETECT[283]	Self-complete	General	Neuropathic pain	APEX
Self-Administrated Patient Satisfaction Scale for Primary Hip and Knee Arthroplasty[284]	Self-complete	Joint specific	Satisfaction with the outcome of joint replacement	ADAPT
Ab-IAP[285]	Self-complete	General	Impairments, activity limitations and participation restrictions	ADAPT, ARENA, PROOF-THR
SF-12[286]	Self-complete	General	HRQoL	ADAPT
MYMOP2[287]	Patient-generated questionnaire completed by patient with assistance from researcher	Joint specific and general	Individualised symptoms and restricted ADL, well-being and medication usage	ADAPT, ARENA
HHS[268]	Assessment by clinician	Joint specific	Joint pain, function, deformity and ROM	ADAPT
AKSS[113]	Assessment by clinician	Joint specific	Joint pain, function, stability, ROM	ADAPT
Timed 20-metre walk[288]	Completed by patient, assessed by clinician	General	Function (locomotion)	ADAPT
Timed get-up-and-go test[289]	Completed by patient, assessed by clinician	General	Function (transfers and locomotion)	ADAPT

TABLE 15 Outcome measures used in the RESTORE programme (*continued*)

Name of measure	Mode of completion	General or joint specific	Health domain measured	Study used in
Sit-to-stand-to-sit[290]	Completed by patient, assessed by clinician	General	Function (transfers)	ADAPT
Step test[291]	Completed by patient, assessed by clinician	General	Function (ascending and descending stairs)	ADAPT
Balance test[292]	Completed by patient, assessed by clinician	General	Function (balance)	ADAPT
Inertial sensor[293]	Completed by patient, assessed by clinician	General	Function	ADAPT, PROOF-THR
LEFS[294]	Self-complete	Specific	Function	ARENA
UCLA Activity Score[295]	Self-complete	General	Activity level	ARENA
Activities-specific Balance Confidence Scale[296]	Self-complete	General	Balance	ARENA
Self-efficacy for Rehabilitation[297]	Self-complete	General	Self-efficacy for rehabilitation	ARENA
NEADL Questionnaire[298]	Self-complete	General	Function	PROOF-THR
ICECAP-O[299]	Self-complete	General	Well-being and utilities	PROOF-THR

Ab-IAP, Aberdeen impairment, activity limitation and participation restriction measure; ICECAP-O, ICEpop CAPability measure for Older people; ICOAP, Measure of Intermittent and Constant Osteoarthritis Pain; LEFS, Lower Extremity Functional Scale; MYMOP2, Measure Yourself Medical Outcome Profile 2; Nottingham Extended ADL; UCLA, University of California at Los Angeles.

Methods

The ADAPT study is a single-centre cohort study at the AOC. Based in the south-west of England, this is one of the largest elective orthopaedic units in the UK, with approximately 800 hip operations and 800 knee operations performed in 2011.[303] The ADAPT study was approved by Southwest 4 Research Ethics Committee (09/H0102/72) and all participants provided their informed, written consent to take part. The study was registered on the NIHR Clinical Research Network Portfolio (UKCRN ID 8311).

Inclusion/exclusion

Recruitment into the study began in February 2010 and finished in November 2011. Patients listed for one of the following operations were eligible: primary TKR, revision TKR, unicompartmental knee replacement, patellofemoral replacement, primary THR, revision THR or hip resurfacing. We included patients with different surgical procedures so that functional measures could be assessed across a range of people with diverse issues and degrees of functional loss.

Patients were excluded from the study if they lacked the capacity to provide informed consent. This was assessed by the research nurse in accordance with guidance from the integrated research application system, which is responsible for providing ethical approval in the UK and the Mental Capacity Act of 2005.[304] This decision was made by a research nurse if the patient met one of the following criteria: (1) they could not understand the information relevant to the decision to participate; (2) they were unable

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

to retain the information about the study; (3) they were unable to use or weigh that information as part of the decision-making process; and (4) they were unable to communicate their decision about participation (whether by talking, using sign language or any other means). Another exclusion criterion was severe functional limitations such that the patient was unable to walk because this would prevent the patient from being able to attempt any of the functional tests. This was assessed in the discussion between the research nurse and the potential participant and was always a mutual decision by the researcher and the patient. Being unable to complete questionnaires in the English language was also an exclusion criterion because not all the validated questionnaires have been translated into other languages.

Participant recruitment

Potential participants were identified from the joint replacement waiting list by the code for the intended operation and sent a postal invitation. Patients who returned a reply form were telephoned by a research nurse to discuss participation. This included a full explanation of study involvement and a preliminary eligibility assessment by asking about the intended operation and assessing understanding of the information provided. Those that did not reply or who were missed from the initial postal invitation list owing to late scheduling of hospital appointments were approached by a research nurse when they attended the pre-operative assessment clinic. These patients were identified by daily checking of the clinic lists. If they were interested, eligibility was assessed and a full explanation of study involvement was provided. The first appointment was arranged then or patients were telephoned a few days later if they needed time to consider. Demographic data (age, sex and postcode) was recorded from all patients.

Assessment times

Participants attended a research appointment, lasting approximately 1 hour, at the AOC. Appointments were scheduled before surgery and then at 3 months and 1 year after surgery. Assessments were conducted at 3 months post operation to coincide with the standard clinical review, by which time most patients should have experienced a large improvement in pain and function.[48] Assessments were also conducted at 1 year post operation as outcomes can continue to improve up until this time point.[48] The inclusion of two postoperative assessments also allowed exploration of outcome trajectories and comparison of rates of improvement between different outcome domains (e.g. pain, function, participation).

At the initial pre-operative appointment, eligibility was confirmed, informed written consent was obtained and a questionnaire was given to participants to return by post before their operation. For the postoperative assessments, a questionnaire was sent out prior to the research appointment. At each time point, participants underwent a clinical assessment. These assessments were conducted by trained research nurses who followed standard operating procedures to ensure consistency and standardisation in data collection and who were assessed for competency in the examination procedures by a senior research nurse and orthopaedic surgeon. Risk assessments of the functional tests were undertaken and safe operating procedures specified. The data collected during the assessments were recorded by the research nurses on standardised proformas.

Selection of outcome measures

Table 16 provides a summary of the functional assessment measures used in the ADAPT study. The table also provides an overview of the ICF domains included within each functional assessment measure, with classification of self-completed PROMs and clinician-administered measures based on the results of an expert consensus study by Pollard and colleagues[60] We also conducted a gait analysis using a single inertial sensor to derive motion parameters during ADL.[305]

There are a number of other measures that could have been included in this study such as the OHS and OKS,[117,274] HSS,[113] KOOS[306] and NHP.[307] However, to avoid participation burden and fatigue only a selection of measures was chosen.

TABLE 16 Measures used in the ADAPT study to assess function pre-operatively and at 3 and 12 months post operation

Measure	ICF domains assessed			Mode of completion	Scoring
	I	A	P		
PROMs[a]					
WOMAC function subscale	–	++	+/–	Patient	0–68
Ab-IAP	++	++	++	Patient	I scale = 9–45, A scale = 17–85, P scale = 9–45
SF-12 PCS	+/–	++	+/–	Patient	0–100
MYMOP2[b]	+/–	+/–	+/–	Patient with assistance from research nurse	0–6
Clinician-administered measures[c]					
AKSS	+	++	–	Research nurse and patient	0–100
HHS	+	++	+/–	Research nurse and patient	0–100
Performance tests and motion analysis[c]					
Timed 20-metre walk	–	++	–	Research nurse and patient	Time, difficulty, motion parameters
Timed get-up-and-go test	–	++	–	Research nurse and patient	Time, difficulty, motion parameters
Sit-to-stand-to-sit test	–	++	–	Research nurse and patient	Completion, difficulty, motion parameters
Step tests	–	++	–	Research nurse and patient	Completion, difficulty, motion parameters
Single stance balance tests	–	++	–	Research nurse and patient	Completion, difficulty, motion parameters
Gait analysis parameters[d]					
Walking speed	++	–	–	Research nurse and patient	Metre/second
Walking cadence	++	–	–	Research nurse and patient	Step/minute
ROM pelvic obliquity	++	–	–	Research nurse and patient	Degree
Time to complete a step	++	–	–	Research nurse and patient	Second
Length of step	++	–	–	Research nurse and patient	Metre
Step Irregularities	++	–	–	Research nurse and patient	Variability in successive steps of the same leg
Asymmetries	++	–	–	Research nurse and patient	Ratio of asymmetry between steps time (seconds) of both legs

A, activity limitations; Ab-IAP, Aberdeen impairment, activity limitation and participation restriction measure; I, impairments; MYMOP2, Measure Yourself Medical Outcome Profile 2; P, participation restrictions.
The extent to which I, A and P is assessed within each tool is indicated using the following symbol system: – no items assessing domain, –/+ a small number of items assessing domain, + some items assessing domain, ++ the majority of items assessing domain.

a Scores were self-completed by the patient in a postal questionnaire, excepting MYMOP2 which was completed during a research appointment.
b The MYMOP2 asks patients to generate two symptoms (impairments or activity limitations) and one activity (which could be activity limitation or participation restrictions) that are restricted by their symptoms.
c Scores and tests were assessed by a research nurse during a research appointment. Participants were also invited to rate their performance on the functional tests.
d Information captured during the 20-metre walk test with body-fixed inertial sensors containing accelerometers and gyroscopes wireless connected to a computer.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Patient-reported outcome measures

The following validated measures were used to provide disease-specific and generic self-reported measures of outcome.

The WOMAC function scale.[114] This disease-specific subscale, validated in osteoarthritis patients, consists of 17 questions assessing the extent of function limitations when performing a range of daily activities. Responses are provided on a 5-point Likert-type scale.

Aberdeen impairment, activity limitation and participation restriction measure (Ab-IAP).[285] This 35-item disease-specific measure, validated in osteoarthritis patients, uses the ICF framework to assess disability and produces scores for impairment, activities limitations and participation restrictions. Responses are provided on a 5-point Likert-type scale.

Short Form questionnaire-12 items.[116] This 12-item general health measure produces a PCS and mental component score scale. Responses are provided as binary options (yes/no) or on a Likert-type scale.

Measure Yourself Medical Outcome Profile 2 (MYMOP2).[287] This patient-generated instrument allows participants to generate and rate the severity of two symptoms that are concerning them and one activity important to them that is restricted by the symptoms. Participants also rate their general well-being, duration of symptom 1 and medication usage for symptom 1. At follow-up, participants are asked to rate the severity of the symptoms and degree of restriction of the activity that they identified at the first data collection point. Ratings are provided on scales of 0–6. The MYMOP2 was completed during research appointments by participants with the assistance of research nurses.

Participants also completed a number of other questionnaires to assess factors that have been found to influence outcomes after total hip or knee replacement (*Table 17*). At each assessment time, participants completed the HADS[281] and the WOMAC pain and stiffness subscales.[114] Participants were also asked to rate how disabled they perceived themselves because of their joint problems and why, and to list three things that they were hoping for from their total hip or knee replacement. Pre-operatively, medical comorbidities were recorded using the Functional Comorbidity Index[279] and information was collected about socioeconomic status (marital status, living arrangements, educational attainment, employment

TABLE 17 Measures used to assess factors influencing function in the ADAPT study

Measure	Dimensions	Mode of completion	Scoring	Assessment times		
				Pre-operation	3 month	1 year
WOMAC pain subscale	Joint pain	Patient	0–20	✓	✓	✓
WOMAC stiffness subscale	Joint stiffness	Patient	0–8	✓	✓	✓
HADS	Depression, anxiety	Patient	0–21	✓	✓	✓
SF-12 mental component score	Mental health	Patient	0–100	✓	✓	✓
Perceived level of disability	Function	Patient	0–10	✓	✓	✓
Three things hoping for from surgery	Expectations	Patient	Categorical	✓	✓	✓
Functional Comorbidities Index	Comorbidities	Patient	0–18	✓		
Arthritis and surgery in other joints	Comorbidities	Patient	By joint/count	✓		
Socioeconomic status	Socioeconomic	Patient	Categorical	✓		
Self-Administered Patient Satisfaction Scale	Satisfaction	Patient	0–100			✓

status), joints affected by arthritis and previous surgery on other joints. In the 1-year postoperative questionnaire, satisfaction with the outcome of surgery was assessed using the Self-Administered Patient Satisfaction Scale for Primary Hip and Knee Arthroplasty.[284]

Clinician-administered measures

The HHS was completed with patients receiving hip replacement.[268] This assessment measure provides a total score of between 0 and 100 (worst to best) collected over four domains. Function, which includes limp, use of assistive devices, walking distance, managing stairs, using public transport, sitting comfortably and putting on shoes and socks, is weighted the most heavily and is assigned 47 points. Pain is assigned 44 points. The physical examination involves assessing deformity (4 points) and ROM (5 points).

The AKSS was completed with patients receiving knee replacement.[113] This assessment consists of a knee score and a function score, both with a total score ranging from 0 to 100 (worst to best). The knee score incorporates examiner's rating of patients' pain (50 points) and a clinical assessment of stability (25 points) and ROM (25 points), with deductions for flexion contracture, extension lag and misalignment. The function score consists of questions about walking distance (50 points) and stair climbing ability (50 points), with deductions for the use of walking aids.

Performance tests

Before performing each of these tasks, participants were asked if they thought that they would be able to perform the task and estimate how difficult they thought the test would be to perform on a 0–10 scale (no difficulty at all to impossible). After they had completed the test, they were asked to rate how difficult the task actually was to perform on the same 0–10 scale. The research nurse conducting the assessment also provided a rating of how difficult it appeared to be for the participant to perform the task. If participants were unwilling to attempt the test or the research nurse was unhappy to proceed because of safety concerns, the test was not performed. All tests were performed without the use of supportive aids except the timed 20-metre walk and are described in the order in which they were performed.

Timed 20-metre walk[288]

Participants were timed as they walked a 20-metre straight distance on level ground at their normal, comfortable speed. If the participant normally used a walking aid they were asked to try without it but, if they felt unable to do so, they completed the test using the walking aid. The recorded outcome was the time taken to complete the test.

Timed get-up-and-go test[289]

Participants sat on a height-adjustable chair such that a 90° angle was formed when the femur was horizontal and the tibia vertical with their feet shoulder width apart and their arms crossed against their chest. Participants were timed as they stood up from the chair without using their hands, walked at a normal pace past a marker 3 metres away, turn around, walked back and sat down again. The recorded outcome was whether or not participants were able to complete the activity and how long it took.

Sit-to-stand-to-sit[290]

Participants sat on a height-adjustable chair as described for the previous test. Participants then stood up, waited 2 seconds and sat down again without using their hands. The recorded outcome was whether or not participants were able to complete the activity.

Step test[291]

Participants stepped up onto a 20-cm-high block leading with the contralateral leg, waited 2 seconds and then stepped down from the block with the index leg leading, without using their arms. The test was then repeated with the index leg leading. If participants successfully completed this test, the test was repeated with a 30-cm-high block. The recorded outcome was whether or not participants were able to complete the activity.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Single stance balance test[292]

Participants stood with their feet together facing the research nurse and placed their palms gently on top of the research nurse's palms. Participants then lifted their index leg and attempted to balance on their contralateral leg for 15 seconds. If the participant lost balance within 3 seconds, then the test was reattempted. If the participant lost balance before 15 seconds, the length of time was recorded. This test was then repeated while balancing on the index leg. If these tests were completed successfully, the participant repeated the tests with no stability support from the research nurse. The recorded outcome was whether or not participants were able to maintain the stance for 15 seconds.

Inertial sensor-based motion and gait analyses

Movement analysis by body-fixed inertial sensors containing accelerometers and gyroscopes enables the objective assessment of the translational and angular movements of body segments outside a gait laboratory.[293,308] We used a single 3 dimensional (3D) inertial sensor [41 × 63 × 24 mm; 39 g; Microstrain Inertia Link (Williston, VT)] containing accelerometers (± 5 g) and gyroscopes (± 300°/second) along the three orthogonal axes in frontal, sagittal and transverse plane and positioned centrally between both posterior superior iliac spines to measure trunk movements near the centre of gravity. Based on the 3D linear accelerations, angular rates and angular positions put out by the sensor and sent wirelessly to a computer at a 100 Hz sampling frequency via a Bluetooth® (Bluetooth SIG, Inc., Kirkland, WA) link, analysis algorithms calculated motion parameters such as step frequency, step asymmetry or trunk sway.

The inertial sensor was used to derive motion parameters from a battery of movement tasks which were clinically feasible to perform during a routine outpatient visit and which challenged the patient's functional capacity in different ways: (1) locomotion (walking), (2) transfers (sit-to-stand-to-sit test, get-up-and-go test), (3) rising and descending (step test) and (4) balance tests (single-leg stance). The walk test[309] and the step-test were repeated twice and the sit-to-stand-to-sit test was repeated three times to derive representative mean values or study possible effects of fatigue or warming up.

Data collection

Information on BMI, diagnosis, side of surgery, type of surgery and surgical approach was extracted from participants' medical records.

Data recording

All data were entered into a password-protected database by research nurses or study administrators. The study was overseen by an independent Steering Committee which met every 6 months to discuss the progress of the study. Data monitoring, which involved double data entry and quality checks, was conducted every 3 months. All data were cleaned before data analysis was performed. Any inconsistencies were collegially discussed by an internal board of researchers involved in the data collection.

Sample size

This study involved exploratory analysis to compare different measures to assess function after total hip or knee replacement. Therefore, no formal sample size calculation was performed, although we aimed to recruit a sufficient number of patients to allow meaningful data analysis. We approached all patients listed for surgery with participating surgeons between February 2010 and November 2011. Previous longitudinal studies comparing measures of function in an orthopaedic population have included between 30 and 200 patients.[310–318]

Analysis

The statistical methods used to analyse the data are described in each section of the results, which have been divided into three sections:

- baseline demographic data
- cross-sectional correlations of baseline data
- analysis of change from longitudinal data including preliminary results from the gait analysis.

Results

Demography of the cohort

A total of 130 patients receiving hip replacement and 133 patients receiving knee replacement were recruited to the ADAPT study.

The patients listed for a hip surgery were planned to receive a primary THR ($n = 78$), revision THR ($n = 44$) or a hip resurfacing ($n = 8$). The 133 patients listed for a knee surgery were planned to receive a primary TKR ($n = 51$), revision TKR ($n = 45$), unicompartmental knee replacement ($n = 32$) or patellofemoral replacement ($n = 5$). The five patients awaiting patellofemoral joint replacement were excluded from the cross-sectional analysis owing to the isolated nature of their knee disease.

Not all data were available on all 258 patients and at each measurement point, so the subsequent analyses reported below are often on slightly smaller groups.

Patient demographics for the 249 participants with available pre-operative data (125 listed for hip replacement and 124 listed for knee replacement) are summarised in *Table 18*.

Cross-sectional analysis of the different measures of function

Introduction

As noted above, one of the main aims of this study, within the overall programme was to improve our understanding of the best ways of measuring function before and after hip or knee joint replacement. In this section of the results, we describe the correlations between the different measures of function that we have data on at the baseline visit. We also describe the disparities/similarities in the associations between these measures and patient characteristics. Investigating these issues provides insight into how the outcomes as measured by these various tools can be interpreted and sheds insight into the comparability of the tests. The data should also aid those investigating disability caused by severe hip and knee pathology to make an informed choice of measurement tool.

Statistical analysis

The relationships between the different functional measures were assessed with correlation statistics. Spearman's rank-order coefficients were used to assess correlations between continuous variables and point-biserial coefficients to assess correlations between continuous and dichotomous variables. These measures range from –1 to 1. The strength of correlation was interpreted as |0.00–0.25| = none–little, |0.26|–|0.49| = low, |0.50|–|0.69| = moderate, |0.70|–|0.89| = high, |0.90|–|1.00| = very high. Correlations between two binary measures were assessed with Cramér's V-statistic, which ranges from 0 to 1. A value > 0.3 was considered very strong.

The association between participants' characteristics and functional measures was investigated with linear regression for HHS, AKSS, WOMAC function, Aberdeen activity limitation subscale (Ab-A), Aberdeen participation restriction subscale (Ab-P) [transformed as root squared (score)], walking speed and get-up-and-go tests (transformed as 1/time). The step and balance tests produced dichotomous outcomes (able/unable to do test) and were investigated with a modified Poisson regression with robust variance estimation.

Individual patient characteristics were first considered in a univariate model. Factors that were found to be significant ($p \leq 0.05$) were then investigated in a multivariate analysis to determine if their effects were confounded by other factors.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 18 Characteristics of participants in the ADAPT study

Characteristic		Hip ($n = 125$)	Knee ($n = 124$)
Surgery type (%)	Primary replacement	65.6	40.3
	Revision surgery	34.4	33.9
	Unicompartmental surgery	–	25.8
Sex (%)	Female	50.4	51.6
Age (years)	Median (25th, 75th)[a]	64.4 (57.1, 72.5)	68.3 (60.5, 73.9)
Pain[b]	Mean (95% CI)	53.9 (50.0 to 57.8)	44.1 (40.7 to 47.4)
Psychological distress[c] (%)		32.0	33.1
BMI, kg/m^2 (%)	Median (25th, 75th)[a]	27.0 (24.3, 30.4)	30.4 (27.4, 34.5)
	Overweight	41.0	39.8
	Obese	26.8	52.7
Comorbidities (%)	0 comorbidities	46.0	36.0
	1 comorbidity	35.9	27.3
	≥ 2 comorbidities	18.1	36.8
Arthritis (%)	0 joint	21.3	14.9
	1 joint	25.0	21.1
	2 joints	19.7	14.1
	3 joints	15.0	16.4
	≥ 4 joints	19.0	33.5
Living alone (%)		24.2	29.3
Education (%)	Normal leaving-school age or before	54.2	61.1
	College	23.0	25.1
	University	22.8	13.8
Working status (%)	Paid or volunteer activity	46.4	30.7
	Retired	48.0	62.9
	Unemployed	5.6	6.4

Q, quartile.
a Q1 = 25th percentile and Q3 = 75th percentile.
b (WOMAC) pain subscale; the higher the score the better the outcome (range 0–100).
c HADS.

The analyses were conducted separately for hip and knee patients. Although few participants had missing information for one or more of the considered variables, missing data were addressed using a multiple imputation by chained equations approach. Ten imputations were generated and estimates were combined using Rubin's rules. Statistical analyses were performed in Stata 12.1.

Results

The mean/median and range of scores for each of the functional measures are shown in *Table 19*. These data show that most participants had significant functional limitations, although the wide range of each of the measures suggests considerable variability.

TABLE 19 Pre-operative function in ADAPT participants

	Hip ($n = 125$)				Knee ($n = 124$)			
Outcome measure	Mean	SD	Minimum	Maximum	Mean	SD	Minimum	Maximum
Patient-reported measures (mean score)								
WOMAC[a] function	55.3	22.0	0.0	100.0	50.9	18.5	0.0	97.0
Ab-A[b]	23.9	11.6	0.0	56.0	25.1	10.7	2.0	50.0
Ab-P[c,d]	8.0	9.0	0.0	31.0	10.0	10.0	2.0	28.0
Clinician-administered measures (mean score)								
HHS[e]	54.0	17.5	23.2	97.0				
AKSS-function[f]					53.7	15.4	0.0	90
AKSS pain, stability and ROM[g]					43.1	15.2	10.0	82.4
Performance tests								
Walking speed[e] (m/second)	0.9	0.4	0.2	1.7	0.9	0.5	0.3	2.0
Get-up-and-go test duration[e] (seconds)	17.0	11.0	9.0	118.0	17.2	10.6	8.0	56.0
Stepped 20-cm achievement (mean %)	81.4				77.4			
Stepped 30-cm achievement (mean %)	60.4				55.6			
Balance test achievement (mean %)	46.6				33.9			

a Range 0–100, worst to best.
b Range 0–68, best to worst.
c Range 0–36, best to worst.
d For these outcomes, the median and IQR (75th percentile – 25th percentile) are reported instead of the mean and SD.
e Range 0–100, worst to best.
f Range 0–100, worst to best.
g Range 0–100, worst to best.

Relationships between functional measures

Correlations between the different functional measures were all statistically significant, but some were much stronger than others (*Table 20*). The HHS correlated relatively well with PROMS and with walk time in patients with hip disease, but not so well with the other performance tests. The AKSS correlated poorly with all other types of functional measures in patients with knee disease. The highest correlations, in both hip and knee patients, were between the WOMAC and Ab-A scores – the two PROMs for disability; between the walking speed and the get-up-and-go test – the two timed tests; and between the balance test and 30-cm step test.

Associations between patient characteristics and functional measures

Associations between patient characteristics and the different functional measures are shown in *Tables 21* (hip) and *22* (knee). Pain was an important determinant of all measures of function in both patient groups. In contrast, age, sex and comorbidities discriminated between hip and knee patients as well as between the different methods of assessing disability. Sex affected most measures of disability in hip patients, but not in knee patients. Age affected the performance tests more than the PROMs or clinician-administered tests, whereas anxiety and depression had much more effect on the PROMs and clinician-administered measures than on the performance tests. BMI does not seem to be important and other comorbidities have more effect on tests of function in people with knee disease than those with hip disease.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 20 Correlations between functional measures in ADAPT participants

Outcome measure		WOMAC	Ab-A	Ab-P	AKSS function	AKSS pain, stability and ROM	HHS	Walking speed[a]	Get-up-and-go test[b]	20-cm step test[c]	30-cm step test[c]
Hip	Ab-A	–0.87									
	Ab-P	–0.71	0.73								
	HHS	0.71	–0.73	–0.67							
	Walking speed	0.56	–0.65	–0.52			0.67				
	Get-up-and-go test	–0.56	0.63	0.42			–0.59	–0.85			
	20-cm step test	0.33	–0.38	–0.28			0.50	0.48	–0.44		
	30-cm step test	0.37	–0.49	–0.28			0.48	0.60	–0.50	0.58	
	Balance test[d]	0.27	–0.32	–0.17[e]			0.38	0.58	–0.39	0.44	0.66
Knee	Ab-A	–0.88									
	Ab-P	–0.63	0.69								
	AKSS function	0.46	–0.47	–0.51							
	AKSS pain, stability and ROM	0.40	–0.33	–0.37							
	Walking speed	0.51	–0.54	–0.51	0.67	0.29					
	Get-up-and-go test	–0.46	0.50	0.43	–0.60	–0.21		–0.73			
	20-cm step test	0.25	–0.28	–0.27	0.50	0.27		0.46	–0.60		
	30-cm step test	0.34	–0.37	–0.37	0.57	0.31		0.57	–0.60	0.43	
	Balance test	0.22	–0.29	–0.26	0.33	0.21		0.27	–0.29	0.31	0.61

a Walking speed in metres per second.
b Duration in seconds to complete the test.
c Achievement of the 20-/30-cm step test.
d Achievement of the balance test.
e All the correlations are statistically significant ($p < 0.05$) except the point-biserial correlation coefficient between the Ab-P score and the balance test for hip patients.

Note

The correlations involving the 20-metre walk and the get-up-and-go tests were derived only on the patients who completed these task ($n = 124$ and $n = 111$ among hip patients, respectively, and $n = 122$ and $n = 110$ among knee patients, respectively). The other correlations were performed on all the 125 hip/124 knee patients. All the functional measures are continuous variable except the 20-cm step, 30-cm step and balance tests, which are binary measures. Correlations between two continuous measures were assessed with the Spearman's rho statistics, ranging from –1 to 1. Correlations between continuous and binary measures were assessed with the point-biserial correlation coefficients, ranging from –1 to 1. Correlations between two binary measures were assessed with the Cramér's V-statistics, ranging from 0 to 1.

TABLE 21 Patients waiting for hip replacement: associations between patient characteristics and functional measures

Hip	WOMAC function[a]	Ab-A[a]	Ab-P[a,b]	HHS[a]	Walk (speed)[a]	Get-up-and-go test[a,c]	20-cm step test[d]	30-cm step test[d]	Balance[d]
Age (years)					**< 0.0001**	**< 0.001**		**< 0.05**[e]	**< 0.0001**
Sex	**< 0.05**	**< 0.05**			**< 0.0001**	**< 0.001**		**< 0.01**	< 0.05
Pain	**< 0.0001**	**< 0.0001**	**< 0.0001**	**< 0.0001**	**< 0.0001**	**< 0.0001**	**< 0.05**	**< 0.01**	**< 0.05**
HADS	**< 0.0001**	**< 0.0001**	**< 0.0001**	< 0.0001	< 0.01	< 0.05			
BMI									
Functional Comorbidity Index		**< 0.05**			< 0.01	< 0.05		**< 0.01**	
Arthritis									
Living alone					< 0.05				**< 0.05**
Education									< 0.05
Working status				**< 0.01**	< 0.01	< 0.05		< 0.05	< 0.01

a Associations investigated with linear regressions.
b Ab-P score modelled as root squared (score).
c Get-up-and-go test time (modelled as 1/time).
d 20-cm step and 30-cm step and balance tests achievement; associations investigated with modified Poisson regressions with robust variance estimation.
e The relationship between age and achieving the 30-cm step test is modelled as age, age^2 and age^3.
Associations which remained statistically significant ($p \leq 0.05$) in multivariate analysis are highlighted in bold.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 22 Patients waiting for knee replacement: associations between patient characteristics and functional measures

Knee	WOMAC function[a]	Ab-A[a]	Ab-P[a,b]	AKSS-f[a]	AKSS[a]	Walking speed[a]	Get-up-and-go test[a,c]	20-cm step test[d]	30-cm step test[d]	Balance[d]
Age (years)						**< 0.05**[e]	**< 0.001**[e]	**< 0.05**[e]		**< 0.05**[e]
Sex									**< 0.01**	
Pain	**< 0.0001**	**< 0.0001**	**< 0.0001**	**< 0.0001**	**< 0.0001**	**< 0.0001**	**< 0.01**		**< 0.05**	
HADS	**< 0.0001**	**< 0.0001**	**< 0.0001**	**< 0.0001**		< 0.01	< 0.05			
BMI										
Functional Comorbidity Index	< 0.01	**< 0.001**	< 0.05	< 0.01	< 0.05		**< 0.05**	**< 0.05**	**< 0.01**	
Arthritis										
Living alone	< 0.05			< 0.05						
Education						< 0.05		< 0.05		
Working status								**< 0.001**	< 0.05	

a Associations investigated with linear regressions.
b Ab-P score modelled as root squared (score).
c Get-up-and-go test time (modelled as 1/time).
d 20- and 30-cm step and balance tests achievement; associations investigated with modified Poisson regressions with robust variance estimation.
e The relationship between age and these outcomes is modelled as age and age^2.
Associations which remained statistically significant ($p \leq 0.05$) in multivariate analysis are highlighted in bold.

Discussion

This study compared different ways of assessing function in patients awaiting hip or knee replacement. Correlations were stronger within the same type of measures (PROMS, clinician-administered or performance test) than between approaches. Correlations that were usually < 0.9 imply that each of these measures describes a slightly different construct of function and that several of them would be needed to provide an accurate and exhaustive assessment of function. Nevertheless, the WOMAC function, Ab-A, HHS, walking test and the get-up-and-go tests had satisfactory convergence validity (correlation ≥ 0.3). This suggests that each of these measures can individually provide a reasonably comprehensive description of function if it is possible to conduct only one test. However, the AKSS and the balance test correlated poorly with most of the measures and should not be used alone. These findings are consistent with previous research which found moderate to strong (> 0.4) correlations with the WOMAC function and stair climbing, walking or the get-up-and-go test.[319–323] Moderate to strong correlations have also been reported pre-operatively between the WOMAC function and the HHS or its components,[319,321,324] and small to moderate correlations have been found between the WOMAC function and the AKSS.[319,325,326] Our finding of a strong relationship between the Ab-A and WOMAC function score is not surprising as the Ab-A is based on several items of the WOMAC.[285] In this study, the Ab-A measure had slightly better correlations than the WOMAC function with all the other measures. This suggests that it may be the preferred tool for assessment of function in this population.

Previous inconclusive studies exploring the association between the HHS or AKSS and performance tests were based on moderate sample sizes, and mainly focused on associations between joint ROM and performance tests.[285,327–329] Our study highlighted that associations between patient characteristics and function differed according to the measurement approach used. For example, obesity was associated with poor AKSS but not with functional outcomes as measured any other way.

Responses to PROMs are influenced by factors including age, sex, mental health or socioeconomic characteristics.[322,330–333] Clinical assessments can also be influenced by patients' characteristics; for instance, fat mass and bony structure affect the reliability and validity of extremity measurements,[334] while age and vulnerability may influence communication with health professionals or interviewers.[335] Performance testing may not always assess ADL of relevance to an individual and may not take into account environmental or behavioural adaptations.[336] Tests are also likely to be confounded by factors such as sarcopenia, which in turn can be influenced by other patient characteristics such as activity or self-efficacy.[337]

Although pain is a major determinant of function irrespective of measurement method, we found that psychological health influenced self-assessment more than performance-based methods. In addition, age affected performance measures, but not self-assessment. This has several implications. First, a causal investigation of function will be accurate, exhaustive and corroborative only if conducted simultaneously with several measures of function. Second, the investigation of any risk factor of function should be adjusted for the patient's psychological status (if a self-assessment measure is used) or for patient age (if a performance test is used), and in both cases for pain. Third, any comparison of measures of function obtained with different measurement methods is flawed unless the effects of pain, age and psychological status are considered. Fourth, there is an age-related decline in function when measured objectively, but this is not evident on PROMs. Fifth, the effect of psychological factors on self-reported function, but not on objective measures, indicates that psychological status influences the perception of function more than the ability to do something; patients may be able to do more than they say they can do and may need encouragement to overcome anxiety. Finally, it seems that any assessment of function should be accompanied by pain assessment to obtain unconfounded assessment. The association of pain with function, even after taking into account the age and psychological status of the patients, confirms the lack of discriminant validity of currently used functional measures. This is to be expected with the clinician-completed HHS and AKSS, which include a pain component. It has also been observed previously between self-reported measures of pain function.[318] However, the association with the performance tests is more problematic as even the most 'objective' measures of function are confounded by pain.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

These findings were obtained on patients from a single-centre orthopaedic unit; however, this is a large sample with a representative age range undergoing a diversity of procedures. The study also focused on a discrete number of assessment measures and did not include measures such as the OHS, OKS, KOOS or HOOS. Measures were selected to include a broad range of tools that could be administered at the same time alongside demographic information. Through this, we were able to compare effectively the measures and the influence of patient characteristics.

Conclusion

Our study shows that associations between patient characteristics and function differed according to the measurement approach used. Measures of pain and psychological health could be routinely used alongside self-report of activity limitations to enable appropriate adjustments. Performance-based tests are strongly influenced by age, possibly owing to age-related sarcopenia. If this is correct, for research purposes the inclusion of a simple muscle strength test, such as grip strength, alongside performance-based methods might aid interpretation of the findings.

Cross-sectional analysis of joint range of motion and its relevance to functional measures

Introduction

Range of motion is often routinely assessed in orthopaedic surgery. Measures of ROM are included in both the AKSS[113] and HHS.[268] However, the relationship between ROM and function is contested, with some authors regarding ROM as a good determinant of function[329] but others reporting poor correlations.[317,338] In view of ongoing use of ROM and continuing uncertainty about its relationship with function, this analysis of the ADAPT data was undertaken to investigate the relationship between ROM and our other measures of function. In this analysis we have also specifically looked at the different domains of function as described in the WHO ICF, that is, we have analysed the relationships between ROM and impairment, activities limitations and participation restriction separately.

Statistical analysis

Analyses were conducted separately for patients listed for hip and knee replacement. Spearman's rank-order correlation coefficients were used to assess correlations between continuous variables. Point-biserial correlation coefficients were used to assess correlations between continuous and dichotomous variables. These correlation measures range from –1 to 1. The strength of correlation was interpreted as |0.00|–|0.25| = none–little, |0.26|–|0.49| = low, |0.50|–|0.69| = moderate, |0.70|–|0.89| = high, |0.90|–|1.00| = very high. Linear regression was conducted to adjust for the effect of demographic factors (age, sex, socioeconomic status, joints affected by arthritis, comorbidities and psychological status) on the relationship between WOMAC pain and self-report activity limitations. To adjust for the effect of demographic factors on the relationship between WOMAC pain and participation restrictions, the participation restrictions scale of the Aberdeen impairment, activity limitation and participation restriction measure (Ab-P) was transformed with a root square function to comply with the assumptions of the linear model.

To compare functional measures between patients with low and high active flexion, patients were dichotomised into those with low flexion ($< 110°$ for knee patients and $< 95°$ for hip patients) and those with high flexion ($\geq 110°$ for knee patients and $\geq 95°$ for hip patients). This cut-off was chosen because 90° of hip and knee flexion is required when rising from sitting to standing in order for the centre of gravity in the sagittal plane to transfer from behind the midline (in sitting) to in front of the midline (in standing). Continuous variables were compared between these two groups using unpaired *t*-tests or Mann–Whitney *U*-tests for non-normally distributed variables. Categorical variables were compared using chi-squared tests. Statistical analysis was performed using Stata 12.

Results

Relationship between measures of impairment and activity limitations Correlations between the measures of impairment (ROM and WOMAC pain) and measures of activity limitations [WOMAC function, activity limitations scale of the Aberdeen impairment, activity limitation and participation restriction measure (Ab-A), performance tests] are displayed in *Table 23*.

Hip and knee ROM correlated weakly with self-report (Spearman's rank-order correlation coefficients ranging from |0.11| to |0.43|) and observed activity limitations (|0.09| to |0.38|). In comparison, correlations between pain and self-report activity limitations were moderate to high (|0.63| to |0.80|) and remained so after adjustment for demographic factors (data not shown). However, correlations between pain and observed activity limitations were low (|0.13| to |0.44|). Correlations between individual WOMAC function items and ROM measurements were investigated to determine if ROM correlated with specific functions. All correlations were found to be low (|0.01| to |0.40|). The highest correlation in patients listed for hip replacement was between flexion and getting on/off toilet (–0.37) and in patients listed for knee replacement it was between flexion and getting in/out of a car (–0.40) and putting on socks/stockings (–0.40).

Relationship between measures of impairment and participation restrictions

Correlations between measures of impairment and participation restrictions (Ab-P) are displayed in *Table 23*. Hip and knee ROM correlated poorly with participation restrictions (|0.06| to |0.32|). In comparison, correlations between pain and participation restrictions were high in patients listed for hip replacement (–0.71) and moderate in patients listed for knee replacement (–0.53), and these correlations remained strong after adjustment for demographic factors.

TABLE 23 Correlations of ROM and pain with measures of activity limitations and participation restrictions

	Self-report activity limitations		Function performance tests			Self-report participation restrictions
Outcome measure	WOMAC function	Ab-A	20-metre walk	Sit-to-stand-to-sit test	20-cm step test	Ab-P
Patients listed for hip replacement						
Flexion	0.29**	–0.35***	–0.29**	0.30***	0.34***	–0.17
Abduction + adduction	0.29***	–0.32***	–0.36***	0.16	0.13	–0.23*
Arc of rotation	0.20*	–0.27**	–0.36***	0.11	0.25**	–0.17
Pain	0.80***	–0.71***	–0.44***	0.13	0.23**	–0.71***
Patients listed for knee replacement						
Active flexion	0.43***	–0.35***	–0.38***	0.31***	0.31***	–0.32***
Active extension	–0.18	0.11	0.09	–0.19*	–0.35***	0.06
Pain	0.78***	–0.63***	–0.32***	0.18*	0.17	–0.53***

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.
Correlations = Spearman's rank-order correlation coefficients for continuous variables and point-biserial correlation coefficients for continuous and dichotomous variables. Correlation interpretation: |0.00|–|0.25| = none–little correlation, |0.26|–|0.49| = low correlation, |0.50|–|0.69| = moderate correlation, |0.70|–|0.89| = high correlation, |0.90|–|1.00| = very high correlation.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Comparison of functional measures between patients with low and high active flexion

Patients listed for knee replacement with low flexion had significantly worse results on all measures of impairment, activity limitations and participation restrictions than patients with high flexion (*Table 24*). Patients listed for hip replacement with low flexion had significantly worse activity limitations than patients with high flexion.

Discussion

The WHO ICF model offers a theoretical framework for describing and assessing disability. The data from this study show that in patients listed for joint replacement, there is a poor relationship between ROM and any of the disability measures used in this study, which contrasts with the strong relationship found between pain, activity limitations and participation restrictions. Previous studies have arrived at discordant conclusions about the relationship between function and ROM. Some reports suggest that ROM is an important determinant of function[321,329] while others disagree.[317,338] Furthermore, it is suggested that ROM is important for some specific functions, or that a threshold of around 95–100° of flexion is required for adequate function.[338] Our data suggest that there may be such a threshold, but that ROM does not correlate with specific activities on the WOMAC function and modest restrictions of ROM are of little relevance to functional outcomes.

These findings are important for two reasons. First, commonly used methods of assessing patients' disability, such as the AKSS and HHS, include ROM. Second, many orthopaedic surgeons often consider the achieved ROM of a replaced joint to be an important measure of surgical outcomes and discuss this with their patients. We suggest that as a measure of impairment, ROM is of little relevance to function and the only concern should be whether or not knee flexion is restricted to < 110° and, to a lesser extent, whether or not hip flexion is limited to < 95°.

TABLE 24 Comparison of functional measures between patients with low and high active flexion

	Patients listed for knee replacement			Patients listed for hip replacement		
Outcome measure	Low flexion (< 110°) (*n* = 54)	High flexion (≥ 110°) (*n* = 67)	*p*-value	Low flexion (< 95°) (*n* = 77)	High flexion (≥ 95°) (*n* = 48)	*p*-value
Impairment measures						
WOMAC pain score (mean, 95% CI)	37 (32 to 42)	50 (46 to 54)	< 0.0001	54 (49 to 58)	54 (47 to 62)	0.8873
Activity limitation measures						
WOMAC function score (mean, 95% CI)	43 (38 to 47)	58 (53 to 62)	< 0.0001	54 (49 to 59)	59 (52 to 66)	0.2548
Ab-A score (mean, 95% CI)	28 (26 to 31)	22 (19 to 24)	0.0007	25 (23 to 28)	20 (17 to 24)	0.0381
20-metre walk test time in seconds, median (25th, 75th centiles)[a]	28 (22, 36)	20 (17, 27)	0.0002	23 (18, 30)	10 (17, 25)	0.3493
Sit-to-stand-to-sit test (% completed)	78	94	0.0009	84	97	0.048
20-cm step test (% completed)	67	85	0.017	78	91	0.073
Participation restriction measures						
Ab-P, median (25th, 75th centiles)	13 (8, 17)	8 (5, 13)	0.0013	8 (5, 16)	8 (4, 12)	0.2867

a Q1–Q3 = 25th percentile to 75th percentile.
p-values presented are for unpaired *t*-tests or Mann–Whitney *U*-tests.

Weaknesses of the study were the lack of randomisation of the order of the performance tests and inclusion of patients from only one specialist orthopaedic unit. However, by including patients listed for a range of joint replacement procedures, a diverse and varied sample was achieved. Strengths include the study's relatively large size, the extent of and care taken with the measures of ROM and disability, and the good interobserver and intraobserver reliability for ROM.

Conclusion

These findings suggest that measuring ROM adds little value to assessment of impairment in patients undergoing joint replacement, unless hip or knee flexion is restricted to < 90° and, therefore, should not be used to assess disability in a pre-operative context.

Longitudinal analysis of changes in the different measures of function over time

Introduction

One of the main aims of the ADAPT study was to assess the responsiveness of various different measures of function and, in particular, to contrast the value of the three main different approaches (self-assessment, clinician-administered tools and functional tests) in assessing change after joint replacement. An important part of such an analysis is to assess which measures might have an important ceiling effect, that is which measures often reach their limits after joint replacement surgery, such that they cannot detect further improvement.

In this section we describe the changes seen in function between the pre-operative and 12-month postoperative assessment.

Statistical analysis

Analyses were conducted separately for patients listed for hip and knee replacement.

Change in function ability (as measured by the WOMAC function subscale, the SF-12 physical function subscale, the Ab-IAP, the MYMOP2 score, the get-up-and-go test, the timed 20-metre walk, the HHS and the AKSS) was defined as the 12-month postoperative score minus the pre-operative score. Patients were categorised into three groups: those with deteriorated function, those with unchanged function and those with improved function.

To determine if the individual changes were due to chance or not, we used the following approach. After transformation of the pre- and postoperative scores (using inverse, root square or logarithm function), the changes in physical function were normally distributed. Therefore, we used linear mixed models with random intercept and slope to regress the transformed outcomes on the time of assessment.[339] We then determined if the individual changes between pre- and post-surgery assessments were different from 0 using the 95% CI around each participant's trajectories. This was derived from the post-estimation of the above models using fixed effects and subject-specific random effects. A 95% CI including 0 is not statistically significant, that is, the observed change is no different than a flat trajectory. This approach was preferred over the traditional relative change index measure as it does not depend on a deterministic external measure of test–retest reliability, which was not available for the studied scores. It also allows a better control of the regression to the mean effect by assuming that all scores are drawn from the same population distribution (shrinkage effect).

We also derived the minimum clinical important improvement (MCII) of each score, that is the improvement in functional score between two time points likely to be important from the patient's perspective. We used an anchoring question about participant satisfaction with recreational activities at 12 months post surgery[284] to dichotomise the ADAPT participants into two groups (very or somewhat satisfied vs. somewhat or very dissatisfied). We then calculated the cut-off point (MCII) on the distribution of score change, using a receiver operating characteristic curve analysis, to determine the threshold maximising the sensitivity and specificity. Patients experiencing an improvement greater or equal to this threshold were defined as having a clinically meaningful change in function.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

We also determined the observed ceiling effect for each score at 12 months post operation. The ceiling effect was defined as the percentage of patients with a score equal to the highest possible score. For example, a patient with a WOMAC function subscale score of 100 [score ranges from 0 to 100 (worst to best)] has reached the 'ceiling' of the score and is considered to have the maximum possible functional ability. For ease of interpretation, the lowest values of scores ranging in the opposite direction to the WOMAC function scoring system such as the Ab-IAP measures [Ab-I 0–36, Ab-A 0–68, Ab-P 0–36; best to worst] or the MYMOP2 score [0–6 (best to worst)] were considered as the 'maximum score'.

Results

This analysis was undertaken on patients who participated in both the baseline and 12-month assessments and provided information on at least one of the functional measures. Of the total cohort ($n = 263$, 130 hip replacement and 133 knee replacement patients), there were 104 hip replacement and 101 knee replacement patients who had this full data set and were included in these analyses.

Change in scores

The scores for the various functional measures, at baseline and 12 months post operation, are shown in *Tables 25* and *26*. *Tables 27* and *28* also record the changes in each of the scores between baseline and 12 months.

TABLE 25 Functional assessment measures before and after surgery

		Pre-operative assessment				12-month postoperative assessment			
Outcome measure	Site	*n*	Mean	SD	Median	*n*	Mean	SD	Median
WOMAC function	Hip	103	56.3	22.3	56.7	103	88.9	15.3	95.6
	Knee	101	51.9	18.4	50	101	75.2	23.1	83.8
SF-12 physical function subscale	Hip	100	33.1	8.9	32.3	97	47.5	11.0	51.5
	Knee	92	30.5	7.2	30.3	88	39.4	11.3	38.5
Ab-I	Hip	94	17.9	6.6	18	98	4.5	5.1	3
	Knee	94	19.6	5.4	20.0	99	10.2	7.4	8.0
Ab-A	Hip	99	23	11.7	22	102	7	8.5	4
	Knee	97	24.4	10.5	25.0	97	13.1	12.8	8.0
Ab-P	Hip	100	9.6	7.1	8	102	2.8	4.7	1
	Knee	96	11.0	6.0	10.0	95	5.5	5.8	3.0
MYMOP2	Hip	104	4.1	0.9	4.0	101	1.1	1.2	0.8
	Knee	99	4.3	0.8	4.3	101	2.0	1.5	1.8
Get-up-and-go test time (duration in seconds to complete the test)	Hip	96	20.8	14.8	17	97	13.7	6.0	12.0
	Knee	90	19.4	8.8	17.0	96	16.3	9.1	13.0
20-metre walk time (duration in seconds to walk a 20-metre distance)	Hip	102	25.5	14.8	22	103	18.8	5.8	17
	Knee	99	24.7	9.4	22.0	100	21.2	7.4	18.5
HHS	Hip	103	53.5	16.8	54.8	102	86.9	15.9	93.1
AKSS pain, stability and ROM	Knee	98	44.1	14.9	45	99	73.1	20.6	81
AKSS function	Knee	100	55.9	13.1	52.5	101	66.2	19.5	65.0

n, number of participants who completed the functional measure of interest.

TABLE 26 Functional assessment measures before and after surgery: proportion of participants who achieved performance tests

		Pre-operative assessment		12-month postoperative assessment	
Outcome	Site	*n*	%	*n*	%
Sit-to-stand-to-sit test	Hip	95	91.4	99	96.1[a]
	Knee	90	89.1	95	94.1
Missing	Hip	0		1	
	Knee	0		0	
20-cm step test	Hip	104	81.7	98	94.2
	Knee	82	81.2	92	91.1
30-cm step test	Hip	64	61.5	84	82.4[a]
	Knee	40	40.0[a]	71	70.3
Missing	Hip	0		2	
	Knee	1		0	
Balance	Hip	50	48.1	63	60.6
	Knee	39	38.6	46	46.0[a]
Missing	Hip	0		0	
	Knee	0		1	
Get-up-and-go test	Hip	96	92.3	98	94.2
	Knee	93	92.1	96	95.1
20-metre walk	Hip	104	100.0	103	99.0
	Knee	100	99.0	100	99.0

n, number of participants who achieved the specific test.
a Percentage of participants who achieved a specific performance test derived from the subsample of subjects with available information (e.g. at 12 months postoperatively, 99 participants out of the 103 with available information were able to perform the sit-to-stand-to sit test, i.e. 96.1% of the available sample).

Table 25 demonstrates that, as expected, scores on the function measures improve from baseline to 12 months. People in this cohort had better function after surgery than before they had the surgical intervention.

Table 26 shows similar results, suggesting that people's function improves after surgery. However, a particular feature of these data is the number of participants who were able to complete certain tasks. Nearly everyone could complete most of the tests, both before and after surgery. However, two of the tests appear to be more discriminatory – the 30-cm step test and the balance test. As shown in *Table 26*, only 61.5% of people with hip disease could do the 30-cm step test prior to surgery, and this improved to 82.4% postoperatively; the equivalent figures for those with knee disease were 40.0% and 70.3%, respectively. The balance test was also difficult for patients with knee disease; only 38.6% of patients could perform the test pre-operatively and 46.0% postoperatively. Those with hip disease could do a little better – 48.1% were able to do it pre-operatively, and 60.6% postoperatively.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Change for better or worse and clinically important improvements

The above scores tell only a part of the story. They do not provide information about what proportion of people got better or worse, or whether or not the improvements were clinically, as well as statistically, important. In order to answer these questions, we investigated the following:

1. the number of patients with scores that indicated improvement, deterioration or no change in function between baseline and 12 months
2. the numbers of patients in the improved or deteriorated function categories whose changes were statistically significant
3. the proportion of patients for whom these changes reached clinical significance, using the anchoring satisfaction question.

The results of these analyses are shown in *Tables 27* and *28*. The data also allow us to further compare the degree of improvement following knee or hip replacement.

As shown in *Tables 27* and *28*, there were a small number of people whose function did not change or deteriorate after surgery. Overall, each of the functional assessment methods is telling a similar story of a few people getting worse (but rarely significantly so) and most getting better, often significantly better. The walking time was more likely to show deterioration than other tests and arguably the 'get-up-and-go test' showed more differentiation between changes for the better or worse than other tests. Overall patients having hip surgery were more likely to improve functionally than those having knee replacement, with most of the measures used, although it is interesting to note that walking speed changes were very similar in both groups.

We also looked for ceiling effects on each of the functional measures at baseline and 12 months, as shown in *Tables 29* and *30*.

The striking finding here is that many of the self-assessment questionnaires that are routinely used to assess function in people with lower limb osteoarthritis show an important ceiling effect in response to joint replacement. The problem is particularly evident in the assessment of function after hip replacement; the WOMAC function subscale, SF-12 physical function measure and all three domains of the Aberdeen scale all reach a maximum score in between 20% and 50% of patients postoperatively. Rather fewer patients reached the maximum score after knee surgery, but the problem is a very real one for this intervention as well (between 8% and 22% of patients reaching the maximum on one or other of the scores). Timed tests such as the walk time or 'get-up-and-go' test, cannot, by definition, suffer from this problem and it is interesting to note that very few people achieved 'top marks' on either the HHS or AKSS.

Discussion

It is well known that, on average, people undergoing a hip or knee joint replacement get some functional benefit.[340] Our data support this, showing that, on average, there was a large improvement in the functional scores between baseline and 12 months after surgery. Our data also confirm findings from previous research that those undergoing hip surgery can, on average, expect more improvement in function that those having a knee replacement.[341,342]

However, average scores obscure the fact that there can be big differences in the change and that some people may experience a decline in function. Our data suggest that very few people get worse, although quite a lot of those who improve are not achieving a level of improvement that can be called clinically, rather than statistically, significant. For example, if we examine the data in *Table 27* carefully, they tell us that the WOMAC function score improved in 93% of people having hip replacement and 86% of those having knee replacement, and that this change was statistically significant in 90% and 82%, respectively. However, the change for the better was clinically significant in only some 70% of those having hip replacement and 61% of the knee replacement patients. Clearly, there is a need to be cautious in relation to the information given to people when they have a joint replacement regarding expected functional outcomes (as opposed to pain improvement).

TABLE 27 Changes and MCII in self-reported functional measures between pre- and 12-month postoperative assessments

	Hip						Knee					
	Sample		Statistical change[a]		%MCII[b]		Sample		Statistical change[a]		%MCII[b]	
Outcome	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
WOMAC function												
Deterioration	5	4.9	2	40.0			12	11.9	3	25.0		
No change	2	2.0					2	2.0				
Improvement	95	93.1	90	94.7	66	69.5	87	86.1	82	94.3	62	71.3
Total	102	100.0	92	90.2	66	64.7	101	100.0	85	84.2	62	61.4
Unknown	2						0					
SF-12 physical function												
Deterioration	8	8.4	6	75.0			15	18.8	9	60.0		
No change	0	0.0					0	0.0				
Improvement	87	91.6	78	89.7	70	80.5	65	81.3				
Total	95	100.0	84	88.4	70	73.7	80	100.0	65	81.3	31	38.8
Unknown	9						21					
Ab-I												
Deterioration	2	2.2	1	50.0			11	11.8	7	63.6		
No change	1	1.1					2	2.2				
Improvement	87	96.7	86	98.9	61	70.1	80	86.0	75	93.8	62	77.5
Total	90	100.0	87	96.7	61	67.8	93	100.0	82	88.2	62	66.7
Unknown	14						8					
Ab-A												
Deterioration	6	6.2	4	66.7			15	16.0	7	46.7		
No change	1	1.0					2	2.1				
Improvement	90	92.8	87	96.7	80	88.9	77	81.9	68	88.3	66	85.7
Total	97	100.0	91	93.8	80	82.5	94	100.0	75	79.8	66	70.2
Unknown	7						7					
Ab-P												
Deterioration	5	5.1	2	40.0			8	8.8	4	50.0		
No change	6	6.1					7	7.7				
Improvement	87	88.8	83	95.4	77	88.5	76	83.5	73	96.1	48	63.2
Total	98	100.0	85	86.7	77	78.6	91	100.0	77	84.6	48	52.8
Unknown	6						10					
MYMOP2												
Deterioration	3	3.0	1	33.3			8	8.1	5	62.5		
No change	0	0.0					1	1.0				
Improvement	98	97.0	95	96.9	77	78.6	90	90.9	84	93.3	61	67.8
Total	101	100.0	96	95.1	77	76.2	99	100.0	89	89.9	61	61.6
Unknown	3						2					

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 27 Changes and MCII in self-reported functional measures between pre- and 12-month postoperative assessments (*continued*)

	Hip						Knee					
	Sample		Statistical change[a]		%MCII[b]		Sample		Statistical change[a]		%MCII[b]	
Outcome	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Get-up-and-go test time												
Deterioration	10	11.0	8	80.0			18	20.2	12	66.7		
No change	3	3.3					9	10.1			9	100.0
Improvement	78	85.7	74	94.9	74	94.9	62	69.7	56	90.3	62	100.0
Total	91	100.0	82	90.1	74	81.3	89	100.0	68	76.4	71	79.8
Unknown	13						12					

ROC, receiver operating characteristics curve.
a Proportion of participants who had experienced a statistically significant change. The change and its 95% CI were derived for each participant using a linear mixed model (with random intercept and slope). A participant change was considered statistically significant if the 95% CI of the change did not include 0 (i.e. rejection of the hypothesis of a flat trajectory).
b %MCII is the percentage of patients experiencing a functional improvement equal or larger than a specific threshold. This threshold is estimated from the subgroup of patients satisfied with their recreational activities at 12 months post surgery using a ROC approach.
Deterioration: decrease in functional ability, as measured by the score of interested, between the pre- and 12-month postoperative assessments.
No change: absence of change in functional ability, as measured by the score of interested, between the pre- and 12-month postoperative assessments.
Improvement: improvement in functional ability, as measured by the score of interested, between the pre- and 12-month postoperative assessments.

TABLE 28 Changes and MCII in clinician-administered tools and functional tests between pre- and 12-month postoperative assessments

	Hip						Knee					
	Sample		Statistical change[a]		MCII ROC		Sample		Statistical change[a]		MCII ROC	
Outcome	*n*	%	*n*	%	*n*	%[b]	*n*	%	*n*	%	*n*	%[b]
20-metre walk time												
Deterioration	15	14.9	12	80.0			19	19.4	15	79.0		
No change	10	9.9					12	12.2				
Improvement	76	75.3	67	88.2	67	88.2	67	68.4	57	85.1	47	70.2
Total	101		79	78.2	67	66.3	98		72	73.5	47	48.0
Unknown	3						3					
HHS												
Deterioration	5	5.0	2	40.0								
No change	0	0.0										
Improvement	96	95.1	91	94.8	86	89.6						
Total	101		93	92.1	86	85.2						
Unknown	3											

TABLE 28 Changes and MCII in clinician-administered tools and functional tests between pre- and 12-month postoperative assessments (*continued*)

	Hip						Knee					
	Sample		Statistical change[a]		MCII ROC		Sample		Statistical change[a]		MCII ROC	
Outcome	*n*	%	*n*	%	*n*	%[b]	*n*	%	*n*	%	*n*	%[b]
AKSS – knee score												
Deterioration							10	10.4	6	60.0		
No change							0	0.0				
Improvement							86	89.6	75	87.2	47	54.7
Total							96		81	84.4	47	49.0
Unknown							5					
AKSS – knee function												
Deterioration							15	15.0	15	100.0		
No change							16	16.0				
Improvement							69	69.0	69	100.0	56	81.16
Total							100		84	84.0	56	56
Unknown							1					

ROC, receiver operating characteristics curve.
a Proportion of participants who had experienced a statistically significant change. The change and its 95% CI were derived for each participant using a linear mixed model (with random intercept and slope). A participant change was considered statistically significant if the 95% CI of the change did not include 0 (i.e. rejection of the hypothesis of a flat trajectory).
b %MCII is the percentage of patients experiencing a functional improvement equal or larger than a specific threshold. This threshold is estimated from the sub-group of patients satisfied with their recreational activities at 12-month post-surgery using a ROC approach.
Deterioration: decrease in functional ability, as measured by the score of interested, between the pre- and 12-month postoperative assessments.
No change: absence of change in functional ability, as measured by the score of interested, between the pre- and 12-month postoperative assessments.
Improvement: improvement in functional ability, as measured by the score of interested, between the pre- and 12-month postoperative assessments.

TABLE 29 Ceiling effects in patient-reported function measures at 12 months post operation

	Hip			Knee		
	Sample	Maximum score[a]		Sample	Maximum score[a]	
Outcome	*N* = 104	*n*	%	*N* = 101	*n*	%
WOMAC function						
Deterioration	5			12		
No change	2	2	100.0	2	0	0.0
Improvement	95	23	24.2	87	10	11.5
Total	102	25	24.5	101	10	9.9
Unknown	2			0		

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 29 Ceiling effects in patient-reported function measures at 12 months post operation (*continued*)

	Hip			Knee		
	Sample	Maximum score[a]		Sample	Maximum score[a]	
Outcome	*N* = 104	*n*	%	*N* = 101	*n*	%
SF-12 physical function						
Deterioration	8			15		
No change	0	0	0.0	0	0	0.0
Improvement	87	0	0.0	65	0	0.0
Total	95	0	0.0	80	0	0.0
Unknown	9			21		
Ab-I						
Deterioration	2			11		
No change	1	0	0.0	2	0	0.0
Improvement	87	20	23.0	80	6	7.5
Total	90	20	22.2	93	6	6.5
Unknown	14			8		
Ab-A						
Deterioration	6			15		
No change	1	1	100.0	2	0	0.0
Improvement	90	23	25.6	77	10	13.0
Total	97	24	24.7	94	10	10.6
Unknown	7			7		
Ab-P						
Deterioration	5			8		
No change	6	3	50.0	7	0	0.0
Improvement	87	43	49.4	76	17	22.4
Total	98	52	46.9	91	17	16.8
Unknown	6			10		
MYMOP2						
Deterioration	3			8		
No change	0	0	0.0	1	0	0.0
Improvement	98	22	22.5	90	9	10.0
Total	101	22	21.8	99	9	8.9
Unknown	3			2		

a % of patients with maximum possible functional ability as defined by the score; e.g., a patient with a WOMAC function score of 100 (0 worst to 100 best function); or with a Ab-A score of 0 (0 best to 68 worse function) would be considered by the WOMAC or Ab-IAP scoring system as having reaching the maximum possible functional ability.

Deterioration: decrease in functional ability, as measured by the score of interested, between the pre- and 12-month postoperative assessments.

No change: absence of change in functional ability, as measured by the score of interested, between the pre- and 12-month postoperative assessments.

Improvement: improvement in functional ability, as measured by the score of interested, between the pre- and 12-month postoperative assessments.

TABLE 30 Ceiling effects in clinician-assessed function measures at 12 months post operation

	Hip			Knee		
	Sample	Maximum score[a]		Sample	Maximum score[a]	
Outcome	*N* = 104	*n*	%	*N* = 101	*n*	%
Get-up-and-go test time						
Deterioration	10	NA	NA	18	NA	NA
No change	3	NA	NA	9	NA	NA
Improvement	78	NA	NA	62	NA	NA
Total	91	NA	NA	89	NA	NA
Unknown	13			12		
20-metre walk time						
Deterioration	15	NA	NA	19	NA	NA
No change	10	NA	NA	12	NA	NA
Improvement	76	NA	NA	67	NA	NA
Total	101	NA	NA	98	NA	NA
Unknown	3			3		
HHS						
Deterioration	5					
No change	0	0	0.0			
Improvement	96	4	4.2			
Total	101	4	4.0			
Unknown	3					
AKSS – knee score						
Deterioration				10		
No change				0	0	0.0
Improvement				86		2.0
Total				96	2	2.1
Unknown				5		
AKSS – knee function						
Deterioration				15		
No change				16	0	0.0
Improvement				69		11.0
Total				100	11	11.0
Unknown				1		

NA, not applicable.

a % of patients with maximum possible functional ability as defined by the score; e.g., a patient with a WOMAC function score of 100 (0 worst to 100 best function); or with a Ab-A score of 0 (0 best to 68 worse function) would be considered by the WOMAC or Ab-IAP scoring system as having reaching the maximum possible functional ability.

Deterioration: decrease in functional ability, as measured by the score of interested, between the pre- and 12-month postoperative assessments.

No change: absence of change in functional ability, as measured by the score of interested, between the pre- and 12-month postoperative assessments.

Improvement: improvement in functional ability, as measured by the score of interested, between the pre- and 12-month postoperative assessments.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

The data do suggest that there are important differences in what is being assessed by self-report, clinician-administered tools and functional assessments, as was apparent in our cross-sectional data. An important finding in relation to that is the fact that the self-assessment tests often used by rheumatologists to detect change in response to non-surgical interventions (e.g. WOMAC and SF-12) show a big ceiling effect when used in the surgical setting.

Assessment of the trajectories of change

Introduction

The analysis presented in the previous section (see *Longitudinal analysis of changes in the different measures of function over time*) showed that the majority of participants experienced an improvement in function after joint replacement. To supplement and extend on this work, we undertook further analyses to investigate participants' trajectories of recovery after joint replacement surgery, using data collected pre-operatively and at 3 months and 12 months after surgery.

First, we explored the trajectory of recovery, in terms of pain and function, in the first year postoperatively, with a particular focus on patients undergoing revision joint surgery. By including patients listed for different sort of surgical procedures, the ADAPT cohort study allowed us to investigate the specificities of pain and function changes following revision surgery. We then investigate how recovery of pain and function were interrelated. In these analyses, we used both a self-reported (WOMAC function) and objective measure of function (time to complete a 20-metre walk test) to identify any disparities in recovery pattern induced by assessment measure. Pain is a subjective experience and, therefore, we used the self-report WOMAC pain score for assessing pain severity. Finally, we present findings from a gait analysis study conducted on total primary hip replacement to shed light on the above self-reported versus objective findings comparison.

Statistical analysis

Analyses were conducted separately for patients undergoing hip and knee replacement surgery using Stata 13.1 (StataCorp LP, College Station, TX, USA).

Pain and function were analysed jointly using a multivariate linear mixed (MLM) regression with random intercepts and slopes. This approach allows the modelling of the longitudinal trajectory (patients' trajectory) of each outcome measure and the assessment of the correlations within and between these outcome measures (correlation structure) in a single regression framework while providing unbiased estimations in a context of missing data (under the missing at random assumption). Postoperative change over time was modelled as two linear splines: one spline for the 'immediate change' occurring between the pre-operative assessment and the first postoperative assessment (3 months) and another spline for the 'long-term change' occurring between the two postoperative assessments (3 and 12 months). These changes were normally distributed for each outcome allowing the use of MLM regression. However, the postoperative function and pain scores were not normally distributed preventing the use of this modelling framework to compare participants' scores at specific postoperative time points. Mann–Whitney *U*-tests were used for this purpose. The strength of correlation between parameters was interpreted as |0.00|–|0.25| = none–little, |0.26|–|0.49| = low, |0.50|–|0.69| = moderate, |0.70|–|0.89| = high, |0.90|–|1.00| = very high. *p*-values of ≤ 0.05 were considered statistically significant.

The MLM models were conducted on WOMAC pain and WOMAC function and replicated on WOMAC pain and time to complete the 20-metre walk test to investigate disparities in findings according to the method of functional assessment (self-reported vs. objective). The inverse of the 20-metre walk test completion time ($Time^{-1}$) was derived to facilitate the comparison of the effects between outcomes (lower scores: worse function/pain score/time of test completion; higher scores: best function/pain score/time of test completion).

To assess if the pattern of changes differed by surgery type, patients were split into two groups: primary surgeries (including primary total hip and knee surgeries, knee unicompartmental and patellofemoral surgeries and revision surgeries). WOMAC pain, WOMAC function and Time^{-1} were modelled separately with univariable linear mixed (ULM) regressions. It was not possible to model all these outcomes in a single multivariate framework as the numbers of patients in the subgroups were not sufficient to fit a MLM (hip: revision, $n = 43$; primary, $n = 80$; knee: revision, $n = 42$; primary, $n = 84$). The ULM models were adjusted for the two time splines defined above, surgery type, their interaction and random effects on each of these parameters. Differences in the immediate- and long-term changes by surgery type (primary vs. revision) were tested using appropriate contrasts. A similar approach was used to investigate the influence of pre-operative pain/function score on the postoperative recovery pattern: patients were split into groups of high or low level of pre-operative pain using the pre-operative WOMAC pain median as a cut-off point (hip: median = 55; knee: median = 40); they were also split into groups of high or low level of pre-operative functional ability using the pre-operative WOMAC function and time to complete the 20-metre walk test medians as cut-off points (hip: median WOMAC function = 56, time to complete the 20-metre walk test = 22^{-1} seconds; knee: 50 and 22^{-1} seconds, respectively).

Results

A total of 123 hip replacement participants were considered. Of these patients, 80 (65%) had a primary THR and 43 (35%) had a revision hip replacement. They had a mean age of 65 years (SD 11 years) and BMI of 28 kg/m^2 (SD 5 kg/m^2). Half of them were female ($n = 62$) and retired or unemployed ($n = 67$) and 24% ($n = 30$) were living alone. Approximately 75% ($n = 91$) had osteoarthritis in at least one other joint.

Of the 123 hip replacement participants with a pre-operative assessment, 121 (98%) completed a WOMAC pain and function measure and 118 (96%) performed the timed 20-metre walk test. Of the 112 (91%) patients who participated in a 3-month assessment, all completed the WOMAC pain and function scores and 107 (87%) completed the 20-metre walk test. At 12 months, 110 (89%) hip patients were still in the study, 109 (89%) completed the WOMAC function score, and 108 (88%) completed the WOMAC pain score and the 20-metre walk test.

A total of 126 knee replacement participants were considered. Of these patients, 48 (38%) had a primary TKR, 42 (33%) a unicompartmental knee replacement, 5 (4%) a patellofemoral knee replacement and 42 (33%) a revision knee replacement. They had a mean age of 67 years (SD 10 years) and a BMI of 31 kg/m^2 (SD 6 kg/m^2). Approximately 55% ($n = 69$) were female, 66% ($n = 83$) were retired or unemployed and 29% ($n = 37$) were living alone. Approximately 83% ($n = 104$) had osteoarthritis in at least one other joint.

Of the 126 knee replacement participants with a pre-operative assessment, 123 (98%) completed the three outcome measures. Of the 115 (91%) patients who participated in a 3-month assessment, 113 (90%) completed the WOMAC function score and 114 (91%) the WOMAC pain score and the 20-metre walk test. At 12 months, 112 (89%) patients were still in the study, 111 (88%) completed the WOMAC scores and 102 (81%) the 20-metre walk test.

Pain and function measures at the different assessment points are presented in *Table 31*.

Hip replacement: change in function and pain

As expected, both function (*Figure 13a*) and pain scores (*Figure 13b*) improved after surgery. These improvements occurred mainly within the first 3 months following surgery [*Table 32*: +0.24 of WOMAC function point/day ($p < 0.001$); +0.28 WOMAC pain point/day ($p < 0.001$)]. There was no evidence of further changes after 3 months (see *Table 32*: WOMAC function and WOMAC pain, p-values = not significant). A similar pattern of recovery was observed with the objective measure of function (*Figure 13c* and *Table 32*) with a statistically significant mean immediate change (+0.002 seconds^{-1}/month; $p < 0.001$) but no significant long-term mean change ($p = 0.057$). This latter effect is close to the 0.05 significance level, suggesting a marginal effect, but a larger sample would be required to provide a more definitive answer.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 31 Longitudinal measures of pain and function[a]

Outcome measure			Hip						Knee					
			n	%	Median	25th percentile	75th percentile	*p*-value[b]	*n*	%	Median	25th percentile	75th percentile	*p*-value[b]
WOMAC function	Pre-operative	Total	121	98.4	55.9	38.2	70.6		123	97.6	50.0	39.7	64.7	
		Low level	60	49.6	38.2	30.9	45.5	< 0.001	59	48.0	39.7	27.9	42.9	< 0.001
		High level	61	50.4	70.6	63.3	82.4		64	52.0	64.7	55.9	72.8	
	3 months	Total	112	91.1	89.7	80.9	95.6		113	89.7	72.1	60.3	89.7	
		Low level	56	50.0	86.0	74.3	92.7	< 0.01	52	46.0	65.9	44.1	75.0	< 0.001
		High level	56	50.0	91.4	85.3	97.1		61	54.0	83.8	69.1	94.1	
	12 months	Total	109	88.6	94.1	83.8	98.5		111	88.1	82.4	57.4	94.1	
		Low level	51	46.8	92.7	80.4	98.5	NS	54	48.7	64.7	39.7	85.3	< 0.001
		High level	58	53.2	95.6	87.5	100.0		57	51.4	91.2	73.5	95.6	
Timed 20-metre walk	Pre-operative	Total	118	95.9	22.0	18.0	28.0		123	97.6	22.0	18.0	30.0	
		Low level	58	49.2	29.0	25.0	35.0	< 0.001	60	48.8	30.0	27.0	38.5	< 0.001
		High level	60	50.9	18.0	16.0	20.0		63	51.2	18.0	16.0	20.0	
	3 months	Total	107	87.0	18.0	16.0	22.0		114	90.5	20.0	18.0	26.0	
		Low level	50	46.7	20.0	18.0	23.0	< 0.001	56	49.1	25.5	22.0	30.5	< 0.001
		High level	57	53.3	17.0	14.0	20.0		58	50.9	18.0	16.0	20.0	
	12 months	Total	108	87.8	17.0	15.0	21.0		102	81.0	18.5	16.0	24.0	
		Low level	50	46.3	20.0	17.0	23.0	< 0.001	47	46.1	24.0	20.0	30.0	< 0.001
		High level	58	53.7	16.0	14.0	17.0		55	53.9	17.0	15.0	18.0	

Outcome measure			Hip						Knee					
			n	%	Median	25th percentile	75th percentile	*p*-value[b]	*n*	%	Median	25th percentile	75th percentile	*p*-value[b]
WOMAC pain	Pre-operative	Total	121	98.4	55.0	35.0	70.0		123	97.6	40.0	30.0	60.0	
		Low level	66	54.6	40.0	30.0	50.0	< 0.001	62	50.4	30.0	20.0	40.0	< 0.001
		High level	55	45.5	70.0	65.0	80.0		61	49.6	60.0	50.0	70.0	
	3 months	Total	112	91.1	95.0	80.0	100.0		114	90.5	75.0	50.0	90.0	
		Low level	61	54.5	95.0	75.0	100.0	0.010	57	50.0	55.0	40.0	80.0	< 0.001
		High level	51	45.5	100.0	90.0	100.0		57	50.0	80.0	70.0	90.0	
	12 months	Total	108	87.8	100.0	85.0	100.0		111	88.1	80.0	55.0	95.0	
		Low level	57	52.8	95.0	75.0	100.0	NS	56	50.5	62.5	45.0	85.0	< 0.001
		High level	51	47.2	100.0	90.0	100.0		55	49.6	90.0	75.0	100.0	

NS, not significant.

a High and low pre-operative level of pain/function status are defined using median scores as cut-off threshold (hip: median WOMAC pain = 55, WOMAC function = 56, time to complete 20-metre walk test = 22^{-1} seconds; knee: 40, 50 and 22^{-1} seconds, respectively).

b Mann–Whitney *U*-tests comparing medians between high and low function groups.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

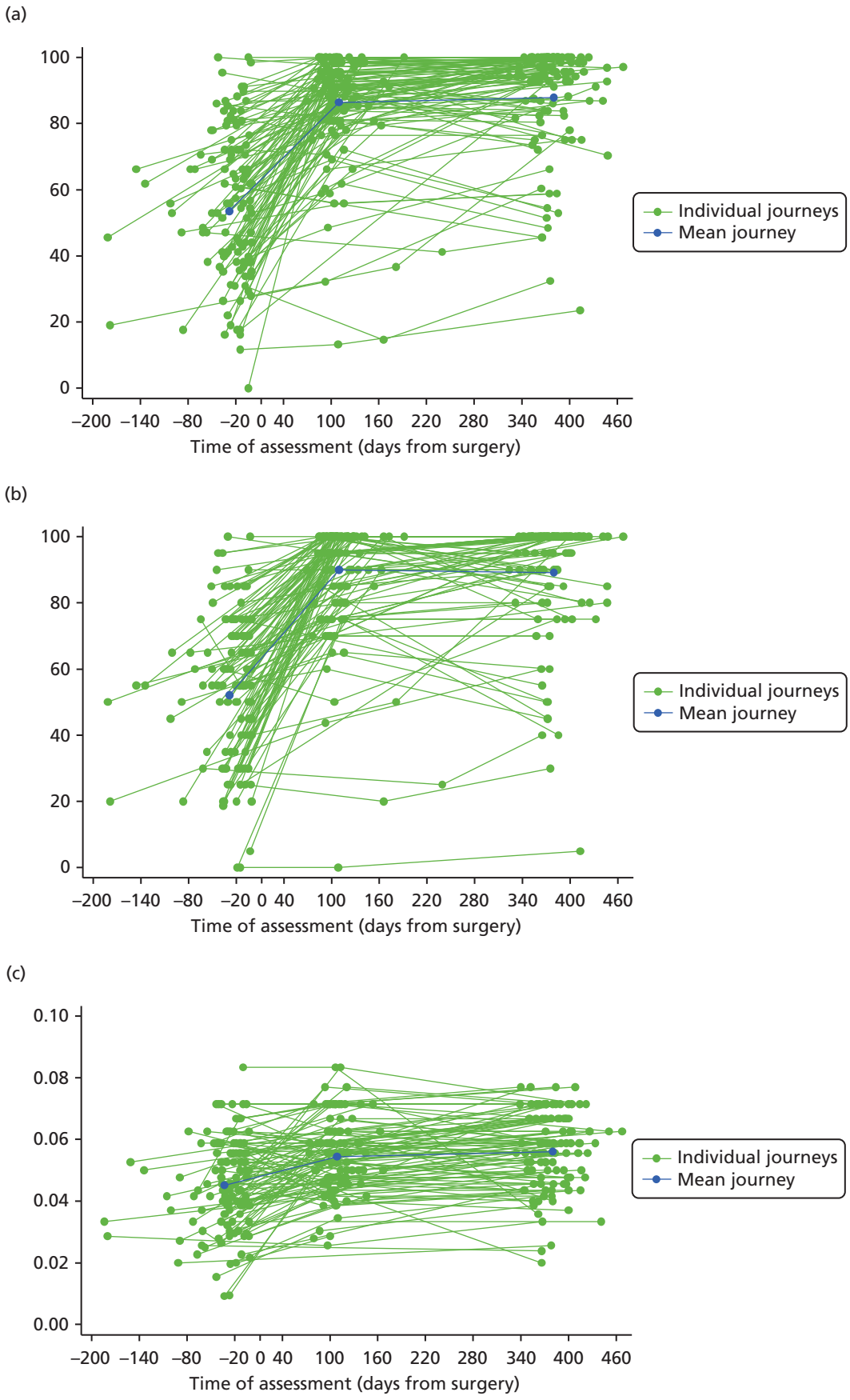


FIGURE 13 Change in pain and function from pre-operative to 12 months after hip replacement. (a) WOMAC function; (b) WOMAC pain; and (c) 20-metre walk test.

TABLE 32 Changes (Δ) and correlations between and within pain and function after hip replacement[a]

Hip	Self-reported function[b] and pain[c]			Objective function[d] and pain[c]		
Fixed effects	***Coefficient***	***95% CI***	***p-value***	***Coefficient***	***95% CI***	***p-value***
Pre-operative score: function[e]	59.93	56.30 to 63.57	< 0.001	0.05	0.04 to 0.05	< 0.001
Immediate Δ:[f] function[g,h]	0.24	0.20 to 0.28	< 0.001	0.002	0.001 to 0.002	< 0.001
Long-term Δ:[i] function[g,h]	0.01	–0.01 to 0.01	NS	0.00	–0.00 to 0.00	0.057
Preoperative score: pain[e]	59.74	56.20 to 63.28	< 0.001	59.74	56.20 to 63.28	< 0.001
Immediate Δ: pain[g]	0.28	0.24 to 0.31	< 0.001	0.28	0.24 to 0.31	< 0.001
Long-term Δ: pain[g]	0.00	–0.01 to 0.01	NS	0.00	–0.01 to 0.01	NS
Random effects	***SD[j]***	***95% CI***		***SD[j]***	***95% CI***	
Pre-operative score: function	20.48	17.72 to 22.92		0.01	0.01 to 0.01	
Immediate Δ: function	0.20	0.17 to 0.22		0.003	0.003 to 0.004	
Long-term Δ: function	0.05	0.04 to 0.05		0.001	0.001 to 0.001	
Preoperative score: pain	19.93	17.24 to 22.30		19.93	17.24 to 22.30	
Immediate Δ: pain	0.20	0.17 to 0.22		0.20	0.17 to 0.22	
Long-term Δ: pain	0.05	0.04 to 0.06		0.05	0.04 to 0.06	
Correlations	***Correlation[k]***	***95% CI***		***Correlation[k]***	***95% CI***	
Preoperative function: preoperative pain	0.78	0.71 to 0.85		0.39	0.24 to 0.54	
Preoperative function: immediate Δ function	–0.61	–0.72 to –0.49		–0.47	–0.62 to –0.33	
Preoperative function: long-term Δ function	–0.12	–0.31 to 0.06		–0.12	–0.31 to 0.07	
Immediate Δ function: long-term Δ function	–0.36	–0.52 to –0.19		–0.33	–0.50 to –0.16	
Preoperative pain: immediate Δ pain	–0.56	–0.69 to –0.44		–0.56	–0.69 to –0.44	
Preoperative pain: long-term Δ pain	0.13	–0.05 to 0.32		0.13	–0.05 to 0.32	
Immediate Δ pain: long-term Δ pain	–0.56	–0.69 to –0.43		–0.56	–0.69 to –0.43	
Preoperative function: immediate Δ pain	–0.45	–0.60 to –0.31		–0.17	–0.35 to 0.01	
Preoperative function: long-term Δ pain	0.06	–0.13 to 0.25		–0.04	–0.23 to 0.15	
Preoperative pain: immediate Δ function	–0.36	–0.52 to –0.20		–0.45	–0.60 to –0.30	
Preoperative pain: long-term Δ function	–0.10	–0.29 to 0.09		0.22	0.03 to 0.40	
Immediate Δ function: immediate Δ pain	0.76	0.68 to 0.84		0.49	0.34 to 0.63	

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 32 Changes (Δ) and correlations between and within pain and function after hip replacement[a] (*continued*)

Hip	Self-reported function[b] and pain[c]		Objective function[d] and pain[c]	
Immediate Δ function: long-term Δ pain	–0.38	–0.54 to –0.21	–0.14	–0.33 to 0.05
Immediate Δ pain: long-term Δ function	–0.25	–0.43 to –0.07	–0.15	–0.34 to 0.04
Long-term Δ function: long-term Δ pain	0.64	0.53 to 0.75	0.05	–0.14 to 0.25

NS, not significant.
a The fixed, random effects and correlations are estimated in one MLM model regressing (WOMAC pain and WOMAC function) and another regressing (WOMAC pain and Time^{-1} to perform 20-metre walk test) on the time of assessment parameterised as two linear splines (to assess immediate changes and long-term changes, see footnotes f and i).
b WOMAC function subscale.
c WOMAC pain subscale.
d Inverse of the time to perform a 20-metre walk-test.
e Intercepts: estimated mean function or pain score on the day of surgery.
f Immediate change: change in function or pain between the pre-operative and first postoperative assessment (≈3 months).
g The fixed-effect coefficient represents the daily change in WOMAC pain or WOMAC function for the period of change of interest (immediate- or long-term change). For example, around one-quarter of a WOMAC function point (0.24) per day during the first 3 months.
h The fixed-effect coefficient represents the monthly change in the inverse of time to complete the 20-metre walk test for the period of change of interest.
i Long-term change: change in function or pain between the first and second postoperative assessments (≈3 and ≈12 months).
j SD of the random effects associated with each of the parameters. Indicate the variability of the parameters across participants.
k Correlation coefficient between set of two parameters derived from the MLM models.

The mean trajectories are derived from the fixed effects of linear mixed models regressing WOMAC pain, WOMAC function and Time^{-1} to perform the 20-metre walk test on the time of assessment parameterised as two linear splines (to assess immediate changes and long-term changes, see *Table 32*, footnotes f and i).

This overall pattern of change in self-reported function was observed in both primary and revision surgery patient groups (*Figure 14a*). However, the immediate change was twice as large ($p < 0.001$) for the primary (+0.28/day, 95% CI 0.24 to 0.33; $p < 0.001$) than for the revision (+0.15/day, 95% CI 0.10 to 0.20; $p < 0.001$) surgery group. No significant long-term improvement in function was observed after 3 months for either group. As a result of the different pace in immediate recovery, and despite similar levels of pre-operative WOMAC function scores, the median level of functional ability observed at 12 months post operation was higher in the primary surgery group ($p = 0.01$).

Similar results were observed for WOMAC pain (*Figure 14b*). Those patients listed for a primary surgery had more pain pre-operatively than those in the revision surgery group ($p = 0.03$), but their immediate improvement was twice as large (+0.33/day, 95% CI 0.29 to 0.38, vs. +0.17/day, 95% CI 0.11 to 0.22); long-term mean changes in pain were not significant for both groups. At 12 months, the primary surgery group had caught up with the revision group and had similar pain score levels ($p =$ not significant).

In contrast, to the two other outcomes, the immediate improvements in walking time were similar for both surgical groups but their changes in objective function after 3 months were different ($p = 0.05$), being nearly flat for the revision group ($p =$ not significant) whereas patients in the primary surgery group continued to experience an improvement in their function ($p < 0.01$). Both groups had the same pre-operative walking speed, but at 12 months the primary surgery group did better ($p < 0.01$).

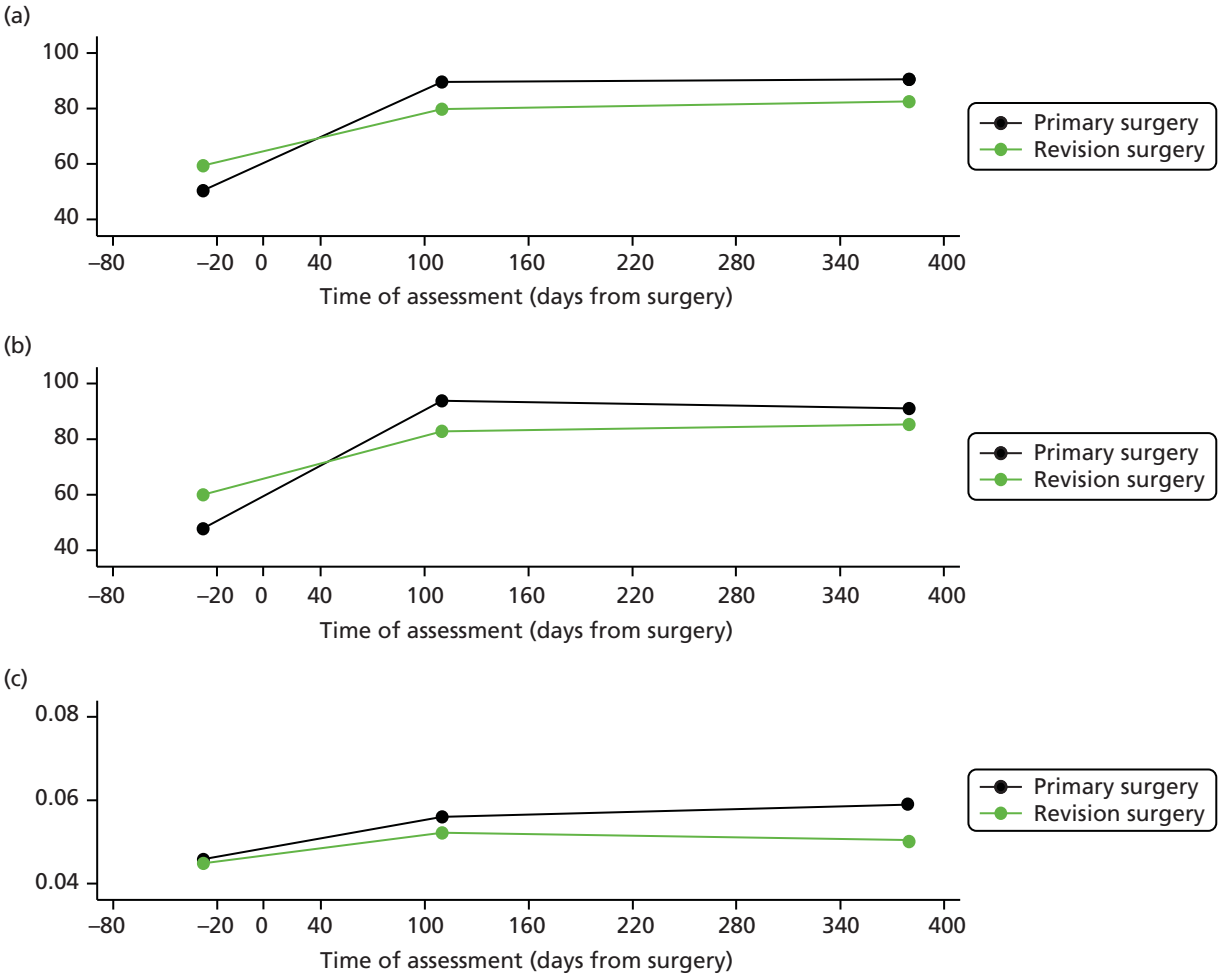


FIGURE 14 Change in pain and function from pre-operative to 12 months after primary and revision hip replacement. (a) WOMAC function; (b) WOMAC pain; and (c) 20-metre walk test. The mean trajectories are derived from the fixed effects of linear mixed models regressing WOMAC pain, WOMAC function and Time^{-1} to perform the 20-metre walk test on the time of assessment parameterised as two linear splines (to assess immediate changes and long-term changes, see *Table 32*, footnotes f and i), the surgery type and their interactions.

Hip replacement: correlation structure between and within pain and function

Two sets of correlations are presented in *Table 32*, one relating to the joint MLM modelling of pain and self-reported function ('self-reported model') and another relating to the modelling of pain and objective measure of function ('objective model').

Participants were more likely to concomitantly report high/low level of pre-operative pain and functional disability (correlation: + 0.78), similar direction of immediate (+ 0.76) and long-term (+ 0.64) pain and function improvements. When an objective measure of function was considered, these correlations were weaker or non-existent (0.39, 0.49 and 0.05). With regard to the 'functional improvement journey', high pre-operative functional disability was correlated with large functional improvement within the first 3 months following surgery and those with more favourable pre-operative functional scores had smaller immediate functional gain (–0.61 in the 'self-reported' and –0.47 in the 'objective' models). This evidence is illustrated in *Figure 15a* and *b*. Participants in the low pre-operative function group had an immediate functional improvement nearly 2.5 times larger than those who were in the high function group (difference in slope between high/low groups: $p < 0.0001$ for both self-reported and objective function). As reported in *Table 31*, the two groups of patients had statistically significantly different levels of pre-operative function but had similar levels of functional ability 12 months after surgery (WOMAC function). A significant difference was still observed after surgery when an objective measure of function was considered but the gap had reduced (see *Figure 15b*).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

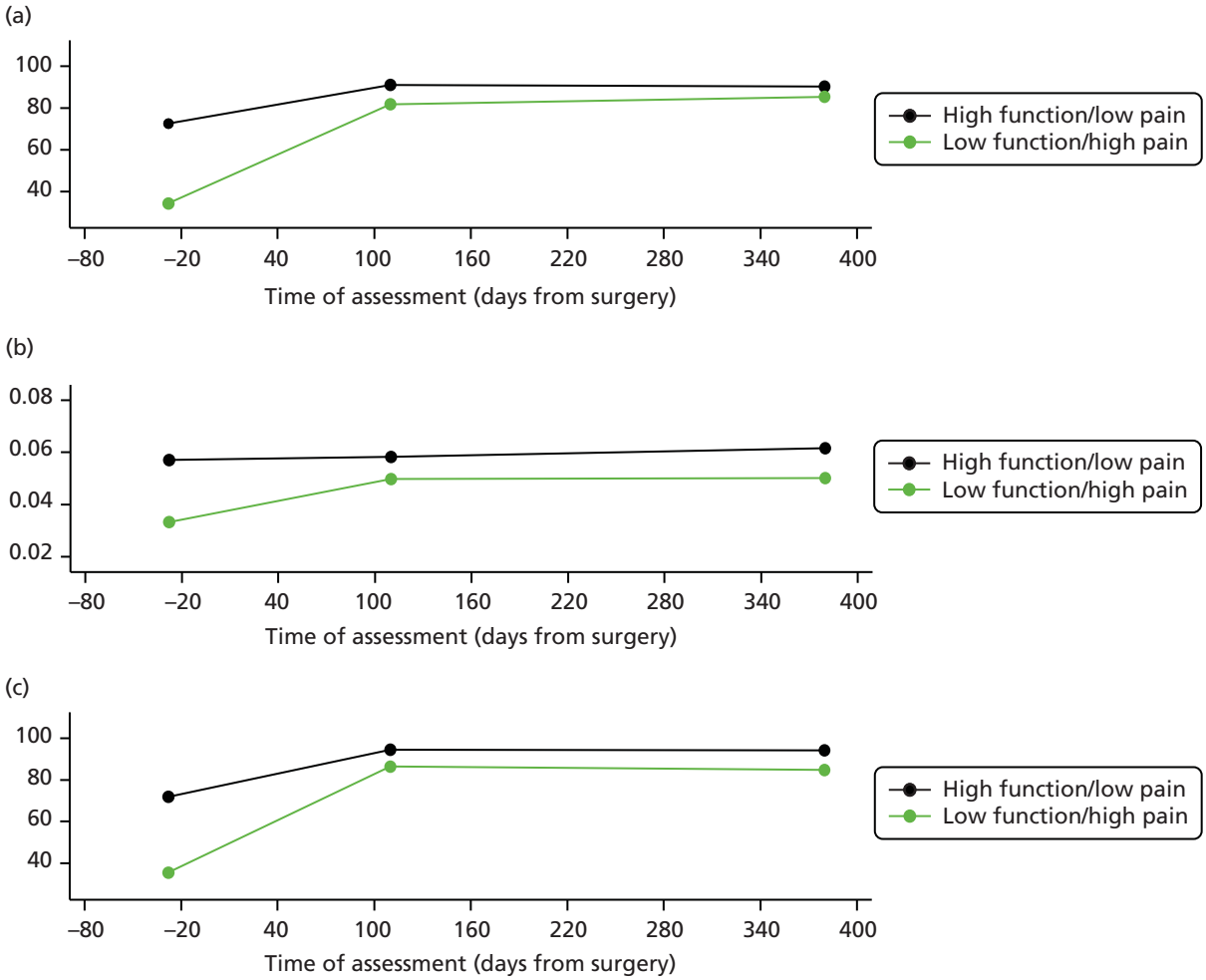


FIGURE 15 Change in pain and function from pre-operative to 12 months after hip replacement by pre-operative pain/function. (a) WOMAC function; (b) 20-metre walk test; and (c) WOMAC pain. The mean trajectories are derived from the fixed effects of linear mixed models regressing WOMAC pain, WOMAC function and Time^{-1} to perform the 20-metre walk test on the time of assessment parameterised as two linear splines (to assess immediate changes and long-term changes, see *Table 32*, footnotes f and i), the pre-operative status and their interactions. Pre-operative level of pain/function status are defined using median scores as cut-off threshold (median WOMAC pain = 55, WOMAC function = 56, time to complete the 20-metre walk test = 22^{-1} seconds).

No relationship was observed between the pre-operative functional scores and long-term changes (see *Table 32*, correlations < 0.25). Large/small immediate functional improvements were correlated with small/large long-term functional improvement (–0.36 in the 'self-reported' and –0.33 in the 'objective' models).

With regard to the 'functional improvement journey', high pre-operative functional disability was correlated with large functional improvement within the first 3 months following surgery while those with more favourable pre-operative functional scores had smaller immediate functional gain (–0.61 in the 'self-reported' and –0.47 in the 'objective' models). This evidence is illustrated in *Figure 15a* and c. Participants in the low pre-operative function group had an immediate functional improvement nearly 2.5 times larger than those who were in the high function group (difference in slope between high/low groups: $p < 0.0001$ for both self-reported and objective function). As reported in *Table 31*, the two groups of patients had statistically different levels of pre-operative function but had similar levels of functional ability 12 months after surgery (WOMAC function). A significant difference was still observed after surgery when an objective measure of function was considered but the gap had reduced (see *Figure 15b*).

No relationship was observed between the pre-operative functional scores and long-term changes (see *Table 32*, correlations < 0.25). Large/small immediate functional improvements were correlated with small/large long-term functional improvement (–0.36 in the 'self-reported' and –0.33 in the 'objective' models).

With regard to the pain improvement trajectory, a similar picture was found, with evidence of relationships between the pre-operative scores and immediate changes (–0.56) and between the immediate- and long-term changes (–0.56). Participants with a high level of pre-operative pain had an immediate change that was twice as large as those in the low-pain group (*Figure 15c*, difference in slope between high/low groups: $p < 0.001$) and the pre-operative difference in pain severity was no longer present at 12 months postoperatively (see *Table 31*).

Pain and function were inter-related and appeared to influence each others 'recovery journey' as shown by the correlations between them. The patient-reported pre-operative level of functional ability was related to immediate change in pain (–0.45), with higher functional improvement for patients with worse pre-operative pain and lower pain improvement for those with better baseline functional ability. This relationship was not observed when function was objectively measured (objective model). Similarly, the level of pre-operative pain was related to the immediate changes in self-reported function (–0.36) as well as with immediate changes in objective function (–0.45). Pre-operative self-reported function did not seem to be correlated with long-term changes in pain and pre-operative pain did not seem to be correlated with long-term changes in self-reported function. Immediate self-reported functional improvement was correlated with long-term pain improvements (–0.38), with smaller long-term changes for those who had large immediate changes or larger long-term changes. Similarly, immediate improvement in pain was correlated with long-term improvement in perceived functional ability (–0.25). These relationships were not observed in the 'objective model'.

Knee replacement: change in function and pain

Patients experienced an improvement in function (*Figure 16a*) and pain (*Figure 16b*) after their knee surgery. The improvements occurred mainly within the first 3 months following surgery (*Table 33*: + 0.18 of WOMAC function point/day, $p < 0.001$; + 0.21 WOMAC pain point/day, $p < 0.001$). There was no evidence of further changes after 3 months for WOMAC function (see *Table 33*: $p =$ not significant) but there was some suggestion of further long-term improvement for pain ($p = 0.051$). Contrary to the self-reported measure of function, the time to complete the 20-metre walk test (*Figure 16c* and see *Table 33*) improved significantly until the 12-month assessment [immediate change + 0.001 seconds^{-1}/month ($p < 0.001$); long-term change + 0.0002 seconds^{-1}/month ($p < 0.01$)], with steeper improvement in the first 3 months (difference between the two slopes, $p = 0.04$).

The differences in improvement patterns by surgical type group are presented in *Figure 17*. Patients in both the revision and primary groups experienced significant improvements within the first 3 months following their surgery in their subjective (*Figure 17a*; $p < 0.0001$ for both groups) and objective (*Figure 17b*, revision surgery, $p = 0.02$; other surgery, $p = 0.01$) measures of function. These immediate improvements in function were higher in the primary surgery group, the difference was not statistically significant ($p > 0.05$). Pain improved for both groups during the first 3 postoperative months (*Figure 17c*) but at a slower pace for the revision surgery group (+ 0.14/day, 95% CI 0.08 to 0.20; $p < 0.0001$) than for the primary surgery group (+ 0.25/day, 95% CI 0.21 to 0.29; $p < 0.0001$). No evidence of function or pain change was observed between 3 and 12 months, except in patients in the primary surgery group who experienced an improvement in their 20-metre walk test time completion (+ 0.0009 seconds^{-1}/month; $p = 0.01$). Pre-operative levels of pain and function (subjective and objective) were similar in both surgery groups ($p > 0.05$), but at 12 months those who had a revision surgery had worse median scores (WOMAC function, $p < 0.02$; WOMAC pain, $p < 0.01$; 20-metre walk test time, $p = 0.03$).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

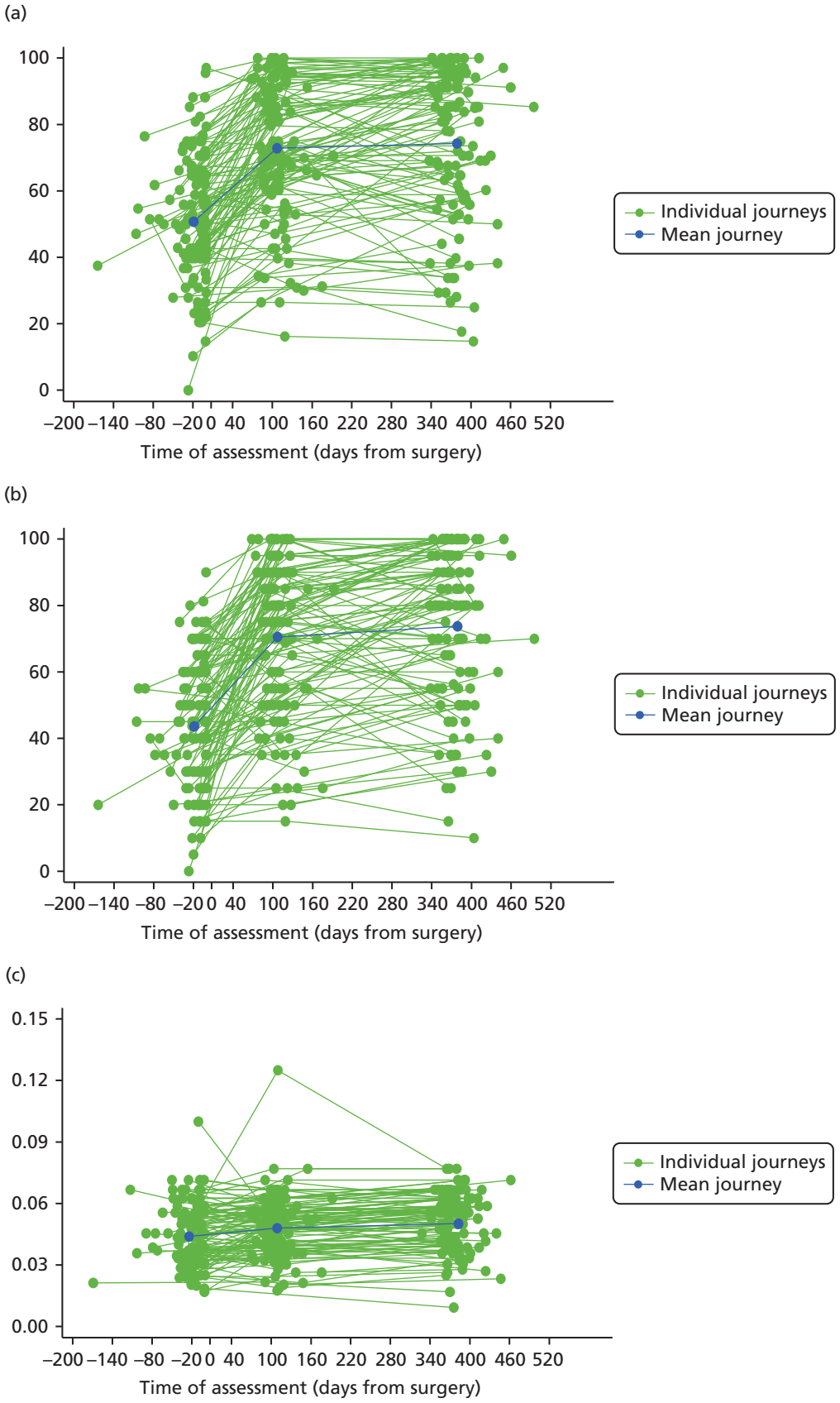


FIGURE 16 Change in pain and function from pre-operative to 12 months after knee replacement. (a) WOMAC function; (b) WOMAC pain; and (c) 20-metre walk test. The mean trajectories are derived from the fixed effects of linear mixed models regressing WOMAC pain, WOMAC function and Time^{-1} to perform the 20-metre walk test on the time of assessment parameterised as two linear splines (to assess immediate changes and long-term changes, see *Table 32*, footnotes f and i).

TABLE 33 Changes (Δ) and correlations between and within pain and function after knee replacement[a]

Knee	Self-reported function[b] and pain[c]			Objective function[d] and pain[c]		
Fixed effects	***Coefficient***	***95% CI***	***p-value***	***Coefficient***	***95% CI***	***p-value***
Pre-operative score: function[e]	54.07	50.86 to 57.28	< 0.001	0.05	0.04 to 0.05	< 0.001
Immediate Δ:[f] function[g,h]	0.18	0.15 to 0.20	< 0.001	0.001	0.000 to 0.002	< 0.001
Long-term Δ:[i] function[g,h]	0.01	–0.00 to 0.02	NS	0.0002	0.0001 to 0.0004	< 0.01
Preoperative score: pain[e]	47.64	44.38 to 50.90	< 0.001	47.64	44.38 to 50.90	< 0.001
Immediate Δ: pain[g]	0.21	0.18 to 0.25	< 0.001	0.21	0.18 to 0.25	< 0.001
Long-term Δ: pain[g]	0.01	–0.00 to 0.02	0.051	0.01	–0.00 to 0.02	0.051
Random effects	***SD[j]***	***95% CI***		***SD[j]***	***95% CI***	
Pre-operative score: function	18.25	15.80 to 20.40		0.01	0.01 to 0.02	
Immediate Δ: function	0.15	0.13 to 0.17		0.003	0.003 to 0.004	
Long-term Δ: function	0.05	0.05 to 0.06		0.001	0.001 to 0.001	
Preoperative score: pain	18.48	16.00 to 20.67		18.48	16.00 to 20.67	
Immediate Δ: pain	0.20	0.18 to 0.23		0.20	0.18 to 0.23	
Long-term Δ: pain	0.06	0.05 to 0.07		0.06	0.05 to 0.07	
Correlations	***Correlation[k]***	***95% CI***		***Correlation[k]***	***95% CI***	
Preoperative function: preoperative pain	0.81	0.75 to 0.87		0.29	0.13 to 0.45	
Preoperative function: immediate Δ function	–0.26	–0.43 to –0.09		–0.31	–0.48 to –0.15	
Preoperative function: long-term Δ function	–0.06	–0.25 to 0.13		–0.08	–0.27 to 0.12	
Immediate Δ function: long-term Δ function	–0.19	–0.37 to –0.01		–0.49	–0.64 to –0.35	
Preoperative pain: immediate Δ pain	–0.30	–0.46 to –0.13		–0.30	–0.46 to –0.13	
Preoperative pain: long-term Δ pain	–0.01	–0.20 to 0.18		–0.01	–0.20 to 0.18	
Immediate Δ pain: long-term Δ pain	–0.38	–0.54 to –0.22		–0.38	–0.54 to –0.22	
Preoperative function: immediate Δ pain	–0.16	–0.33 to 0.02		0.06	–0.12 to 0.24	
Preoperative function: long-term Δ pain	0.03	–0.16 to 0.21		0.12	–0.07 to 0.30	
Preoperative pain: immediate Δ function	–0.22	–0.40 to –0.05		–0.11	–0.29 to 0.07	
Preoperative pain: long-term Δ function	–0.09	–0.28 to 0.10		0.02	–0.18 to 0.21	
Immediate Δ function: immediate Δ pain	0.80	0.74 to 0.87		0.33	0.17 to 0.50	
Immediate Δ function: long-term Δ pain	–0.24	–0.42 to –0.07		–0.07	–0.26 to 0.12	

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 33 Changes (Δ) and correlations between and within pain and function after knee replacement[a] (*continued*)

Knee	Self-reported function[b] and pain[c]		Objective function[d] and pain[c]	
Immediate Δ pain: long-term Δ function	–0.05	–0.24 to 0.14	–0.01	–0.20 to 0.18
Long-term Δ function: long-term Δ pain	0.64	0.52 to 0.75	–0.04	–0.23 to 0.15

NS, not significant.
a The fixed, random effects and correlations were estimated in one MLM model regressing (WOMAC pain and WOMAC function) and another regressing (WOMAC pain and Time^{-1} to perform the 20-metre walk test) on the time of assessment parameterised as two linear splines (to assess immediate changes and long-term changes, see footnotes f and i).
b WOMAC function subscale.
c WOMAC pain subscale.
d Inverse of the time to perform a 20-metre walk test.
e Intercepts: estimated mean function or pain score on the day of surgery.
f Immediate change: change in function or pain between the pre-operative and first postoperative assessment (≈3 months)
g The fixed-effect coefficient represents the gain in WOMAC pain or WOMAC function per day for the period of interest (immediate- or long-term change). For example, around 0.18 WOMAC function point per day during the first 3 months.
h The fixed-effect coefficient represents the monthly improvement in time to perform the walk time.
i Long-term change: change in function or pain between the first and second postoperative assessments (≈3 and ≈12 months).
j SD of the random effects associated with each of the parameters. Indicate the variability of the parameters across participants.
k Correlation coefficient between set of two parameters derived from the MLM models.

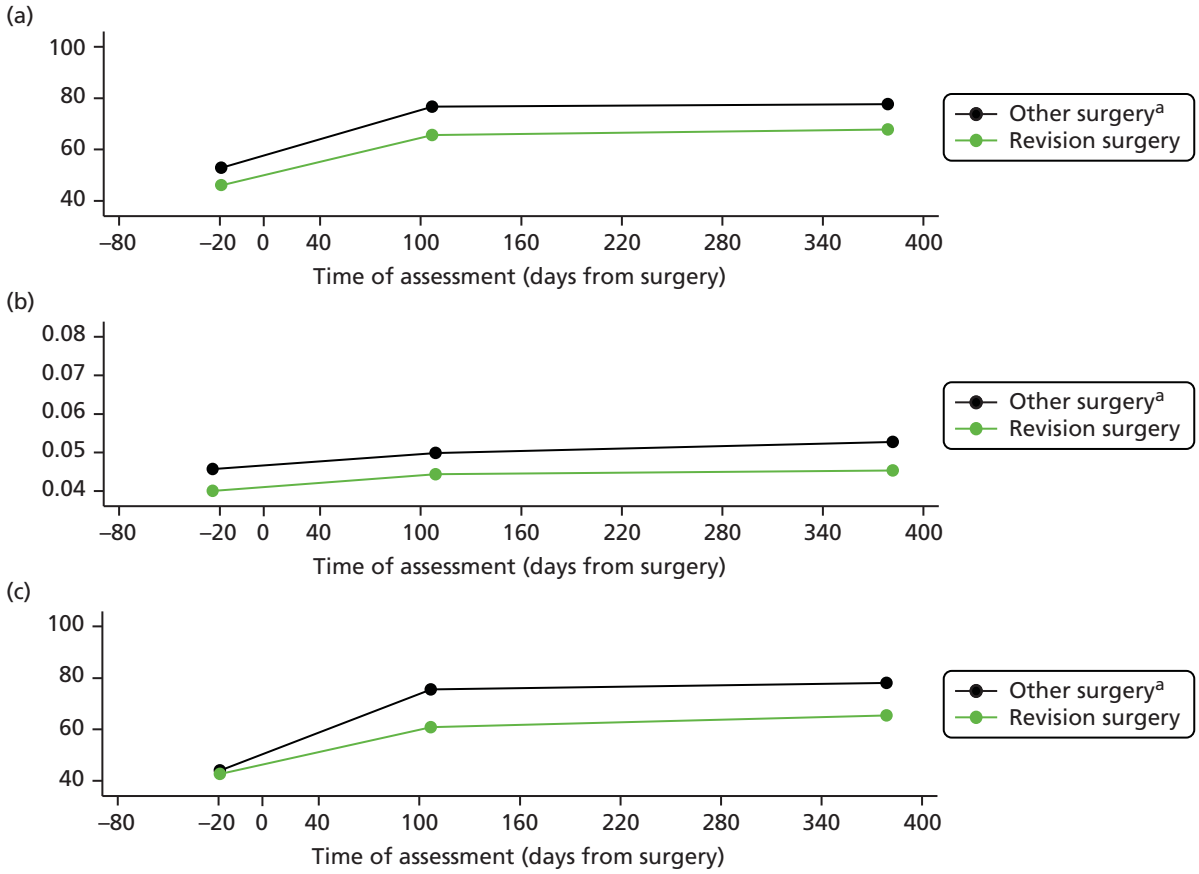


FIGURE 17 Change in pain and function from pre-operative to 12 months after primary and revision knee replacement. (a) WOMAC function; (b) 20-metre walk test; and (c) WOMAC pain. a, Other surgery includes primary, unicompartmental and patellofemoral procedures. The mean trajectories are derived from the fixed effects of linear mixed models regressing WOMAC pain, WOMAC function and Time^{-1} to perform the 20-metre walk test on the time of assessment parameterised as two linear splines (to assess immediate changes and long-term changes, see *Table 33*, footnotes f and i), the surgery type and their interactions.

Knee replacement: correlation structure between and within pain and function

The correlation structures of the 'self-reported' and 'objective' models are presented in *Table 33*.

Participants were more likely to concomitantly report high/low level of pre-operative pain and functional disability (+ 0.81), similar direction of immediate (+ 0.80) and long-term (+ 0.64) pain and functional improvements. When an objective measure of function was considered, the corresponding correlations were much weaker or negligible (+ 0.29, + 0.33 and –0.04).

With regard to the 'functional improvement journey', low/high pre-operative function scores were correlated with high/low immediate improvement in function (self-reported model –0.26, objective model –0.31). In *Figure 18a* and *b*, we can notice steeper immediate improvements for those in the low pre-operative function group than in those in the high pre-operative function group (difference in slope between high/low groups: WOMAC function, $p < 0.001$; Time^{-1}, $p = 0.012$).

The long-term changes in function did not seem to be related with the pre-operative scores (see *Table 33*). A weak relationship between the self-reported immediate- and long-term function change was observed (–0.19) whereas high/small immediate improvement in the 20-metre walk test completion time was correlated with small/high long-term improvement (–0.49).

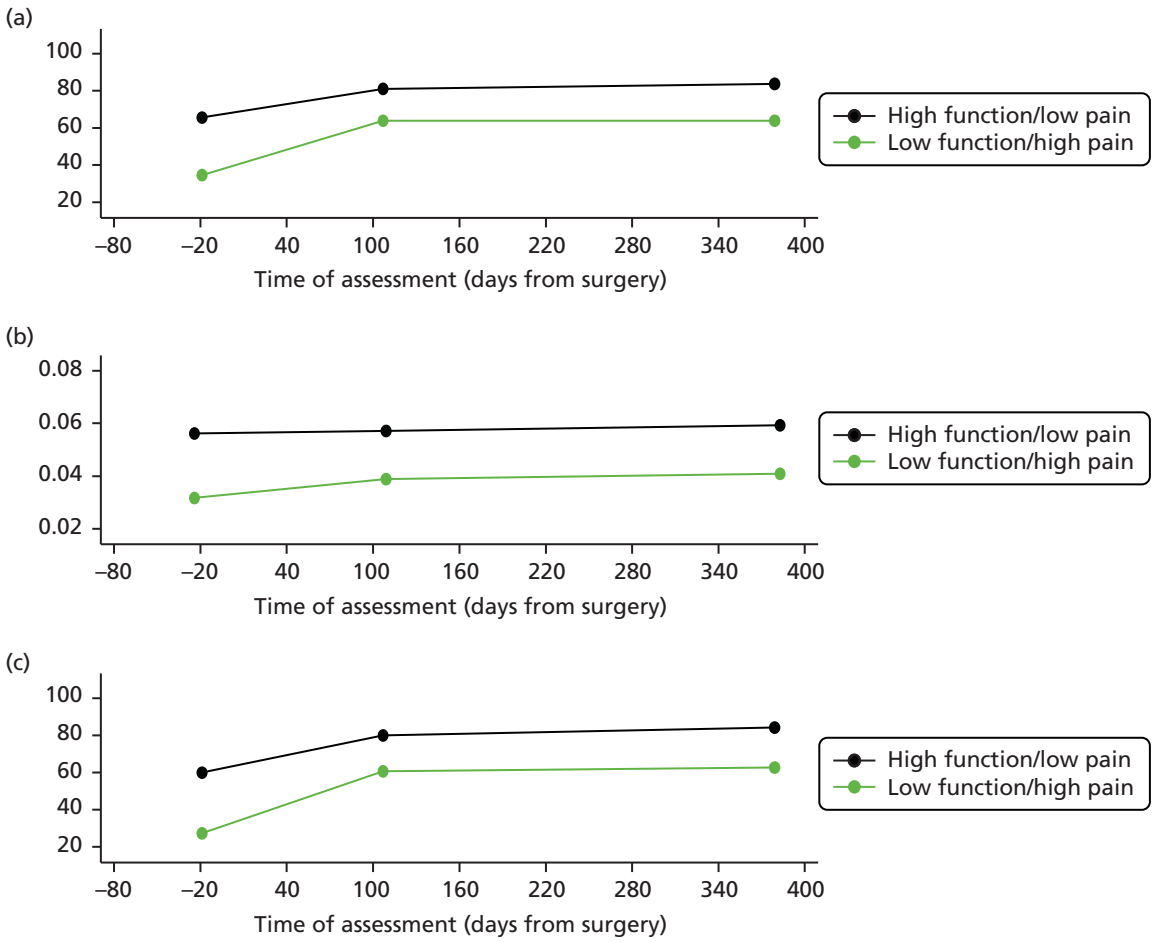


FIGURE 18 Change in pain and function from pre-operative to 12 months after knee replacement by pre-operative pain/function. (a) WOMAC function; (b) 20-metre walk test; and (c) WOMAC pain. The mean trajectories are derived from the fixed effects of linear mixed models regressing WOMAC pain, WOMAC function and Time^{-1} to perform the 20-metre walk test on the time of assessment parameterised as two linear splines (to assess immediate changes and long-term changes, see *Table 33*, footnotes f and i), the pre-operative status and their interactions. Pre-operative level of pain/function status are defined using median scores as cut-off threshold (median WOMAC pain = 40, WOMAC function = 50, time to complete the 20-metre walk test = 22^{-1} seconds).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

With regard to the 'pain improvement journey', large immediate pain improvements were correlated with high pre-operative pain level and small immediate improvement with low pre-operative level of pain (–0.30). This is illustrated in *Figure 18c*, which shows that immediate improvement was steeper for patients in the low pre-operative pain group than for those in the high pre-operative pain group (difference in slope between high/low groups, $p < 0.01$).

The long-term pain change was not related to the pre-operative pain scores (see *Table 33*). Those with larger/smaller immediate pain improvements also had smaller/larger long-term pain improvement (–0.38).

With regard to the pain–function inter-relation, that is, the influence on each other's 'journey', no evidence of relationship between the pre-operative function level and the postoperative changes in pain was observed. Pre-operative pain level was weakly correlated (–0.22) with immediate self-reported function change. This relation was not found with the objective measure of function. Long-term change in function appeared independent of the pre-operative pain severity. The self-reported immediate functional change was weakly correlated (–0.24) with long-term pain change, although this relationship was not observed in the objective model. The immediate pain change was not related to long-term change in function.

Assessment of function using accelerometry in patients receiving hip replacement

Patients were also invited to wear an inertial ambulatory motion sensor incorporating accelerometers and gyroscopes during the completion of the 20-metre walk test (see *Inertial sensor-based motion and gait analyses*). Participants were asked to walk along a straight flat corridor at their own preferred speed. Participants wore their own clothes and shoes but high-heeled shoes were not permitted. After crossing the finish line, one last step was allowed to establish a complete stop avoiding a significant slowdown within the 20 metres. The exact distance covered (20 metres + the last step) was measured and used for the following analyses. The test was conducted on the 36 patients listed for a primary THR without any history of previous lower limb joint surgery and with available longitudinal WOMAC function and ambulatory gait analysis data.

The collected measures are presented in *Table 34* and longitudinal changes are reported in *Figure 19*.

The 36 participants had the same pattern of WOMAC function recovery (see *Figure 19*) as the pattern observed in the overall sample (see *Figure 13*) – a large significant improvement within the first 3 months following the surgery ($p < 0.0001$) but no further improvement between 3 months and 12 months postoperatively ($p > 0.05$).

Pre-operatively, all the gait parameters had some weak to moderate correlations with WOMAC function (see *Table 34*). Apart from the 'range of motion pelvic obliquity' gait parameter, all the others maintained some weak correlations 12 months after the surgery. These findings suggest that the patient-reported measure partially reflect functional aspects captured by the gait analysis objective parameters.

Steps cadence and time to complete a step had the same course of longitudinal changes as the WOMAC function scores (see *Figure 19*).

Conversely, speed, ROM pelvic obliquity and step length continued to improve after the 3-month postoperative assessment ($p < 0.0001$).

The postoperative average changes in step irregularity and asymmetry were not statistically significant, suggesting that these aspects of function are not altered by THR surgery. However, there is a large heterogeneity in the patterns of individual changes (see *Figure 19*).

TABLE 34 Longitudinal measures of WOMAC function score and gait parameters and correlations between each gait parameter and WOMAC function

Outcome measure	Pre-operative			3 months			12 months		
n = 36	Median	IQR	*r*	Median	IQR	*r*	Median	IQR	*r*
WOMAC function	48.50	35.50–71.30		91.20	81.00–95.60		95.60	83.80–100.00	
Speed (metre/second)	0.97	0.81–1.12	0.51[a]	1.12	0.96–1.30	0.31	1.20	1.08–1.33	0.45[a]
Cadence (step/minute)	106.00	98.40–113.90	0.31	110.50	102.30–117.30	0.27	112.70	107.30–119.30	0.37
Step time (second)	0.57	0.53–0.61	–0.31	0.54	0.51–0.59	–0.24	0.53	0.50–0.56	–0.37[a]
Step length (metre)	0.54	0.48–0.62	0.47[a]	0.60	0.53–0.68	0.25	0.64	0.57–0.70	0.32
ROM (degree)	5.70	3.60–6.30	0.43[a]	6.40	5.30–7.90	0.14	7.50	5.50–8.40	0.14
Step irregularity (variability in successive steps of the same leg)	0.05	0.03–0.07	–0.06	0.05	0.03–0.06	–0.26	0.04	0.03–0.06	–0.39[a]
Step asymmetry (ratio of asymmetry between steps time (seconds) of both legs)	4.75	1.78–7.82	–0.11	2.92	1.58–7.05	–0.06	2.67	0.88–5.51	–0.33[a]

a Indicates a significant correlation ($p < 0.05$) of Spearman's r between gait parameter and WOMAC function.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

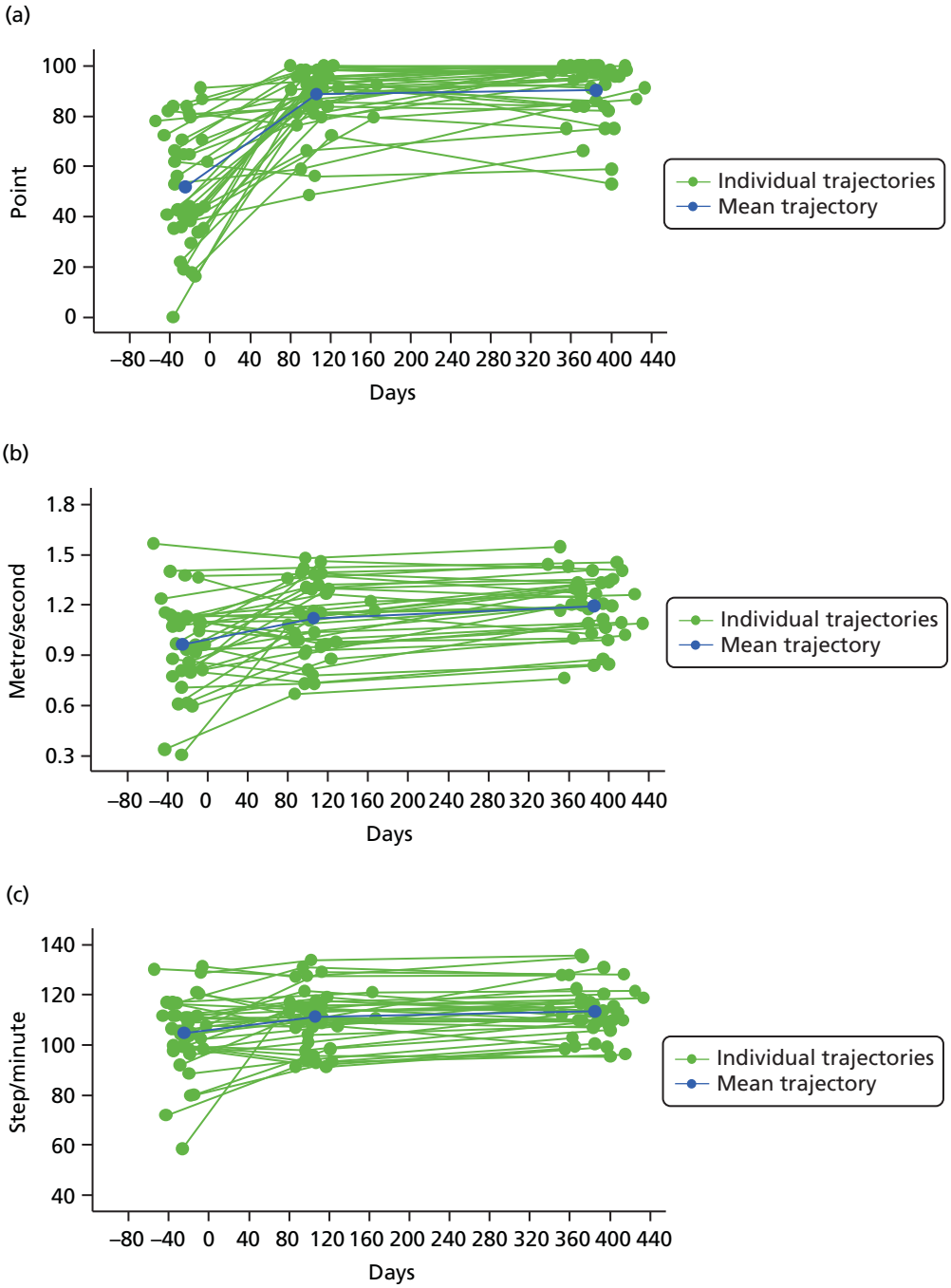


FIGURE 19 Change in patient-reported function and gait parameters from pre-operative to 12 months after hip replacement. (a) WOMAC function; (b) speed; (c) cadence; (d) ROM; (e) step time; (f) step length; (g) irregularities; and (h) asymmetries. The mean trajectories are derived from the fixed effects of linear mixed models regressing teach outcome on the time of assessment parameterised as two linear splines (to assess immediate changes and long-term changes, see *Table 33*, footnotes f and i). (*continued*)

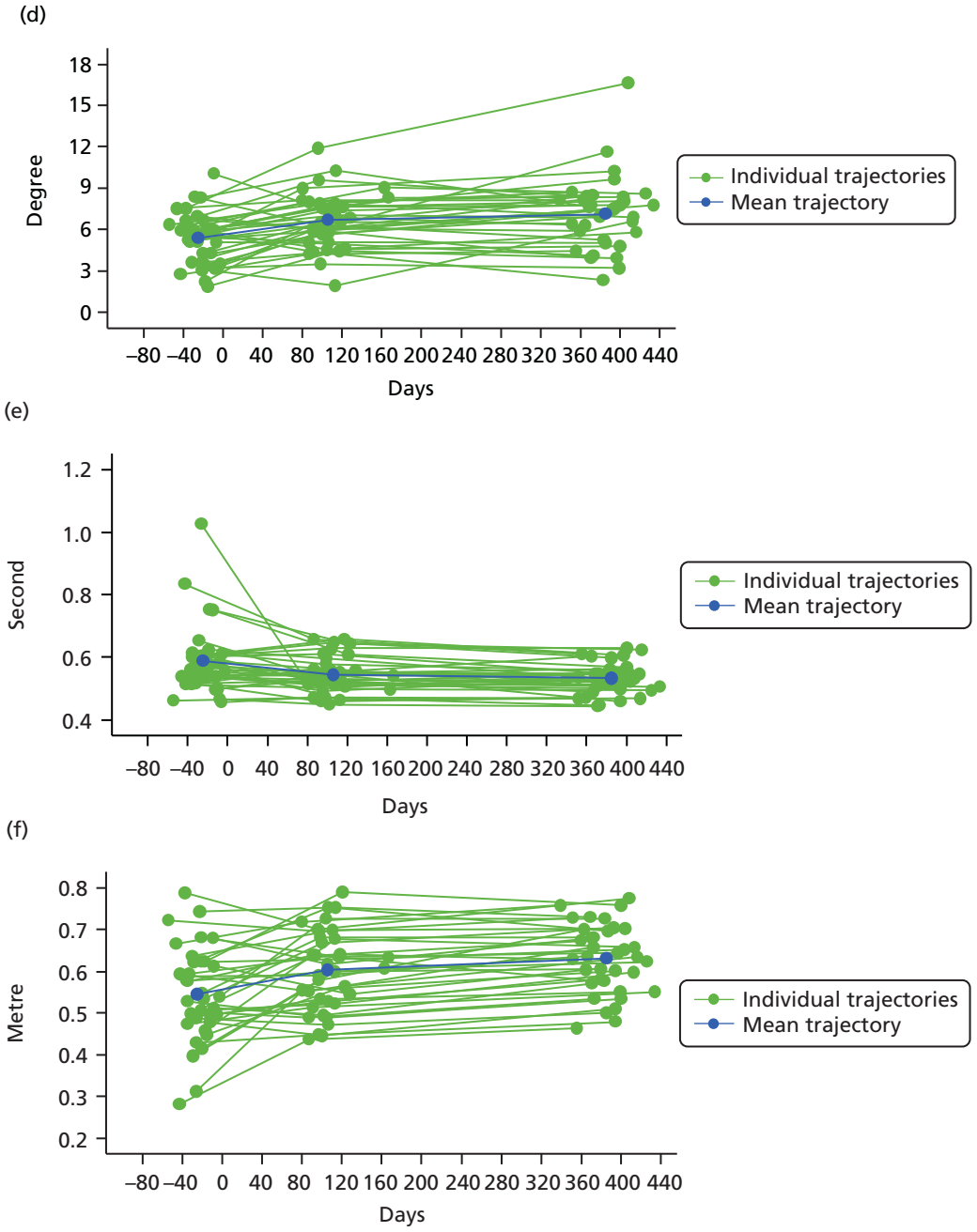


FIGURE 19 Change in patient-reported function and gait parameters from pre-operative to 12 months after hip replacement. (a) WOMAC function; (b) speed; (c) cadence; (d) ROM; (e) step time; (f) step length; (g) irregularities; and (h) asymmetries. The mean trajectories are derived from the fixed effects of linear mixed models regressing teach outcome on the time of assessment parameterised as two linear splines (to assess immediate changes and long-term changes, see *Table 33*, footnotes f and i). (*continued*)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

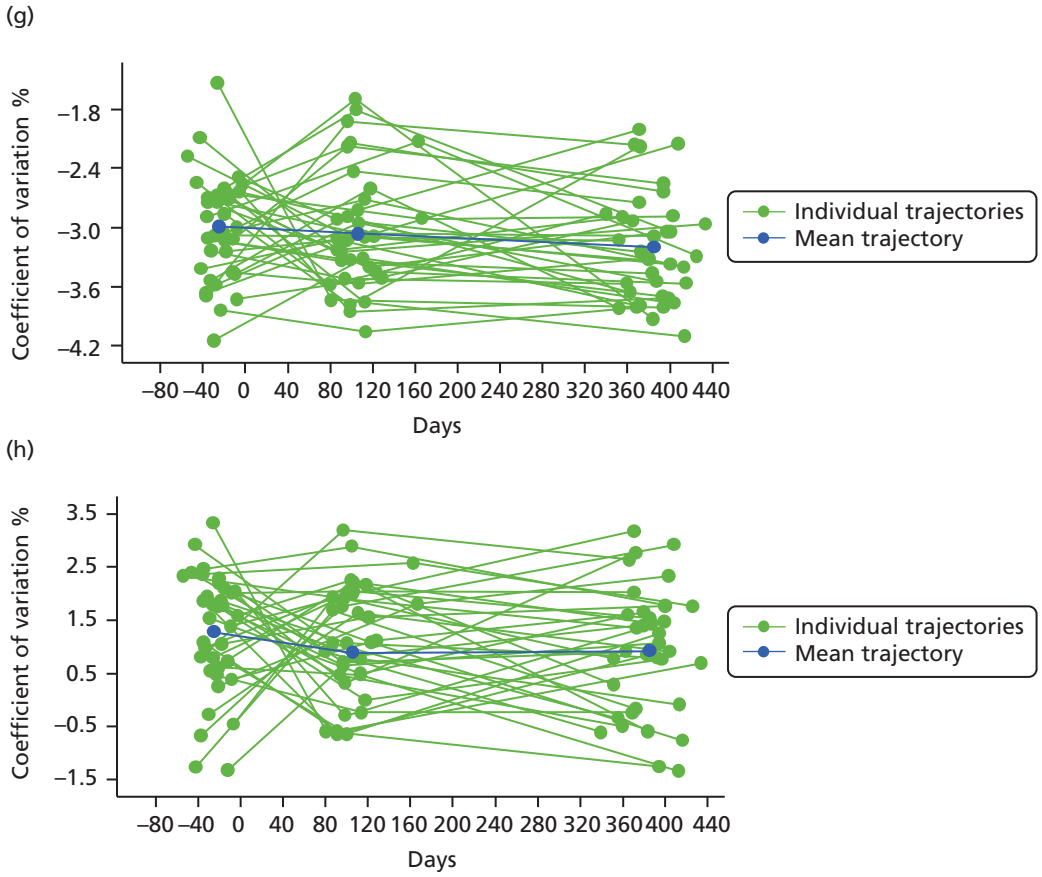


FIGURE 19 Change in patient-reported function and gait parameters from pre-operative to 12 months after hip replacement. (a) WOMAC function; (b) speed; (c) cadence; (d) ROM; (e) step time; (f) step length; (g) irregularities; and (h) asymmetries. The mean trajectories are derived from the fixed effects of linear mixed models regressing teach outcome on the time of assessment parameterised as two linear splines (to assess immediate changes and long-term changes, see *Table 33*, footnotes f and i).

Discussion

These findings indicate that the pain and function trajectories in the first year following hip or knee surgery are similar, with most of the improvement occurring within the first 3 postoperative months. No clear indication of further improvement was observed after the 3 months postoperative assessment for those undergoing hip surgery. However, for those who had knee surgery, function measured objectively (20-metre walk test) continued to improve until 12 months post operation.

The absence of improvement after 3 months post operation could be viewed as an artefact resulting from the ceiling effect inherent to score bounded PROMs such as WOMAC limiting the ability to detect improvement for patients recovering very quickly.[343,344]

However, the long-term mean changes associated with the objective function measures were marginal and much smaller than the one that occurred before 3 months and observed only among patients undergoing knee surgery. The gait analysis also revealed steeper slopes before 3 months and not all gait parameters had a statistically significant improvement beyond 3 months. Only residual changes might have to be expected after 3 months in proportion to those occurring before. The modest sample size of ADAPT limited our ability to adjust for factors known to be associated with the postoperative outcome such as age, sex, mental health and other comorbidities, and adjusted findings might have provided a slightly different picture. Our results are consistent with the existing literature.[48,341,342,345–350] Improvements in WOMAC physical function beyond 3 months were observed by Bachmeier and colleagues[48] in patients who had undergone hip replacement. However, changes in WOMAC pain were marginal. For patients with knee replacement, changes beyond 3 months in both WOMAC function and pain were marginal.

Heiberg and colleagues,[347] in Norway, found a small but significant improvement after 3 months post operation among hip surgery patients for pain and subjective and objective measures of function [HOOS and 6-metre walk test (6MWT)]. Kennedy and colleagues[348,349] found some further improvement between 3 and 6 months post knee or hip surgery but none thereafter using objective or PROMs measure of function [Lower Extremity Functional Scale (LEFS) and 6MWT] in a Canadian population. Halket and colleagues,[341] in Canada, and Naylor and colleagues,[350] in Australia, found hardly any improvement after 3 months in PROM measures of pain including WOMAC pain.

Interesting relationships have been found between the pre-operative score levels and postoperative changes. The pre-operative situation is negatively related to the immediate postoperative changes. The worse the situation before the surgery, the more likely the participants are to improve within the first few postoperative months; therefore, the better the pre-operative situation, the lower the immediate postoperative improvement. These findings can be induced by the ceiling effect inherent in the scoring system of PROMs in which those doing well have less room for improvement, magnifying the effect of those starting with lower scores. However, these negative correlations were also observed with the objective measure of function suggesting that more can be expected from the surgery when the patients have very poor pre-operative pain and function. Twelve months after their hip surgery, patients with poor pre-operative scores had caught up with those who had better pre-operative score. However, after their knee surgery, and despite a faster immediate improvement, participants with low function or high pain before their surgery still had significantly poorer function or pain level, even if the gap had reduced. This suggests that, even if there is a lot to expect from the joint surgery, any delay in the knee surgery might be associated with functional and/or pain degradation, which cannot be corrected by the operation. It is unlikely that these findings are driven by the revision/non-revision status of the knee participants. The prevalence of patients listed for a knee revision did not differ between high- and low-score groups; their pain or function pre-operative median scores did not differ from those listed for a first-time joint surgery.

For both groups, any intervention modifying the pre-operative pain level is likely to affect its course of immediate postoperative improvement, and the same is true for function. However, the relationship between pain and function differed between those having hip or knee surgery. For the hip patients, pain and function were interrelated whereas, for knee disease, no correlation between patients' pre-operative score levels and postoperative changes was found. This could suggest that separate interventions specific to pain and function need to be designed for knee pre- and postoperative rehabilitation whereas more generic hip intervention could affect both domains simultaneously.

Our findings suggest that patients undergoing primary or revision surgery will experience an improvement in pain and function but the pattern of recovery will differ between these two types of surgery. Despite similar or better function and pain scores for patients undergoing a revision surgery than for those undergoing a primary joint surgery, a revision surgery does not seem to bring as much pain and functional improvement 12 months later. This finding is congruent with the existing literature[351,352] and needs to be kept in mind when patients and clinicians discuss post-surgical expectations.

Finally, the pattern of functional recovery seems to be influenced by the method used to assess function, with significant long-term improvement observed in objective measure of function, but not with the self-reported measure. This could reflect the well-documented ceiling effect of the WOMAC function score. However, some of the gait analysis parameters, less subject to a ceiling effect, have a similar course of postoperative improvement as the self-reported measure of function. As the WOMAC function score is capturing information on several daily activities, this might also suggest that the potential loss of information induced by the use of a score-bounded instrument might not be as important as we think. It might also reflect the actual improvement pattern of some specific dimensions of function. Moreover, pain appears more correlated with the self-reported than with the objective measure of function. This might confirm previous work by Stratford and Kennedy[353] which suggested an internal limitation of the WOMAC index scores: 'activity overlap on the pain and function subscales plays a causal role in limiting the WOMAC physical function subscale's ability to detect change'.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

In all cases, these findings imply that it is valuable to use both self-reported and objective measures of function whenever possible. Doing so will capture a comprehensive longitudinal functional ability picture of patients undergoing joint replacement.

Discussion and conclusions

The ADAPT study aimed to investigate the different measures used to assess function in people undergoing hip or knee replacement and their responsiveness to the change resulting from joint replacement. The cohort included 263 people undergoing a mixture of hip and knee replacement, and primary and revision surgeries. This provided a mix of patients with a wide variety of different levels of disability, but the disadvantage of lacking homogeneity.

Our theoretical basis for the assessment of disability was the ICF, which differentiates between impairments, activities limitations and participation restrictions. We deliberately chose a number of different types of approach to functional assessment:

- standard self-report measures widely used in rheumatology practice (the WOMAC and SF-12)
- the Aberdeen measure, a recently developed self-assessment tool which differentiates between impairments, activities limitations and participation restrictions
- clinician-administered tools widely used by orthopaedic practitioners (HHS and AKSS)
- performance-based tests widely used by geriatricians ('get-up-and-go test', step tests, balance tests and walking time)
- accelerometry tests, which are a recent development and have the promise of providing us with a more objective way or assessing function.

Measures were made immediately prior to surgery, at the standard 3-month follow-up visit and at 1 year.

Our key findings are:

1. There is no 'right' way to assess function in patients undergoing joint replacement.

We had hoped at the outset of this study that we might be able to conclude that some measures should be used, and others discarded, but the data do not support this. Arguably the 'knee score' component of the AKSS is of questionable value because it correlates poorly with other measures. Each of the different methods of assessing function appears to be measuring something a little different and is influenced by different covariates, so nothing is 'right' and nothing is 'wrong'. The strongest correlations were between the different self-assessment measures and also between the different performance tests. However, the correlations between self-assessment measures and performance tests were much lower. This suggests that it might be wise to use one of each type of measure to obtain a satisfactory picture of the degree of functional loss in any individual patient. This is also confirmed by our comparisons of the longitudinal changes between patient-reported and performance test functional measures.

2. Self-assessment measures and functional tests are influenced by different factors.

We have shown that:

- Pain affects every type of functional assessment measure.
- Mental health status has a large influence on self-assessment measures but little effect on functional testing.
- Age (and sex in the case of the hip replacement) affects laboratory tests of function but not self-assessment measures.

We interpret this as confirming previous research that suggests pain and function are inextricably linked in musculoskeletal disability, that people with anxiety or depression may assess themselves as being worse off than they objectively are and that the influence of age on functional tests may be mediated by sarcopenia (a hypothesis that requires further investigation).

The implication is that measures of function may need adjustment for pain, psychological status, age and perhaps muscle strength if we are to obtain a satisfactory picture of functional loss.

3. Range of joint motion is not a satisfactory surrogate measure for function.

It is relatively easy to assess the ROM of the hip or knee and this measure is commonly carried out in clinical practice. Health-care professionals and patients often assume that it provides a useful surrogate measure of osteoarthritis severity and/or functional problems. It constitutes an important part of both the HHS and the AKSS.

Our data indicate that ROM does not correlate well with other measures of disease severity and we would suggest that it should not be given any weight in patient assessment.

The ROM, within the ICF classification, is a measure of impairment. Pain is generally considered to be an impairment measure as well[300] but in contrast to ROM correlates well with measures of activities limitations and participation restrictions. We would argue that it may be inappropriate to classify pain as an impairment measure in this context.

4. Function is improved 1 year after surgery in most, but not all, people.

Data on the outcomes of joint replacement are usually presented simply as the average difference in pain or function before and after surgery.

However, 'averages' do not tell us how many people might have got significantly (for them) better and, conversely, how many did not change or got worse. Our data are presented in such a way as to make these aspects of outcome totally explicit. They show that improvement that is both clinically and statistically significant will occur in some 90% of patients having a hip replacement and 70% of those having a knee replacement (an important difference between the two joint sites) and that, in contrast, some 5% of those having a hip replacement and 10% of those having a knee replacement will stay much the same or experience a deterioration in function 1 year after surgery. However, the degree of deterioration is rarely of clinical significance.

These data are important to patients and surgeons counselling them about the likely outcome of a joint replacement.

5. 'Ceiling effects' are a major problem for many measures of function.

A possible limitation of a measure of function, and one that we were keen to explore, is that it reaches a ceiling, so that patients cannot improve further on that score, even if their clinical status does improve. Our data indicate that this is a significant problem for self-assessment measures such as WOMAC in the context of joint replacement and, to a lesser extent, for the clinician-administered HHS and AKSS. The longitudinal and gait analyses revealed that some 'objective' functional parameters were still improving after the surgery when the WOMAC function scores were reaching a plateau. However, other 'objective' gait parameters did have a similar pattern of improvement, suggesting that perhaps this ceiling effect is not necessarily as extensive as we might think and the WOMAC function score is still providing an acceptable reflection of functional change.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

6. Walking speeds tell a different story.

We have put a reasonable amount of emphasis on the walking speed of patients in this study for three main reasons: first, it is a reasonably objective measure; second, it does not have a ceiling effect; and, third, it is a widely used surrogate measure of participation.[354–356] It also has some correlation with life expectancy.[357–362]

Our data indicate that walking does not show such as good a response to joint replacement as most of the other measures used. Patients are more likely to be worse 1 year after surgery on their walking time than on other measures and the amount of improvement is rarely large. We believe that walking time is more dependent on other variables, many of which are age related, than the other measures.

7. Patients with hip and knee disease respond differently to joint replacement.

It is widely thought that people have a better outcome after a hip replacement than after a knee replacement, and our data support this idea. The likelihood of improvement and the amount of improvement is much greater for people having hip replacement than knee replacement, and there are subtle but important differences in the nature of the response and its determinants.

Patients and joint replacement surgeons need to consider hip and knee osteoarthritis as different diseases. Pain and function seem also to be differently inter-related over time between these two diseases. A more tailored course of intervention may be required for knee osteoarthritis to tackle pain and function, whereas an intervention tackling one of these domains is also likely to affect the other one for hip osteoarthritis.

8. The chances of a good response to joint replacement depend on the severity of the disease at the time of surgery.

Our data show this very clearly. This is not a new finding, but the ADAPT cohort does shed some new light on this important aspect of joint replacement.

Our findings suggest that we should think about the journey (the amount of change after surgery) and the destination (the 'final' point reached 1 year after surgery). Patients with very severe disease at the time of surgery are more likely to have a good journey (i.e. pain and functional ability will probably improve substantially), whether patients have hip or knee disease. But the destination differs for the two joint sites. Those with hip disease can have a similar good destination, irrespective of the starting point, whereas those with knee disease can never 'catch up' (i.e. have as good a final outcome or destination) if they start off with very severe disease at the time of surgery. This is an important finding with the possibility that we may be delaying surgery too long for many people with knee disease.

Finally, our findings show that patients listed for a revision surgery had slightly better pre-operative pain and similar functional ability than those listed for primary surgery. However, their postoperative gains do not seem to be as large as the improvement experienced by patients with primary joint surgery. Clinicians and patients should be aware of this to discuss and set the expectations from a revision surgery.

Chapter 6 Perioperative pain management with local anaesthetic infiltration in total hip and knee replacement: systematic review, randomised controlled trial, cost-effectiveness study, evaluation of nurse recruitment methods and qualitative study of views and experiences of trial participation and use of analgesics

Parts of this chapter have been reproduced with permission from Horwood and colleagues.[363] Crown Copyright © 2015 Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/). Some parts have also been reproduced from Marques and colleagues[364] © 2015 Marques *et al.* This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated; and from Wylde and colleagues[365] © 2011 Wylde *et al*; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. In addition, some parts of this chapter have been reproduced from Marques and colleagues[366] © 2014 Marques *et al.*; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated; from Wylde and colleagues[367] © 2015 International Association for the Study of Pain. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 3.0 Licence; and from Mann C, Delgado D, Horwood J, Evaluation of internal peer-review to train nurses recruiting to a randomized controlled trial – Internal Peer-review for Recruitment Training in Trials (InterPReTiT), *J Adv Nurs* 2014, vol. 70, pp. 777– 90, with permission from John Wiley & Sons Ltd. © 2013 John Wiley & Sons Ltd.[368]

Abstract

Background

We evaluated the clinical effectiveness and cost-effectiveness of perioperative local anaesthetic infiltration on long-term pain after joint replacement. We also studied the experience of trial involvement for health-care professionals and patients.

Methods

In the APEX RCTs, 322 patients receiving total hip and 316 patients receiving TKR were randomised to local anaesthetic infiltration or standard anaesthesia. All patients with TKR received a femoral nerve block (FNB). We also appraised existing research in a systematic review and conducted qualitative interviews with 24 patients and 15 health-care professionals about involvement in the APEX trials.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Results

In the APEX RCTs, local anaesthetic infiltration was associated with reduced pain 1 year after THR. In patients receiving TKR, there was no strong evidence that local anaesthetic infiltration reduced pain additional to that provided by FNB. From the NHS and PSS perspective, local anaesthetic infiltration is a cost-effective treatment option in THR.

Systematic review identified 36 RCTs. Local anaesthetic infiltration was effective in reducing short-term pain, particularly with addition of post-closure analgesia. In TKR, there was no evidence of benefit additional to a FNB.

Patients and health-care professionals recognised the importance of participating in RCTs.

Conclusions

Patients with THR should receive local anaesthetic infiltration, which is a cost-effective treatment option for the management of long-term pain. For patients receiving TKR, it may not provide additional benefit to FNB.

Background

Many patients undergoing total hip or knee replacement experience significant pain while in hospital.[70] In addition to the obvious benefits of reducing patient suffering and distress, good perioperative pain control has the added advantage of allowing early mobilisation and rehabilitation.[67] This minimises risks of complications such as deep-vein thrombosis, pulmonary embolus, muscle and joint contractures, physical deconditioning and chest infection. Early mobilisation allows early discharge, with short-term inpatient cost-savings for the NHS. Unfortunately, many of the traditional methods of achieving perioperative pain relief, such as spinal or epidural anaesthetics and the use of opioids, can preclude early mobilisation.[71,72]

In diverse surgeries there is also evidence that increased levels of perioperative pain are associated with long-term pain, for example after breast surgery,[369] inguinal hernia repair[370] and thoracic surgery.[371] Large amounts of noxious input induced by surgery may contribute to the transition from acute to chronic pain through hyperexcitability and sensitisation of neurones within the central nervous system, leading to long-lasting amplification of pain signalling within the spinal cord.[66]

Perioperative pain is managed with multimodal pain control strategies, with analgesics relieving pain with additive or synergistic effects.[372] Incorporation of high-volume local anaesthetic infiltration into the multimodal regimen has been used during different surgical procedures. In a systematic review of local anaesthetic infusion into wounds at the end of surgical procedures, Liu and colleagues[373] identified studies dating from as early as 1983. The authors concluded that local anaesthetic infusion can improve analgesia, reduce opioid use and side effects, increase patient satisfaction and lead to reduced hospital stay. However, only one study included patients with TKR or THR.[374] Subsequently, more evaluations of local anaesthetic infiltration in joint replacement have been reported.[365]

Aims

Our aims were to:

- synthesise evidence from RCTs using systematic review and meta-analysis on the effectiveness of perioperative local anaesthetic infiltration for pain control in total hip and knee replacement
- assess, in RCTs, the clinical effectiveness of local anaesthetic infiltration administered before wound closure as part of the multimodal regimen on the short- and long-term severity of joint pain after total hip or knee replacement

- conduct an economic evaluation to determine the cost-effectiveness of local anaesthetic infiltration from a NHS and PSS perspective
- identify and address training needs of nurses involved in patient recruitment to RCTs using embedded qualitative methods
- explore, using qualitative methods, the experience of trial participation and surgery among patients and of trial involvement by health-care professionals.

Systematic review and meta-analysis of the effectiveness of perioperative local anaesthetic infiltration in total hip and knee replacement

Using systematic review methods and meta-analysis, our objective was to synthesise evidence from RCTs evaluating the effectiveness of perioperative local anaesthetic infiltration in reducing short- and long-term pain after hip and knee replacement. Secondary outcomes relate to opioid requirement, mobilisation and hospital stay.

Methods

General methods	As described in *Chapter 2*, *Systematic review methods*
Databases and dates	MEDLINE, EMBASE and The Cochrane Library from inception to 11 December 2012. Citations of key articles in ISI Web of Science and reference lists
Search strategy	Hip or knee replacement/RCTs/anaesthesia and analgesia. MEDLINE search strategy based on terms in *Appendix 3*
Study design	RCTs
Patients	Adults receiving primary total hip or knee replacement
Intervention	Local anaesthetic infiltration before wound closure. In addition, studies with intervention patients receiving additional delivery of analgesics through catheters and injections after wound closure. We excluded studies with interventions applied exclusively after wound closure
Controls	Patients receiving no local anaesthetic infiltration or placebo, or alternative analgesia regimens
Follow-up	Any time post operation
Data extraction	Country, baseline dates, participants (indication, age, sex), inclusion criteria, anaesthesia procedures common to randomised groups, intervention (including content of infiltrate, timing and volume), additional intervention group treatments, and control group treatment including placebo and alternative analgesia regimens
Outcomes	Pain at rest or during activity during hospital admission (24 and 48 hours after surgery); opioid consumption; mobilisation; length of hospital stay; and long-term pain and function. Complications were recorded and classified as serious (altered state of consciousness, atrial fibrillation, cardiac and hemodynamic changes requiring treatment, cardiac toxicity, central nervous system toxicity, dysarthria, dyspnoea, major surgical complications, pneumonia, pulmonary embolism, respiratory depression, seizures, swollen knee) or relating to deep infection. Vomiting and nausea
Quality assessment	Cochrane risk of bias: blind outcome assessment and losses to follow-up

Statistical analyses

We conducted meta-analyses for pain at rest and during activity at 24 and 48 hours, length of hospital stay and complications. Follow-up times were approximated to the closest timing. When not specified, we assumed measurements were taken at rest. Analyses were carried out in Stata 12 and RevMan 5. Results are reported with 95% CIs and funnel plots were inspected to assess for small study effects.[375] Given the number of potential effect modifiers, we used random-effects models for all meta-analyses.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

In meta-analysis, means and SD values of continuous variables, such as pain intensity, are required for intervention and control groups. Pain outcomes are sometimes reported as medians and IQRs owing to the recognised floor and ceiling effects of pain measures after successful pain management. This is less of an issue during early recovery. Kerr and Kohan[376] presented distributions of pain intensity scores at rest and while walking on the first and second day after total hip or knee replacement. The proportion of people reporting no pain and, thus, reflecting a floor effect, ranged from 2% to 35% on days 1 and 2, and pain intensities showed near normal distributions.

When no measures of variance were reported, we contacted authors to obtain SDs. If necessary we estimated means and SDs from medians and IQRs[96] from ranges using the method of Walter and Yao,[377] or imputed values from the average per arm across studies.

As pain scores are reported on different scales we used the SMD as our measure of treatment effect in meta-analyses.[378] To help in the interpretation of these pooled estimates, we multiplied SMD values by the mean SD on the widely reported 100-point VAS scale for the outcome. As the use of this method is entirely dependent on the chosen 'typical' value,[379] we used a mean SD calculated from control groups of all studies reporting the outcome.[96]

For length of hospital stay, we compared means and medians in studies reporting both and examined individual-level data provided by some authors.[380,381] Distributions were right-skewed and followed a log-normal distribution. Some studies reported means and SDs directly. For studies that reported medians and IQRs, or ranges, we estimated means and SDs on the log scale and then back-transformed them to the natural (unlogged) scale.[382]

Complications were compared between randomised groups using meta-analysis with summary statistics calculated as the Peto's OR, the method of choice when event rates are low.[96,383]

Analgesia regimen comparisons

Not all studies compared a local anaesthetic infiltration intervention with no intervention or placebo. Thus meta-analyses are reported separately for different regimen comparisons. These are summarised in *Figure 20*. Studies in patients with THR include comparisons A and B only. We report the combined comparison of groups (A + B) and further report A and B results separately. For studies in patients with TKR, we also report results from a combined meta-analysis across the first two subgroups (A + B), comparing local anaesthetic infiltration with or without further post-closure intervention against control. We further report all comparisons from A to E separately. Although we considered epidural analgesia as 'usual care' and, thus, included studies fort which this was used in comparisons A–E, we provide a summary of results.

Heterogeneity and subgroup analyses

Heterogeneity within meta-analyses was studied using tau-squared and I^2-statistics.[384] Sensitivity and subgroup analyses explored risk of bias in the study, use of additional analgesia delivered through a catheter or injection and inclusion of non-steroidal inflammatory agents or steroids in the infiltrate. We used meta-regression to quantify the differences in treatment effects between groups A and B.

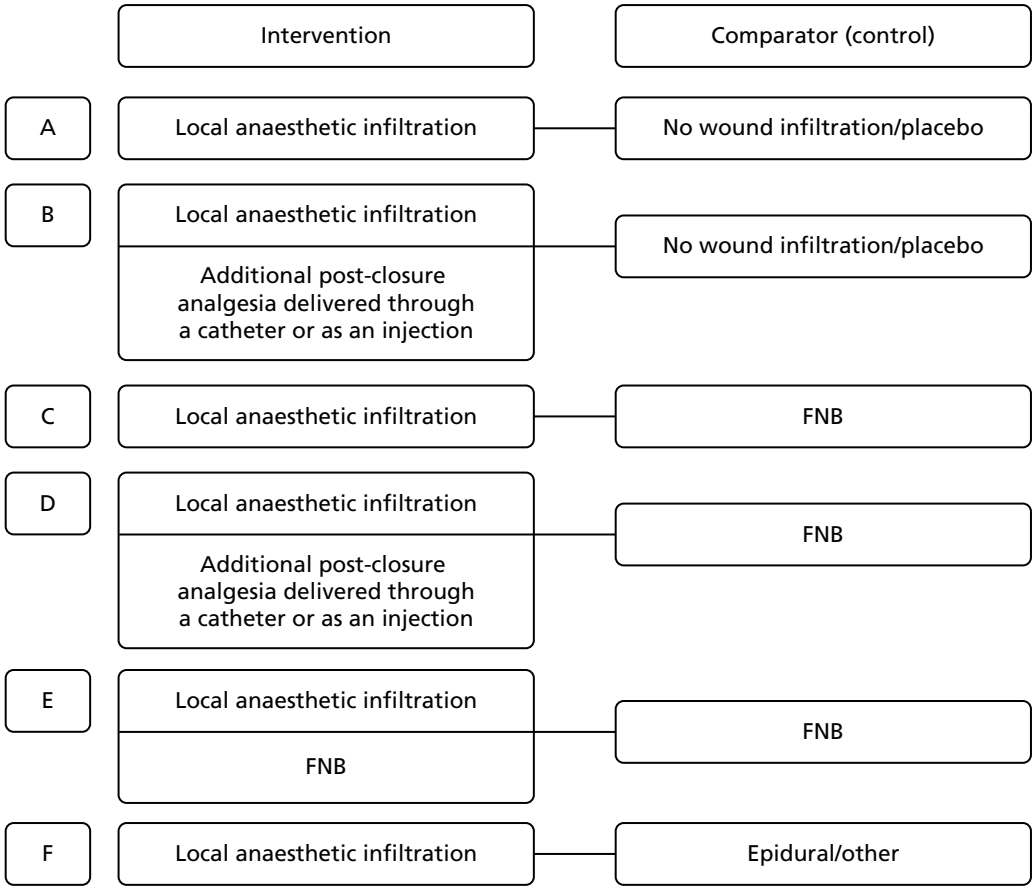


FIGURE 20 Systematic review of the effectiveness of perioperative local anaesthetic infiltration in total hip and knee replacement: possible anaesthesia regimens.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Results

The review process is summarised in *Figure 21*. Searches identified 839 articles, of which 33 described 36 RCTs evaluating local anaesthetic infiltration in total hip or knee replacement. Characteristics of included studies are shown in *Table 35* and a risk-of-bias assessment in *Appendix 9*. Thirteen studies were in patients undergoing THR[385–396] or included a large majority of THR patients.[374] Twenty-three studies were in patients undergoing TKR.[380,381,386,397–414]

Small study effects

Inspection of funnel plots for each meta-analysis gave no strong indication of publication bias or small study effects, but numbers of studies in individual analysis groups were small, such that assessment of asymmetry was difficult.

Total hip replacement

In 13 studies with 909 patients identified by searches, the mean number of patients with THR randomised was 70 (range 37–120). We assessed that 10 studies were at low risk of bias while three studies had unclear risk of bias owing to uncertainty about blinding of outcome assessments.

Results of the meta-analysis are summarised in *Table 36*.

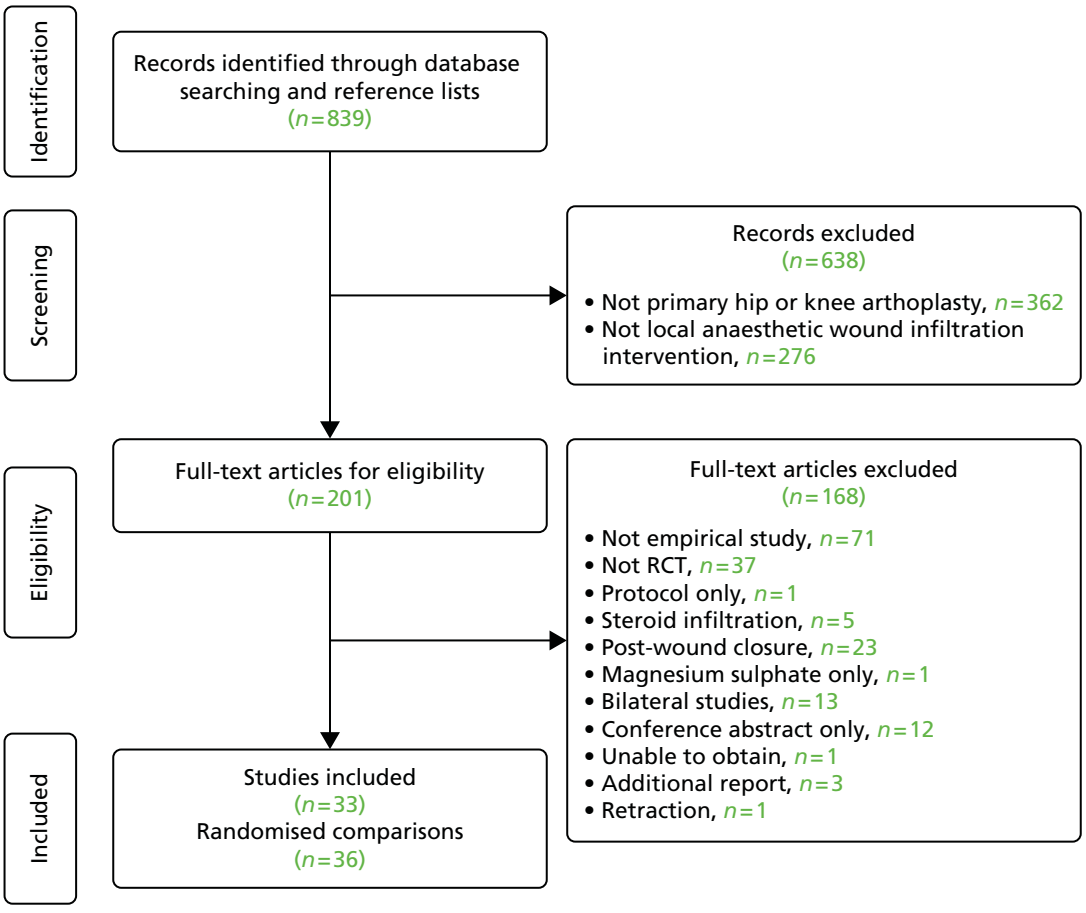


FIGURE 21 Systematic review of the effectiveness of perioperative local anaesthetic infiltration in total hip and knee replacement: flow diagram.

TABLE 35 Systematic review of the effectiveness of perioperative local anaesthetic infiltration in total hip and knee replacement: study characteristics

Study; country (date)	Inclusion; total patients (intervention : control); mean age (intervention : control); percentage female (intervention : control)	Common treatment		Latest post-surgical follow-up; outcomes; losses to follow-up (intervention : control)
		Intervention treatment (volume of infiltrate)		
		Further treatment (if given)	Control	
THR				
Aguirre and colleagues 2012;[387] Switzerland (date not specified)	Minimally invasive; $n = 76$ (38 : 38); 58 : 58 years; 53% : 50%	Spinal anaesthesia, PCA morphine 20 ml of solution containing 60 mg of ropivacaine injected into wound before closure Further continuous infusion through catheter	20 ml of placebo injection of saline Continuous infusion of saline through catheter	48 hours and to 3 months; i.v. morphine consumption, VAS pain at rest and with motion, electrocardiogram, skin inflammation or infection, satisfaction; 4 (2 : 2) lost to follow-up, three caused by catheter dislocation
Andersen and colleagues 2007;[385] Denmark (2005–6)	OA, elective; $n = 80$ (40 : 40); 62 : 61 years; 90% : 85%	Spinal, postoperative oral oxycodone hydrochloride as required 101.5 ml of solution containing 200 mg of ropivacaine, 30 mg of ketorolac (Toradol®, Roche) and 0.5 mg epinephrine infiltrated during surgery Further infiltrate through catheter intra-articularly 8 hours after surgery	Epidural infusion	96 hours; VAS pain, length of stay, time to mobilisation, side effects and complications, motor block (Bromage scale); 5 (2 : 3) patients lost to follow-up
Andersen and colleagues 2007;[388] Denmark (date not specified)	OA, uncemented, > 80 years; $n = 37$ (19 : 18); 62 : 64 years; 84% : 56%	Spinal anaesthesia, self-administered oral oxycodone as rescue medication 151.5-ml saline solution containing 300 mg of ropivacaine, 30 mg of ketorolac and 0.5 mg of adrenaline infiltrated during surgery Further infusion through catheter on day 1	Saline placebo infiltration Saline placebo infused through catheter on day 1	6 weeks; VAS pain at rest and on leg raise up to 8 hours, WOMAC pain to day 4, WOMAC pain, stiffness and function after 1, 2, 4, 6 weeks, EQ-5D at 6 weeks, patient-controlled analgesic use to discharge, adverse events; 3 patients out of 10 not fitting inclusion criteria were identified retrospectively; no losses to follow-up

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 35 Systematic review of the effectiveness of perioperative local anaesthetic infiltration in total hip and knee replacement: study characteristics (*continued*)

Study; country (date)	Inclusion; total patients (intervention : control); mean age (intervention : control); percentage female (intervention : control)	Common treatment		Latest post-surgical follow-up; outcomes; losses to follow-up (intervention : control)
		Intervention treatment (volume of infiltrate)		
		Further treatment (if given)	Control	
Bianconi and colleagues 2003;[374] Italy (date not specified)	THR and TKR (78% THR), elective; $n = 37$ (18 : 19); 66 : 64 years; 79% : 83%	Spinal anaesthesia. Loading dose of i.v. morphine at end of surgery		72 hours; VAS pain at 2, 4, 8, 12, 24, 48, 72 hours, opioid consumption (rescue medication), adverse events, length of hospital stay, patient satisfaction; no losses to follow-up
		40 ml of saline containing 200 mg of ropivacaine (Naropin®, Astra Zeneca) infiltrated at end of surgery	No placebo infiltration during surgery	
		Further ropivacaine infusion through catheter for 55 hours after closure	Saline infusion through catheter for 55 hours after closure	
		i.v. saline infusion for 24 h after surgery	i.v. morphine plus ketorolac infusion for 24 hours	
Busch and colleagues 2010;[389] UK (2003–5)	OA, age < 80 years; $n = 64$ (32 : 32); 61 : 65 years; 50% : 54%	General or spinal anaesthesia, PCA morphine		2 years; VAS at rest and activity, morphine consumption (PCA), VAS satisfaction, complications, HHS, WOMAC, length of hospital stay; no losses to follow-up
		100 ml of saline solution containing 400 mg of ropivacaine (HCl®, Astra Zeneca), 30 mg of ketorolac (Toradol®, Astra Zeneca), 5 mg of morphine (Sabex) and 0.6 ml of epinephrine (1 : 1000) (Abbott Laboratories) infiltrated during surgery	No placebo infiltration	
Dobie and colleagues 2012;[390] UK (2006–7)	OA or RA; $n = 96$ (50 : 46); 67 : 67 years; 38% : 52%	Spinal, general, i.v. morphine after surgery as required		6 days; VAS at 24 hours, morphine consumption, walking and stair test, mobilisation velocity and day, sit-to-stand test, home readiness, hospital stay, ILAS; 4 (4 : 0) patients did not receive intervention as planned. ITT results. Some data missing for one control
		160 ml of saline solution containing 200 mg of levobupivacaine and adrenaline	No local infiltration	

Study; country (date)	Inclusion; total patients (intervention : control); mean age (intervention : control); percentage female (intervention : control)	Common treatment		Latest post-surgical follow-up; outcomes; losses to follow-up (intervention : control)
		Intervention treatment (volume of infiltrate)		
		Further treatment (if given)	Control	
Lee and colleagues 2009;[391] South Korea (2006–7); note: additional pre-emptive analgesia and epidural	13% OA, 72% osteonecrosis; $n = 60$ (30 : 30); 51 : 55 years; 37% : 43%	General anaesthesia		5 days; VAS pain, ambulation, doses of parenteral analgesia, time to straight leg raise, complications; no losses to follow-up described
		Pre-emptive analgesia with oral oxycodone and celecoxib. Epidural anaesthesia	No pre-emptive analgesia	
			No epidural	
		90 ml of saline solution containing 5 mg of morphine, 40 mg of methylprednisolone and 6.8 mg of ropivacaine infiltrated during surgery	No injection during surgery	
		postoperative oral oxycodone and paracetamol	postoperative i.v. PCA and oral and injected analgesics as required	
Liu and colleagues 2011;[392] China (2008–9)	OA, ASA I–III, < 80 years; $n = 82$ (41 : 41); 74 : 74 years; 75% : 77%	Spinal anaesthesia, PCA morphine		15 days and 9 months (range 6–12 months) for infection; morphine use, VAS pain, surgical outcome, mobilisation (time to straight leg raise and 90 degree flexion); 2 (1 : 1) lost to follow-up
		60 ml of saline solution containing 5 mg of morphine, 30 mg of bupivacaine, 1 ml of betamethasone and 0.5 ml of epinephrine infiltrated during surgery	60 ml of saline infiltrated during surgery	
Lu and Li 2010;[393] China (date not specified)	Primary; $n = 40$ (20 : 20); no information on age and sex of patients	No description of common anaesthesia except PCA		48 hours; VAS pain, use of PCA pump, adverse drug reactions; no losses to follow-up apparent
		COX-2 inhibitor before surgery	No COX-2 inhibitor before surgery	
		100-ml solution containing 0.15% of ropivacaine infiltrated at end of surgery	100-ml saline placebo infiltrated at end of surgery	
		COX-2 inhibitor after surgery	No COX-2 inhibitor after surgery	
Lunn and colleagues 2011;[394] Denmark (2009–10)	Age > 18 years; $n = 120$ (60 : 60); 67 : 67 years; 55% : 65%	Spinal with or without general. Multimodal oral analgesia		8 hours and to discharge; VAS pain at rest and during walking and passive hip flexion, oxycodone consumption, complications; no losses to follow-up except 'pain during walking' with 18 (11 : 7) lost to follow-up
		150-ml saline solution containing 0.2% ropivacaine (AstraZeneca) and 10 µg/ml of epinephrine infiltrated during surgery	150 ml of saline placebo infiltrated during surgery	

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 35 Systematic review of the effectiveness of perioperative local anaesthetic infiltration in total hip and knee replacement: study characteristics (*continued*)

Study; country (date)	Inclusion; total patients (intervention : control); mean age (intervention : control); percentage female (intervention : control)	Common treatment		Latest post-surgical follow-up; outcomes; losses to follow-up (intervention : control)
		Intervention treatment (volume of infiltrate)		
		Further treatment (if given)	Control	
Murphy and colleagues 2012;[395] Ireland (2009–10)	OA; $n = 91$ (45 : 46); 57 : 54 years; 49% : 38%	Spinal, PCA opioid analgesia 60 ml of saline containing 150 mg of levobupivacaine infiltrated during surgery	60 ml of saline placebo	72 hours; WOMAC pain, McGill Pain Questionnaire, VAS pain, morphine consumption, complications; 13 (6 : 7) lost to follow-up but some analyses used multilevel modelling to handle missing data
Parvataneni and colleagues Hip 2007;[386] USA (2005–6)	OA; $n = 71$ (35 : 36); 64 : 61 years; 40% : 39%	Spinal anaesthesia with or without FNB Intraoperative infiltration of 200–400 mg of bupivacaine, 4–10 mg of morphine sulphate, 300 µg of epinephrine, 40 mg of methylprednisolone acetate, 75 mg cefuroxime and 22 ml of saline. Total volume approximately 33 ml	No infiltration during surgery Post-surgical PCA	3 months; VAS pain, total narcotic dose, functional recovery including time to straight leg raise, side effects of narcotic use, patient satisfaction; no losses to follow-up reported
Rikalainen-Salmi and colleagues 2012;[396] Finland (2009–10)	OA, ASA I–III; $n = 60$ (30 : 30); 65 : 66 years (followed up); 66% : 61% (followed up)	Spinal, propofol if required, oxycodone (Oxanest®, Nycomed or OxyNorm®, Mundipharma) rescue medication 101 ml of solution containing 125 mg of levobupivacaine (Chirocaine®, Abbott) and 30 mg of ketorolac (Toradol®, Roche) infiltrated during surgery 21 ml of solution containing 100 mg of levobupivacaine and 30 mg of ketorolac administered through catheter on morning of first postoperative day	Intrathecal morphine (2 mg/ml, Nycomed) No placebo infiltration Sham catheter attached to skin with 21 ml of air administered on morning of first postoperative day (not inserted into joint)	8 weeks; NRS pain at rest and motion, oxycodone consumption, mobilisation, fulfilment of discharge criteria, satisfaction, adverse events and complications; 3 (1 : 2) lost to early follow-up; 7 (4 : 3) lost to long-term follow-up

Study; country (date)	Inclusion; total patients (intervention : control); mean age (intervention : control); percentage female (intervention : control)	Common treatment: Intervention treatment (volume of infiltrate); Further treatment (if given)	Control	Latest post-surgical follow-up; outcomes; losses to follow-up (intervention : control)
TKR				
Affas and colleagues 2011;[397] Sweden (2007–8)	77.5% OA, 22.5% RA, age > 18 years, ASA I–III, primary; $n = 40$ (20 : 20); 67 : 69 years; 45% : 60%	Spinal anaesthesia, PCA morphine 110 ml containing approximately 200 mg of ropivacaine (Narop®, Astra Zeneca), 20 mg of ketorolac (Toradol®, Roche) and 0.33 mg of epinephrine (Adrenalin®, NM Pharma) infiltrated during surgery Further intra-articular infiltration through catheter after surgery	FNB (Narop®, Astra Zeneca) i.v. ketorolac (Toradol®, Roche) after surgery No placebo infiltration	24 hours; NRS pain intensity at rest and on movement, 24-hour morphine PCA consumption; no losses to follow-up. Missing data analysis reported
Andersen and colleagues 2010;[398] Denmark (2007–8)	Age > 18 years; $n = 49$ (24 : 25); 67 : 69 years; 43% : 26%	Spinal anaesthesia, PCA morphine 151.5 ml of saline solution containing 300 mg of ropivacaine, 30 mg of ketorolac and 0.5 mg of epinephrine infiltrated during surgery Further continuous infusion through catheter after closure	Epidural infusion of ropivacaine Postoperative i.v. ketorolac	72 hours and to discharge, infection to 30 days; VAS/NRS pain, morphine requirement, side effects and complications, time to achieve discharge criteria, length of stay; 9 (3 : 6) patients lost to follow-up
Busch and colleagues 2006;[399] Canada (date not specified)	Age < 80 years; $n = 64$ (32 : 32); 66 : 70 years; 50% : 59%	General or spinal anaesthesia, PCA morphine 100 ml of saline solution containing 400 mg of ropivacaine, 30 mg of ketorolac (Toradol®, Roche), 5 mg of epimorphine and 0.6 ml of epinephrine (1 : 1000) infiltrated during surgery	No placebo infiltration	6 weeks; VAS at rest and activity, morphine consumption (PCA), VAS satisfaction, complications, Knee Society Score, WOMAC, length of hospital stay; no losses to follow-up

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 35 Systematic review of the effectiveness of perioperative local anaesthetic infiltration in total hip and knee replacement: study characteristics (*continued*)

Study; country (date)	Inclusion; total patients (intervention : control); mean age (intervention : control); percentage female (intervention : control)	Common treatment		Latest post-surgical follow-up; outcomes; losses to follow-up (intervention : control)
		Intervention treatment (volume of infiltrate)		
		Further treatment (if given)	Control	
Carli and colleagues 2010;[400] Canada (2007–8)	OA, tricompartmental, cemented.; $n = 40$ (20 : 20); 71 : 71 years; 75% : 70%	Spinal, FNB and periarticular knee catheter inserted, PCA morphine		6 weeks; morphine consumption, NRS pain at rest and walking, functional capacity, ability to walk 30 m, physical activity, SF-12, WOMAC; no losses to follow-up
		Solution of ropivacaine (0.2%), 1 ml of ketorolac (30 mg/ml), and 0.5 ml of epinephrine (1 mg/ml) with a total volume of 100 ml infiltrated during surgery	Continuous FNB Saline injection	
		Further infusion through catheter after closure	Post-surgical infusion of saline	
Chen and colleagues 2012;[401] China (2008)	OA, age < 76 years.; $n = 81$ (40 : 41); 66 : 65 years; 75% : 78%	Spinal anaesthesia, PCA morphine		15 days and infection to 6 months; total morphine consumption, VAS pain at rest and motion, time to straight leg raise and 90 degree flexion, adverse events including delayed infection; 1 (0 : 1) patient lost to follow-up
		Intraoperative injection of a solution of magnesium sulphate (50 mg/kg) and 190 mg ropivacaine in normal saline to a volume of 100 ml	Intraoperative intra-articular injection of 100 ml normal saline	
Essving and colleagues 2010;[402] Sweden (2007–8)	OA, ASA I–III, 20–85 years; $n = 48$ (24 : 24); 72 : 70 years; 54% : 54%	General anaesthesia, PCA morphine		3 months; PCA morphine consumption, VAS pain at rest and on knee flexion, time to home readiness, length of hospital stay, surgical outcome, functional outcome tests, OKS, EQ-5D, patient satisfaction, adverse events; 1 (0 : 1) patient lost to follow-up
		116 ml of saline containing 300 mg of ropivacaine, 30 mg of ketorolac and 0.5 mg of epinephrine infiltrated during surgery. 50 ml of saline containing 100 mg of ropivacaine infiltrated before closure	No placebo injections during surgery Post-surgical injection of saline at 21 hours	
		Further injection of mixture 21 hours after closure		
Essving and colleagues 2011;[403] Sweden (2009–10)	OA, ASA I–III, age 40–85 years; $n = 50$ (25 : 25); 71 : 71 years; 64% : 60%	Spinal anaesthesia, PCA morphine		3 months; VAS pain, PCA morphine, verbal rating scale of satisfaction, functional tests, time to home readiness, OKS, EQ-5D, adverse events; 2 (0 : 2) patients lost to follow-up
		Spinal plus intrathecal saline	Spinal plus intrathecal morphine	
		Injection during surgery of 400 mg of ropivacaine (160 ml), 30 mg of ketorolac (1 ml) and 0.5 mg of epinephrine (5 ml)	No injection during surgery	
		Further infiltrate through catheter on days 1 and 2	Post-surgical infusion of saline through catheter	

Study; country (date)	Inclusion; total patients (intervention : control); mean age (intervention : control); percentage female (intervention : control)	Common treatment		Latest post-surgical follow-up; outcomes; losses to follow-up (intervention : control)
		Intervention treatment (volume of infiltrate)		
		Further treatment (if given)	Control	
Fu and colleagues 2009;[404] China (2006–7)	OA, age < 80 years; $n = 80$ (40 : 40); 69 : 68 years; 75% : 78%	Spinal anaesthesia, PCA morphine 60 ml of saline containing 5 mg of morphine, 30 mg of bupivacaine and 1 ml of betamethasone infiltrated during surgery	60 ml of saline infiltrated during surgery	15 days except ROM 90 days, infection 12 months; morphine consumption, VAS pain at rest and activity, ROM, time to straight leg raise, surgical outcomes, complications; no losses to follow-up. Missing data imputation described
Fu and colleagues 2010;[405] China (2008–9)	OA, age < 80 years; $n = 100$ (50 : 50); 68 : 67 years; 76% : 80%	Spinal anaesthesia, PCA morphine Oral COX-2 inhibitor and tramadol 1 day before to 1 month after surgery	Oral placebo 1 day before to 1 month after surgery	15 days except ROM at 90 days and infection to mean 7.5 months (range 6–9 months); VAS pain, morphine consumption (PCA and intramuscular), time to straight leg raise and 90 degree flexion, surgical outcomes, adverse reactions; no losses to follow-up
		50 ml of saline containing 5 mg of morphine, 150 mg of ropivacaine, 0.5 ml of adrenaline and 1 ml of betamethasone infiltrated during surgery	50 ml of saline placebo infiltrated during surgery	
Han and colleagues 2007 interventions 1 and 2;[406] Korea (2005–6); note: 2 intervention groups	Primary; $n =$ (intervention 1 30 : intervention 2 30 : control 30); 69 : 68 : 67 years; 90% : 80% : 90%	Spinal and epidural anaesthesia, PCA morphine 50 ml saline solution containing 300 mg of ropivacaine, epinephrine (0.25 ml, 1 : 200,000) and 5 mg of morphine injected before wound closure	50 ml of saline placebo	48 hours; incidence of booster PCA for 24 hours, amount of i.v. tramadol, VAS pain at rest and exercising, side effects, range of flexion; no losses to follow-up reported
		50 ml of saline solution containing 300 mg of ropivacaine and epinephrine (0.25 ml, 1 : 200,000) injected before wound closure		
Koh and colleagues 2012;[407] Korea (2008–9)	OA, unilateral; $n = 101$ (49 : 52); 70 : 70 years; 89% : 91%	FNB, spinal anaesthesia, PCA morphine 50 ml of saline containing 300 mg of ropivacaine, 10 mg of morphine sulphate, 30 mg of ketorolac, epinephrine of 0.3 mg and 750 mg of cefuroxime injected/infiltrated during surgery	No placebo infiltration reported	7 days; VAS pain at rest (day 1) and on movement (days 4 and 7), PCA opioid consumption, use of rescue medication, pain compared with expectations, functional recovery (straight leg raise and flexion), satisfaction, side effects and complications, length of stay; 14 (4 : 10) did not receive treatment as planned. Results reported by ITT

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 35 Systematic review of the effectiveness of perioperative local anaesthetic infiltration in total hip and knee replacement: study characteristics (*continued*)

Study; country (date)	Inclusion; total patients (intervention : control); mean age (intervention : control); percentage female (intervention : control)	Common treatment		Latest post-surgical follow-up; outcomes; losses to follow-up (intervention : control)
		Intervention treatment (volume of infiltrate)		
		Further treatment (if given)	Control	
Krenzel and colleagues 2009;[408] USA (2007–8)	96% OA elective.; $n = 67$ (35 : 32), one patient with staged bilateral TKR included twice; 67 : 65 years; 57% : 72%	FNB, spinal anaesthesia, PCA fentanyl 20 ml infiltration of 100 mg of ropivacaine during surgery	20 ml of saline placebo infiltrated during surgery	24 hours; PCA fentanyl consumption, NRS pain, functional tests, time to straight leg raise, ambulation distance, surgical outcomes, adverse events; no losses to follow-up
Mahadevan and colleagues 2012;[409] UK (date not specified)	OA or RA, unilateral; $n = 52$ (26 : 26); 68 : 67 years; 54% : 58%	FNB, general anaesthesia, PCA morphine 25 ml of saline containing 0.375% levobupivacaine infiltrated during surgery	Sciatic nerve block No placebo infiltration reported	48 hours and to discharge; VAS pain, morphine consumption, active ROM, length of hospital stay; no losses to follow-up reported
Meftah and colleagues 2012;[410] USA (2010–11)	Unilateral; $n = 90$ (45 : 45); 65 : 67 years; 64% : 64%	Pre-emptive analgesia 45.1 ml of saline solution containing 400–800 mg of marcaine, 8 mg of morphine sulphate, 0.3 mg of adrenaline, 750 mg of antibiotic and 40 mg of corticosteroids injected during surgery	FNB. PCA epidural No placebo injection reported	3 days and to discharge, 6 months for infection, fracture and reoperation; pain at rest and ambulation, readiness for discharge; 1 (1 : 0) lost to all follow-up, 6 (4 : 2) lost to readiness for discharge follow-up
Ng and colleagues 2012;[411] China (2008–10); note: crossover design. Patients having both knees replaced	OA; $n = 32$ (16 : 16) surgeries but 16 patients only having two TKRs 3 months apart; 70 : 70 years; 88% : 88%	General anaesthesia, remifentanil infusion, PCA morphine 101.5 ml of saline solution containing 300 mg of ropivacaine, 1 mg of adrenaline and 40 mg of triamcinolone acetonide infiltrated during surgery Femoral catheter inserted and saline infused	FNB Wound infiltration with 101.5 ml of saline	3 days and to discharge; pain score at rest and motion, total morphine consumption, Knee Society Score, ROM, quadriceps power, satisfaction, adverse events and complications; no losses to follow-up reported

Study; country (date)	Inclusion; total patients (intervention : control); mean age (intervention : control); percentage female (intervention : control)	Common treatment		Latest post-surgical follow-up; outcomes; losses to follow-up (intervention : control)
		Intervention treatment (volume of infiltrate)		
		Further treatment (if given)	Control	
Parvataneni and colleagues 2007;[386] USA (2005–6)	OA; $n = 60$ (31 : 29); 69 : 71 years; 45% : 52%	Spinal anaesthesia with or without FNB Intraoperative infiltration of 200–400 mg of bupivacaine, 4–10 mg of morphine sulphate 300 µg of epinephrine, 40 mg of methylprednisolone acetate, 75 mg of cefuroxime and 22 ml of saline. Total volume approximately 33 ml	No infiltration during surgery FNB at end of surgery Post-surgical PCA Effort to conceal allocation but no sham epidural	3 months; VAS pain, total narcotic dose, functional recovery including time to straight leg raise, side effects of narcotic use, patient satisfaction; no losses to follow-up reported
Spreng and colleagues no i.v. injection 2010;[412] Norway (2007–9)	Unilateral, non-cemented, no patella resurfacing, age > 17 years, ASA I–III; $n = 68$ (34 : 34); 67 : 66 years; 61% : 67%	Spinal. Propofol if indicated. PCA morphine 150 ml of saline solution containing 150 mg of ropivacaine, 0.5 mg of epinephrine, 30 mg of ketorolac and 5 mg of morphine infiltrated during surgery Knee injected through catheter with ropivacaine and ketorolac solution after 22–24 hours i.v. injection with saline at 22–24 hours	48 hours of epidural analgesia as soon as spinal started to wear off No wound infiltration during surgery. No injections through sham catheter. No sham epidurals	72 hours and to discharge; VAS at rest and during knee flexion, morphine consumption, functional recovery, length of stay, satisfaction, mobilisation including walking distance, adverse events; 2 (1 : 1) lost to follow-up
Spreng and colleagues with i.v. injection 2010;[412] Norway (2007–9)	Unilateral, non-cemented, no patella resurfacing, age > 17 years, ASA I–III.; $n = 68$ (34 : 34); 67 : 66 years; 61% : 67%	Spinal anaesthesia, propofol if indicated, PCA morphine 150 ml of saline solution containing 150 mg of ropivacaine and 0.5 mg of epinephrine infiltrated during surgery In addition, i.v. injection of 1 ml of ketorolac (30 mg/ml) and 5 ml of morphine (1 mg/ml) Knee injected with saline at 22–24 hours (catheter) i.v. injection with ketorolac at 22–24 hours	48 hours of epidural analgesia as soon as spinal anaesthetic started to wear off No wound infiltration during surgery. No injections through sham catheter	72 hours and to discharge; VAS at rest and during knee flexion, morphine consumption, functional recovery, length of stay, satisfaction, mobilisation including walking distance, adverse events; 2 (1 : 1) lost to follow-up

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 35 Systematic review of the effectiveness of perioperative local anaesthetic infiltration in total hip and knee replacement: study characteristics (*continued*)

Study; country (date)	Inclusion; total patients (intervention : control); mean age (intervention : control); percentage female (intervention : control)	Common treatment		Latest post-surgical follow-up; outcomes; losses to follow-up (intervention : control)
		Intervention treatment (volume of infiltrate)		
		Further treatment (if given)	Control	
Thorsell and colleagues 2010;[381] Sweden (not specified)	OA or RA; $n = 85$ (46 : 39); 69 : 72 years (followed up); 81% : 73% (followed up)	Not specified, probable PCA		4 days and to discharge; VAS pain, morphine consumption, satisfaction, mobilisation getting out of bed without assistance, walking with crutches), functional recovery, length of hospital stay; 21 (13 : 8) patients lost to follow-up data reported
		Spinal anaesthesia	Spinal or epidural analgesia	
		156 ml of solution with 300 mg of ropivacaine, 0.5 mg of adrenaline and 30 mg of ketorolac infiltrated during surgery	No placebo infiltration reported	
		Further infiltrate through catheter intra-articularly on postoperative day 1	Postoperative pain relief with ropivacaine infusion through epidural catheter	
Toftdahl and colleagues 2007;[380] Denmark (2005–6)	OA with planned spinal anaesthesia; $n = 77$ (40 : 37); 70 : 72 years; 63% : 60%	Spinal and after surgery immediate-release oxycodone and i.v. morphine if required		4 days and to discharge; NRS pain, opioid consumption, mobilisation (able to walk > 3 metres, able to hold quadriceps tension for > 5 seconds), length of hospital stay, adverse events and complications; 4 (3 : 1) patients lost to follow-up
		152 ml of solution containing 300 mg of ropivacaine, 30 mg of ketorolac and 0.5 mg of epinephrine infiltrated during surgery	FNB prior to spinal anaesthesia	
			No placebo infiltration	
		Further infiltrate through catheter intra-articularly on day of surgery and postoperative day 1	Post-surgical continuous FNB	
Vendittoli and colleagues 2006;[413] Canada (2003–4)	95.2% OA; $n = 42$ (22 : 20); ages not specified; 73% : 70%	Spinal anaesthesia, PCA morphine		5 days and to discharge; VAS pain at rest and during physiotherapy exercise, PCA morphine consumption, functional recovery, side effects; no losses to follow-up described
		160 ml of solution containing, in total, 400 mg of ropivacaine (Naropin®, Astra Zeneca), 30 mg of ketorolac and 0.5 ml of adrenaline (1 : 1000) infiltrated during surgery	No placebo infiltration	
		Infiltrate through catheter intra-articularly on day 1		
Zhang and colleagues 2007;[414] China (2006–7)	Unilateral; $n = 60$ (30 : 30); mean 68 years; 83% : 80%	PCA morphine		72 hours; VAS pain at rest and activity, functional recovery; no losses to follow-up described
		60 ml of solution containing 0.25% bupivacaine, epinephrine (1 : 200,000) and 10 mg of morphine infiltrated during surgery	No placebo injection	

ASA, American Society of Anesthesiologists; ILAS, Iowa Level of Assistance Scale; ITT, intention to treat; i.v. intravenous; NRS, numerical response scale; OA, osteoarthritis; PCA, patient-controlled analgesia; RA, rheumatoid arthritis.

TABLE 36 Systematic review of the effectiveness of perioperative local anaesthetic infiltration in THR: meta-analyses

THR studies	*n*	Method	Pooled effect size (random effects)	95% CI	*p*-value	I^2 (%)	τ^2
(A + B) any local anaesthetic infiltration + usual anaesthesia vs. usual anaesthesia							
Pain at rest at 24 hours	12	SMD	–0.605	–1.051 to –0.160	0.0078	89	0.541
Pain during activity at 24 hours	9	SMD	–0.848	–1.450 to –0.246	0.0058	92	0.765
Pain at rest at 48 hours	11	SMD	–0.285	–0.520 to –0.050	0.018	58	0.09
Pain during activity at 48 hours	8	SMD	–0.432	–0.776 to –0.089	0.014	71	0.171
Length of hospital stay	9	WMD	–0.829	–1.540 to –0.118	0.022	84	0.866
(A) local anaesthetic infiltration + usual analgesia vs. usual anaesthesia							
Pain at rest 24 hours post operation	7	SMD	–0.633	–1.208 to –0.059	0.031	90	0.529
Pain during activity 24 hours post operation	4	SMD	–0.241	–0.637 to 0.155	0.23	68	0.11
Pain at rest 48 hours post operation	6	SMD	–0.134	–0.348 to 0.080	0.22	19	0.014
Pain during activity 48 hours post operation	3	SMD	–0.225	–0.559 to 0.109	0.19	35	0.03
Length of hospital stay	5	WMD	–0.257	–0.622 to 0.108	0.17	14	0.029
(B) local anaesthetic infiltration + post-closure analgesia + usual anaesthesia vs. usual anaesthesia							
Pain at rest 24 hours post operation	5	SMD	–0.572	–1.383 to 0.240	0.17	90	0.767
Pain during activity 24 hours post operation	5	SMD	–1.378	–2.499 to –0.257	0.016	94	1.525
Pain at rest 48 hours post operation	5	SMD	–0.489	–0.963 to –0.015	0.043	73	0.209
Pain during activity 48 hours post operation	5	SMD	–0.599	–1.158 to –0.040	0.036	80	0.319
Length of hospital stay	4	WMD	–1.117	–2.474 to 0.239	0.11	88	1.621

WMD, weighted mean difference.

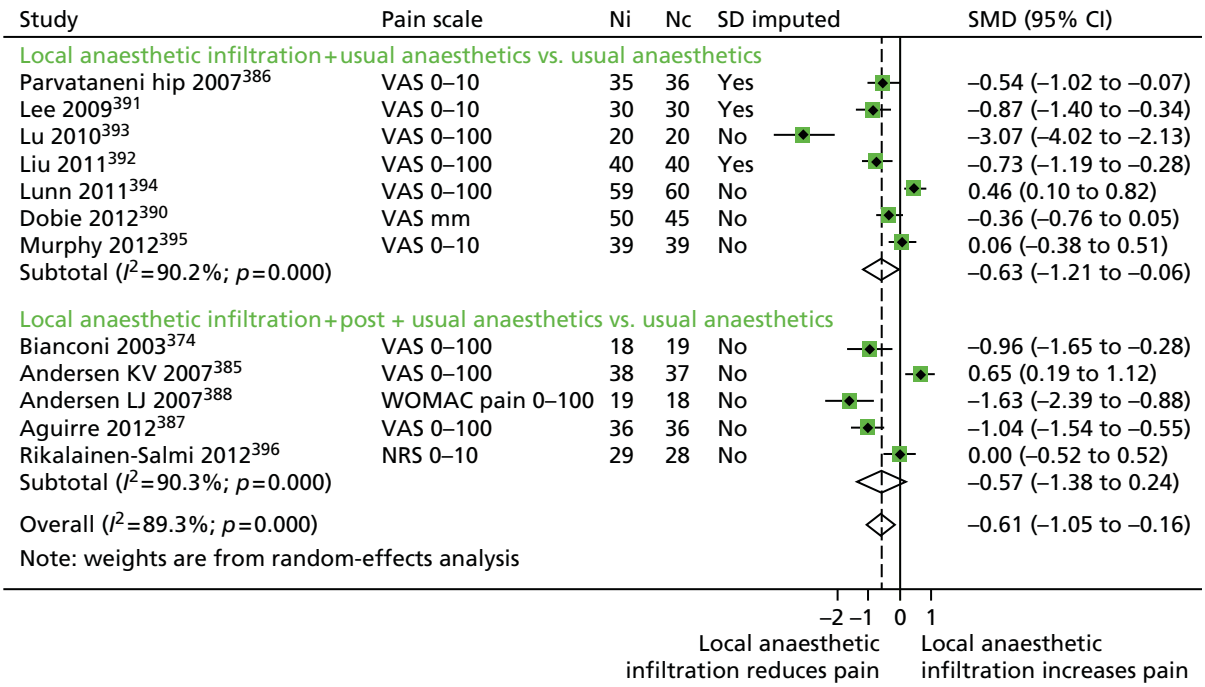
Pain

Data for meta-analysis were available for up to 12 studies depending on follow-up.[374,385–388,390–396] Overall, as shown in *Table 36* and *Figures 22* and *23*, there was a reduction in pain at 24 and 48 hours at both rest and activity. For example, at rest at 24 hours, the average SMD favouring local anaesthetic infiltration was –0.61 (95% CI –1.05 to –0.16; $p = 0.008$) and during activity at 48 hours was –0.85 (95% CI –1.45 to –0.25; $p = 0.006$). This reflected reduced pain at 24 hours at rest by an estimated 12 points (95% CI 3 to 21 points $p = 0.008$) and during activity by 24 points (95% CI 7 to 42 points; $p = 0.006$) on a 100-point scale. Average effect sizes at 48 hours were smaller for pain at rest (SMD –0.29, 95% CI –0.52 to –0.05; $p = 0.018$) and during activity, (SMD –0.43, 95% CI –0.78 to –0.09; $p = 0.014$), corresponding to 5 and 10 points on a 100-point scale, respectively.

In seven studies, the comparison was between patients receiving local anaesthetic infiltration with no additional analgesia delivered through a catheter or injection (A group), and controls receiving no intervention or saline infiltration.[386,390–395] At rest at 24 hours, the local anaesthetic infiltration group reported reduced pain (average SMD –0.63, 95% CI –1.21 to –0.06; $p = 0.031$), equivalent to an estimated 12 points lower pain. There was no strong evidence that the intervention had an effect during activity or at 48 hours.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

(a)



(b)

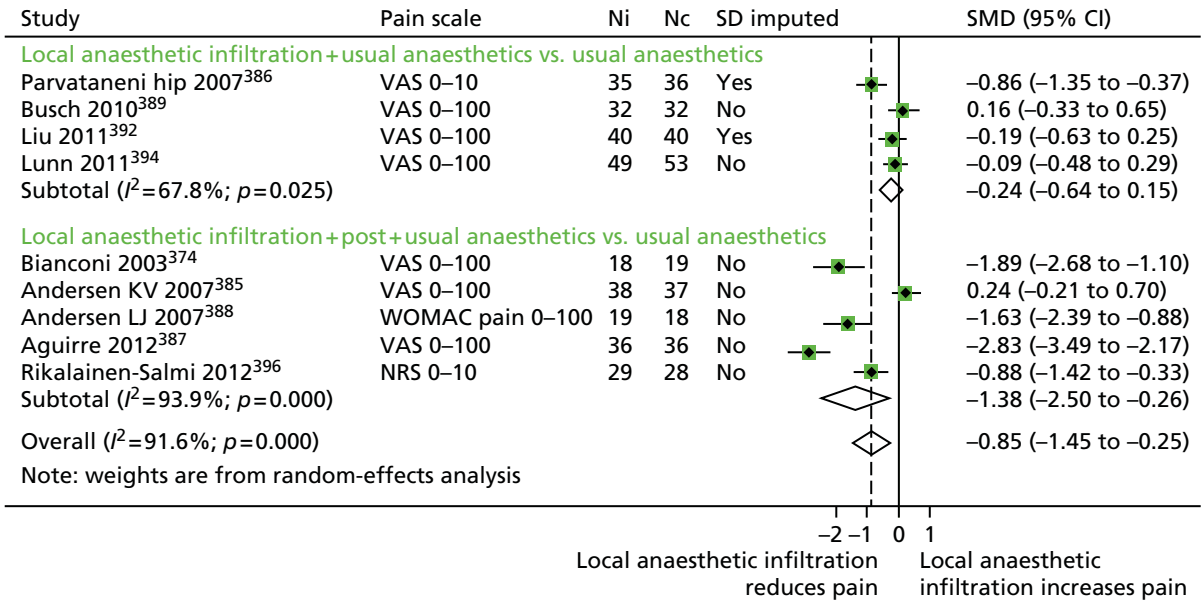
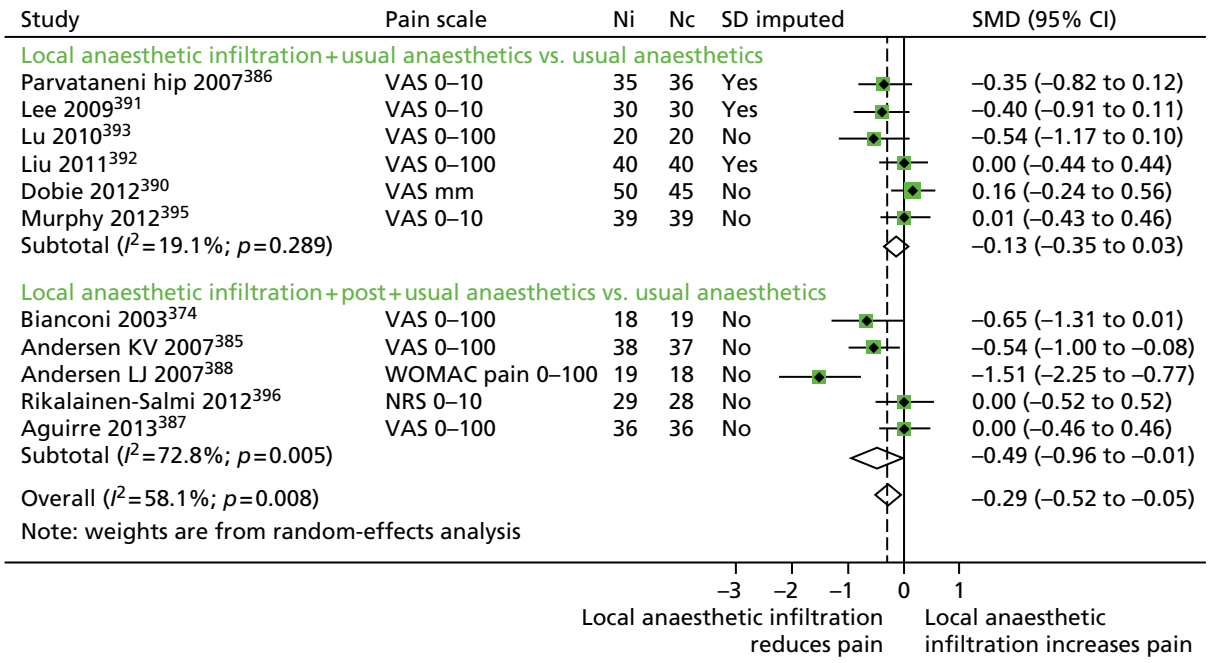


FIGURE 22 Total hip replacement: 24-hour VAS pain score at rest and during activity by local anaesthetic infiltration grouping. SMD in pain at 24 hours post surgery. Nc, number in the control group; Ni, number in the intervention group. (a) Pain at rest; and (b) pain during activity.

(a)



(b)

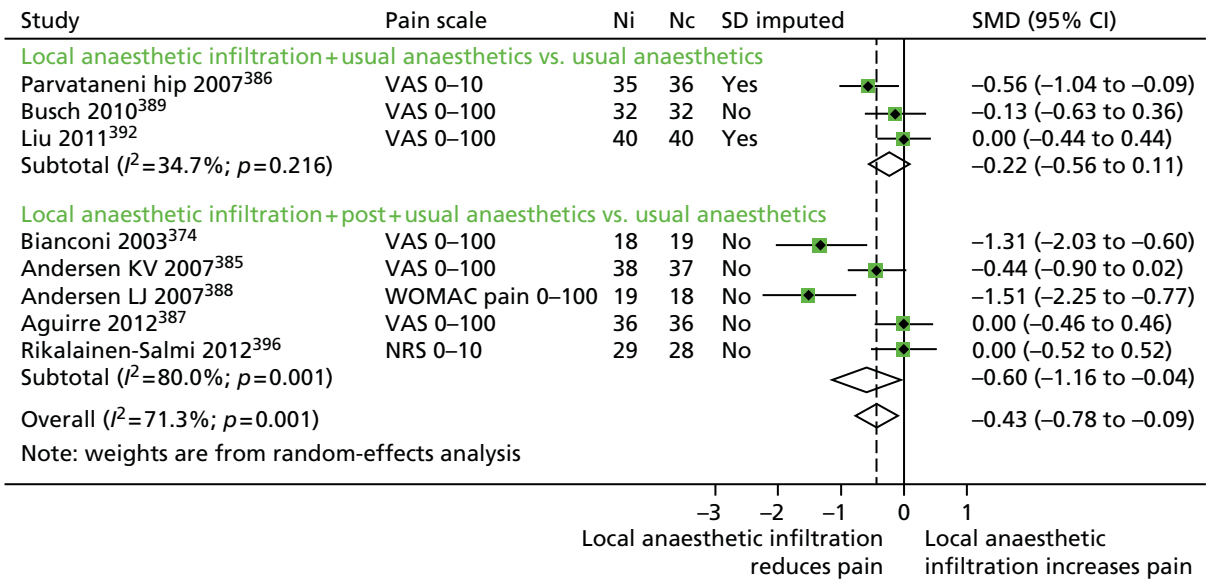


FIGURE 23 Total hip replacement: 48-hour VAS pain score at rest and during activity by local anaesthetic infiltration grouping. SMD in pain at 48 hours post surgery. Nc, number in the control group; Ni, number in the intervention group. (a) Pain at rest; and (b) pain during activity.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

In five studies, the intervention group received local anaesthetic infiltration and further analgesia through a catheter or injection after wound closure (B group).[374,385,387,388,396] Pain was reduced on average at 24 hours during activity (SMD –1.38, 95% CI –2.5 to –0.26; $p = 0.016$), equivalent to a 40-point decrease, and at 48 hours at rest (SMD –0.49, 95% CI –0.96 to –0.02; $p = 0.043$) and during activity (SMD –0.6, 95% CI –1.16 to –0.04; $p = 0.036$) equivalent to 8- and 14-point decreases, respectively.

In one study, control patients received an epidural analgesia infusion.[385] Pain was lower for the duration of the epidural infusion but, at 48 hours, pain was higher in the control group than in the local anaesthetic infiltration group. In a study in which control patients received additional intrathecal morphine, there was no difference in pain outcomes at any time point.[396]

Heterogeneity as expressed by the between-study variance (τ^2) and the I^2-statistic (see *Table 36*) was high and separate analysis for A and B groups did not appear to reduce this heterogeneity.

Considering nine studies with low risk of bias, the benefit for any local anaesthetic infiltration was still apparent.[374,386–388,390,392,394–396] Studies with low risk of bias had a marginally smaller reduction in pain after 24 hours at rest, averaging (SMD –0.49, 95% CI –0.89 to –0.09; $p = 0.017$), but during activity average pain reduction was greater (SMD –0.99, 95% CI –1.64 to –0.35; $p = 0.003$), corresponding to 28 points on a 100-point scale.

Opioid consumption

In 11 studies reporting an appropriate outcome, opioid consumption was reduced in local anaesthetic infiltration groups compared with controls.[374,385,387–390,392–396] The difference ranged from 12% to 92%. There was no suggestion of different effects in groups with or without additional post-closure analgesia through a catheter or injection. In the studies in which control patients received epidural[385] or intrathecal analgesia,[396] patients receiving local anaesthetic infiltration consumed 20% and 12% less morphine, respectively.

Mobilisation

Several different measures of mobilisation were reported. In three studies, patients receiving local anaesthetic infiltration with no additional postoperative component achieved a straight leg raise earlier than control patients.[386,391,392]

More patients were able to walk during the first postoperative day in two studies in which further postoperative analgesia was provided through a catheter.[385,396] In one study with no additional analgesia, with the exception of those with adverse events, all patients were mobilised on the first postoperative day.[390] However, the mean walking speed over 6 metres was improved in intervention patients at a 2-day functional assessment.

In one study, 35% of patients receiving local anaesthetic infiltration were able to walk after 8 hours, compared with 87% of control patients receiving an epidural infusion.[385] In the study for which control patients received intrathecal morphine, 33% of these patients could walk further than 5 metres on the first postoperative day, compared with 71% of patients receiving local anaesthetic infiltration.[396]

Length of hospital stay

As shown in *Table 36* and *Figure 24*, patients receiving local anaesthetic infiltration spent an average of 0.83 fewer days (95% CI 0.12 to 1.54 fewer days; $p = 0.022$) in hospital than control patients. Benefit was mainly limited to local anaesthetic infiltration interventions with additional analgesia through a catheter (B group). Heterogeneity across studies was high ($I^2 = 84\%$), mainly in studies with additional postoperative analgesia.

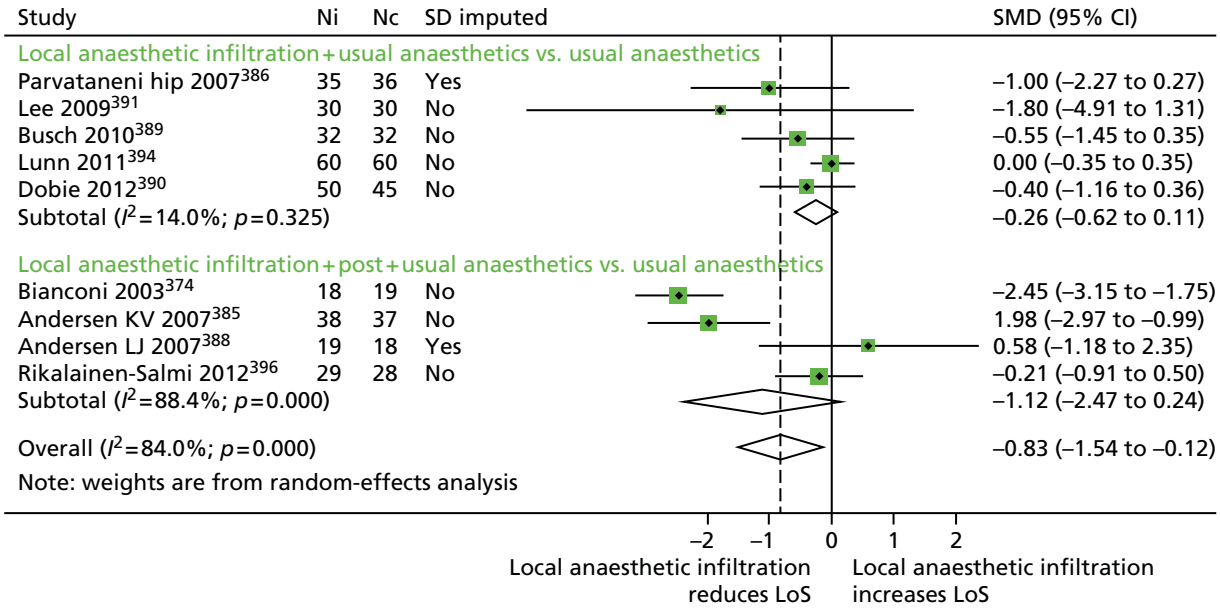


FIGURE 24 Total hip replacement: length of hospital stay by local anaesthetic infiltration grouping. Weighted mean difference in days. LoS, length of hospital stay. Nc, number in the control group; Ni, number in the intervention group.

When the comparison group received an epidural infusion, patients with local anaesthetic infiltration had on average a 2-day shorter hospital stay. In the study in which the comparison group received intrathecal morphine, there was no clear difference in discharge times.

Complications

The Peto's OR for a major complication in patients with local anaesthetic infiltration compared with controls was 0.30 (95% CI 0.05 to 1.77; $p = 0.18$). This was based on only one major complication in 448 patients randomised to local anaesthetic infiltration and four major complications in 448 controls. Across all studies with 909 patients, five deep infections were reported, four in local anaesthetic infiltration patients and one in controls (Peto's OR 3.47, 95% CI 0.58 to 20.81; $p = 0.17$). Four infections occurred in the 218 patients who received post-closure delivery of infiltrate through a catheter.

The incidence of vomiting (or vomiting and nausea if not reported separately) was reduced in patients receiving local anaesthetic infiltration in the five studies with data, (Peto's OR 0.46, 95% CI 0.27 to 0.80; $p = 0.006$). There was only slight heterogeneity between studies.

Long-term outcomes

Five studies reported long-term outcomes. In the study of Andersen and colleagues,[388] the median WOMAC pain scores at 6 weeks in intervention and control groups were 2 (range 0–50) and 7 (range 0–13), but this difference favouring intervention was not statistically significant ($p = 0.07$). At the 8-week follow-up, Rikalainen-Salmi and colleagues[396] reported no significant differences in mobilisation or intensity or duration of pain. Parvataneni and colleagues[386] reported that VAS pain scores 3 months after surgery were 'comparable between groups'. Similarly Aguirre and colleagues[387] reported no difference in analgesic consumption or pain during normal daily activities between groups at 3 months. In the study of Busch and colleagues,[389] mean overall WOMAC scores at 2 years were more favourable in the intervention group (69.3, SD 23.5) than in the control group (76.6, SD 25.9) but this was not statistically significant ($p = 0.24$).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Total knee replacement

Searches identified 23 studies with 1439 patients with TKR randomised. The mean number of patients randomised was 63 (range 32–101). We assessed that 17 studies were at low risk of bias[386,399–409,411–413] and that five studies had unclear risk of bias based on uncertainty about blinding of outcome assessments.[380,397,398,410,414] One study was assessed to be at high risk of bias owing to a large uneven loss to follow-up between randomised groups.[381]

Results of the meta-analysis are summarised in *Table 37*.

Pain

In patients receiving patients receiving local anaesthetic infiltration (A and B groups), pain at rest at 24 hours and during activity at 48 hours was reduced by SMD –0.40 (95% CI –0.58 to –0.22; $p < 0.001$) and –0.27 (95% CI –0.50 to –0.05; $p = 0.018$), respectively. This reflected reductions in pain at rest at 24 hours by an average of 10 points (95% CI 6 to 15 points; $p < 0.001$) and during activity at 48 hours by 8 points (95% CI 1.5 to 15 points; $p = 0.018$) on a 100-point scale.

TABLE 37 Systematic review of the effectiveness of perioperative local anaesthetic infiltration in TKR: meta-analyses

TKR studies	Number of studies	Method	Pooled effect size (random effects)	95% CI	*p*-value	I^2 (%)	τ^2
(A + B) any local anaesthetic infiltration + usual anaesthesia vs. usual anaesthesia							
Pain at rest at 24 hours	12	SMD	–0.398	–0.576 to –0.219	< 0.001	32	0.032
Pain during activity at 24 hours	12	SMD	–0.453	–0.671 to –0.235	< 0.001	54	0.078
Pain at rest at 48 hours	12	SMD	–0.325	–0.546 to –0.103	0.0041	56	0.084
Pain during activity at 48 hours	11	SMD	–0.273	–0.500 to –0.046	0.018	56	0.081
Length of hospital stay	8	WMD	–0.866	–1.622 to –0.109	0.025	77	0.805
(A) local anaesthetic infiltration with no additional post-wound closure analgesia + usual anaesthesia vs. usual anaesthesia							
Pain at rest 24 hours post operation	6	SMD	–0.248	–0.452 to –0.044	0.017	14	0.009
Pain during activity 24 hours post operation	6	SMD	–0.283	–0.470 to –0.096	0.0031	0	0
Pain at rest 48 hours post operation	6	SMD	–0.155	–0.458 to 0.148	0.32	61	0.086
Pain during activity 48 hours post operation	6	SMD	–0.077	–0.263 to 0.110	0.42	0	0
Length of hospital stay	1	WMD	0.092	–0.890 to 1.073	0.85	100	< 0.001
(B) local anaesthetic infiltration + post-wound closure analgesia + usual anaesthesia vs. usual anaesthesia							
Pain at rest 24 hours post operation	6	SMD	–0.587	–0.829 to –0.346	< 0.001	9	0.008
Pain during activity 24 hours post operation	6	SMD	–0.693	–1.152 to –0.234	0.0031	74	0.24
Pain at rest 48 hours post operation	6	SMD	–0.52	–0.778 to –0.262	< 0.001	21	0.022
Pain during activity 48 hours post operation	5	SMD	–0.594	–0.997 to –0.191	0.0039	61	0.128
Length of hospital stay	7	WMD	–1.023	–1.822 to –0.224	0.012	76	0.761

TABLE 37 Systematic review of the effectiveness of perioperative local anaesthetic infiltration in TKR: meta-analyses (*continued*)

TKR studies	Number of studies	Method	Pooled effect size (random effects)	95% CI	*p*-value	I^2 (%)	τ^2
(C) local anaesthetic infiltration + FNB + usual anaesthesia vs. FNB + usual anaesthesia							
Pain at rest 24 hours post operation	3	SMD	0.253	–0.514 to 1.021	0.52	81	0.37
Pain during activity 24 hours post operation	3	SMD	0	–0.317 to 0.317	1	0	0
Pain at rest 48 hours post operation	2	SMD	0.254	–0.429 to 0.937	0.47	67	0.166
Pain during activity 48 hours post operation	2	SMD	–0.073	–0.446 to 0.299	0.7	0	0
Length of hospital stay	2	WMD	0.07	–0.838 to 0.978	0.88	0	0
(D) local anaesthetic infiltration + usual anaesthesia vs. FNB + usual anaesthesia							
Pain at rest 24 hours post operation	3	SMD	–0.241	–0.604 to 0.122	0.19	44	0.046
Pain during activity 24 hours post operation	0						
Pain at rest 48 hours post operation	1	SMD	–0.18	–0.571 to 0.211	0.37	100	0
Pain during activity 48 hours post operation	1	SMD	0.094	–0.296 to 0.485	0.64	100	0
Length of hospital stay	1	WMD	1.52	0.054 to 2.986	0.042	100	0
(E) local anaesthetic infiltration + post-wound closure analgesia + usual anaesthesia vs. FNB + usual anaesthesia							
Pain at rest 24 hours post operation	3	SMD	–0.076	–0.632 to 0.480	0.79	69	0.166
Pain during activity 24 hours post operation	3	SMD	0.159	–0.869 to 1.187	0.76	90	0.741
Pain at rest 48 hours post operation	2	SMD	0.056	–0.300 to 0.412	0.76	0	0
Pain during activity 48 hours post operation	2	SMD	–0.202	–1.034 to 0.631	0.63	75	0.275
Length of hospital stay	2	WMD	–0.069	–0.634 to 0.497	0.81	0	0

WMD, weighted mean difference.

Heterogeneity as expressed by the between-study variance (τ^2) and the I^2-statistic was moderate to low. Among studies with low risk of bias, heterogeneity reported was higher, possibly owing to variability across comparators and surgical characteristics.

Data were available for up to six trials comparing local anaesthetic infiltration with no additional post-closure analgesia (A group), with controls receiving no intervention or saline infiltration.[401,404–406,414] As shown in *Table 37* and *Figure 25*, pain at 24 hours was reduced both at rest and during activity [SMDs –0.25 (95% CI –0.45 to –0.04; $p = 0.017$) and –0.28 (95% CI –0.47 to –0.10; $p = 0.003$), respectively]. In six trials where additional analgesia was delivered through a catheter or as an injection after wound closure (B group),[398,402,403,412,413] reduction in pain at 24 hours was somewhat greater than controls at both rest and activity [SMDs –0.59 (95% CI –0.83 to –0.35; $p < 0.001$) and –0.69 (95% CI –1.15 to –0.23; $p = 0.003$)].

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

(a)

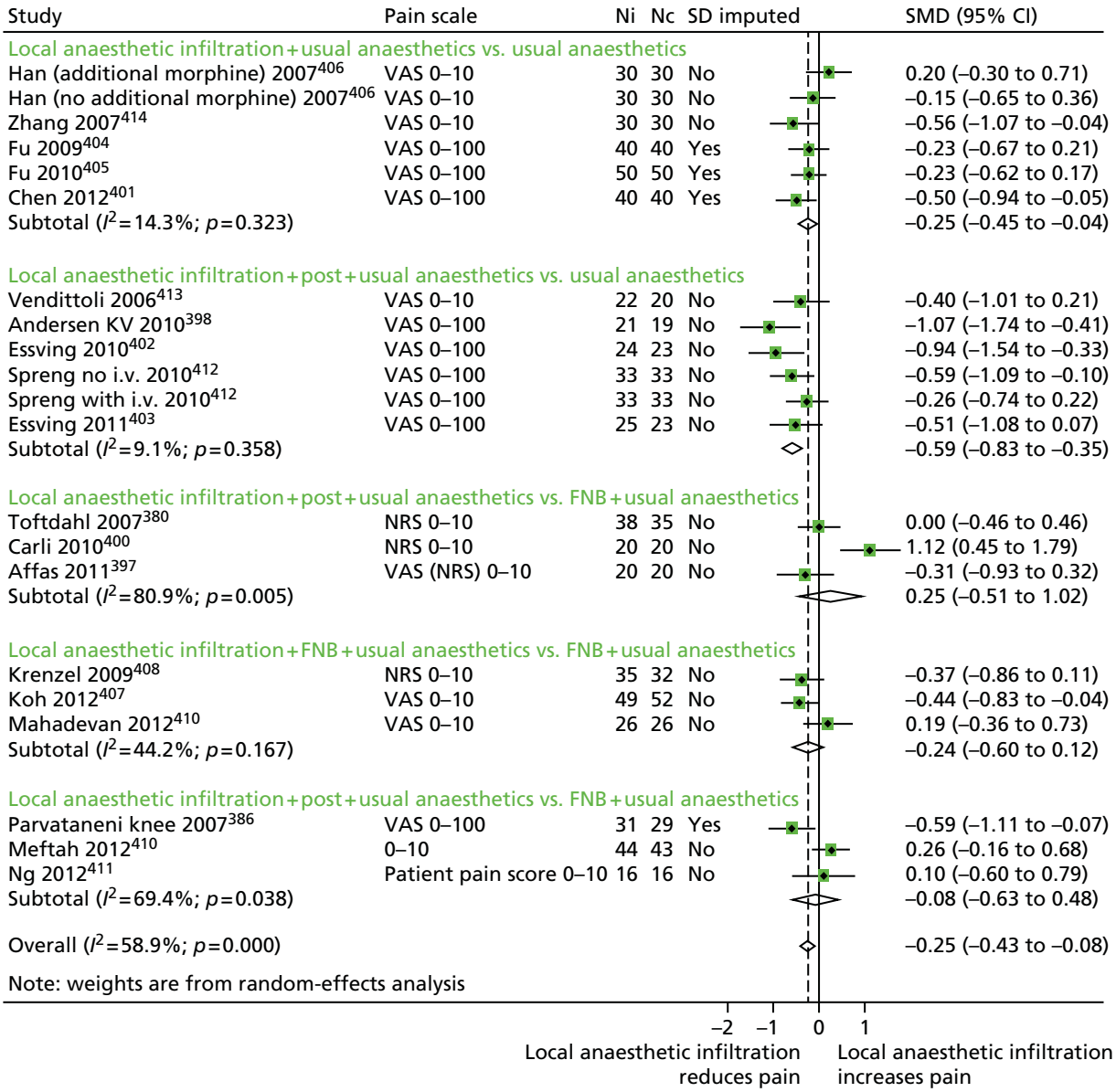


FIGURE 25 Total knee replacement: 24-hour VAS pain score at rest and during activity by local anaesthetic infiltration grouping. SMD in pain at 24 hours post surgery. i.v., intravenous; Nc, number in the control group; Ni, number in the intervention group; NRS, numerical response scale. (a) Pain at rest; and (b) pain during activity. (*continued*)

(b)

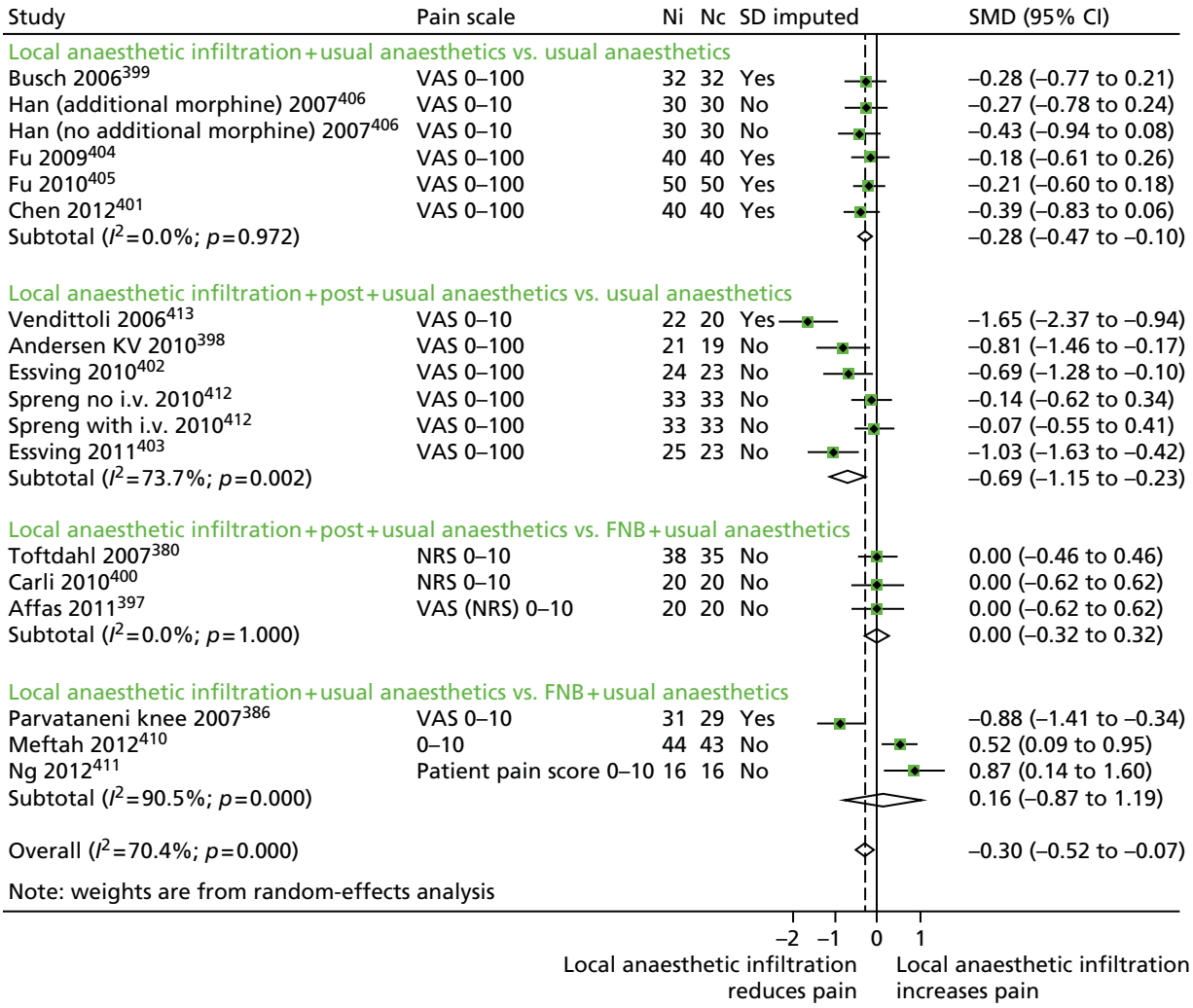


FIGURE 25 Total knee replacement: 24-hour VAS pain score at rest and during activity by local anaesthetic infiltration grouping. SMD in pain at 24 hours post surgery. i.v., intravenous; Nc, number in the control group; Ni, number in the intervention group; NRS, numerical response scale. (a) Pain at rest; and (b) pain during activity.

As shown in *Figure 26*, improvement in pain relief was sustained at 48 hours, but only if additional analgesia was provided postoperatively (B group), (SMD –0.52, 95% CI –0.78 to –0.26; $p < 0.001$) at rest and during activity (SMD –0.59, 95% CI –1.0 to –0.19; $p = 0.004$).

Heterogeneity as expressed by the between-study variance (τ^2) and the I^2-statistic was moderate to low.

Nine studies in TKR included a FNB analgesia regimen.[380,386,397,400,402,407–410] In three studies for which both randomised groups received a FNB (E),[407–409] there was no evidence for added benefit of local anaesthetic infiltration in any outcome. In the six studies of a direct comparison of local anaesthetic infiltration with or without post-closure analgesia with a FNB in addition to usual analgesia (C and D),[380,386,397,400,410,411] there was also no evidence of improved pain at any time point.

In eight comparisons between local anaesthetic infiltration with controls,[381,398,399,402,403,412,413] additional ketorolac was included in the wound infiltrate. In seven comparisons with data, patients receiving additional analgesia in the infiltrate had lower pain than controls.[398,399,402,403,412,413] For example, pain was reduced on average at rest at 24 hours by SMD –0.68 (95% CI –0.94 to –0.42; $p < 0.001$) and during activity at 48 hours by SMD –0.59 (95% CI –1.01 to –0.17; $p = 0.006$), equivalent to a reduction of 17 and 30 points, respectively, on a 100-point scale compared with controls.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

(a)

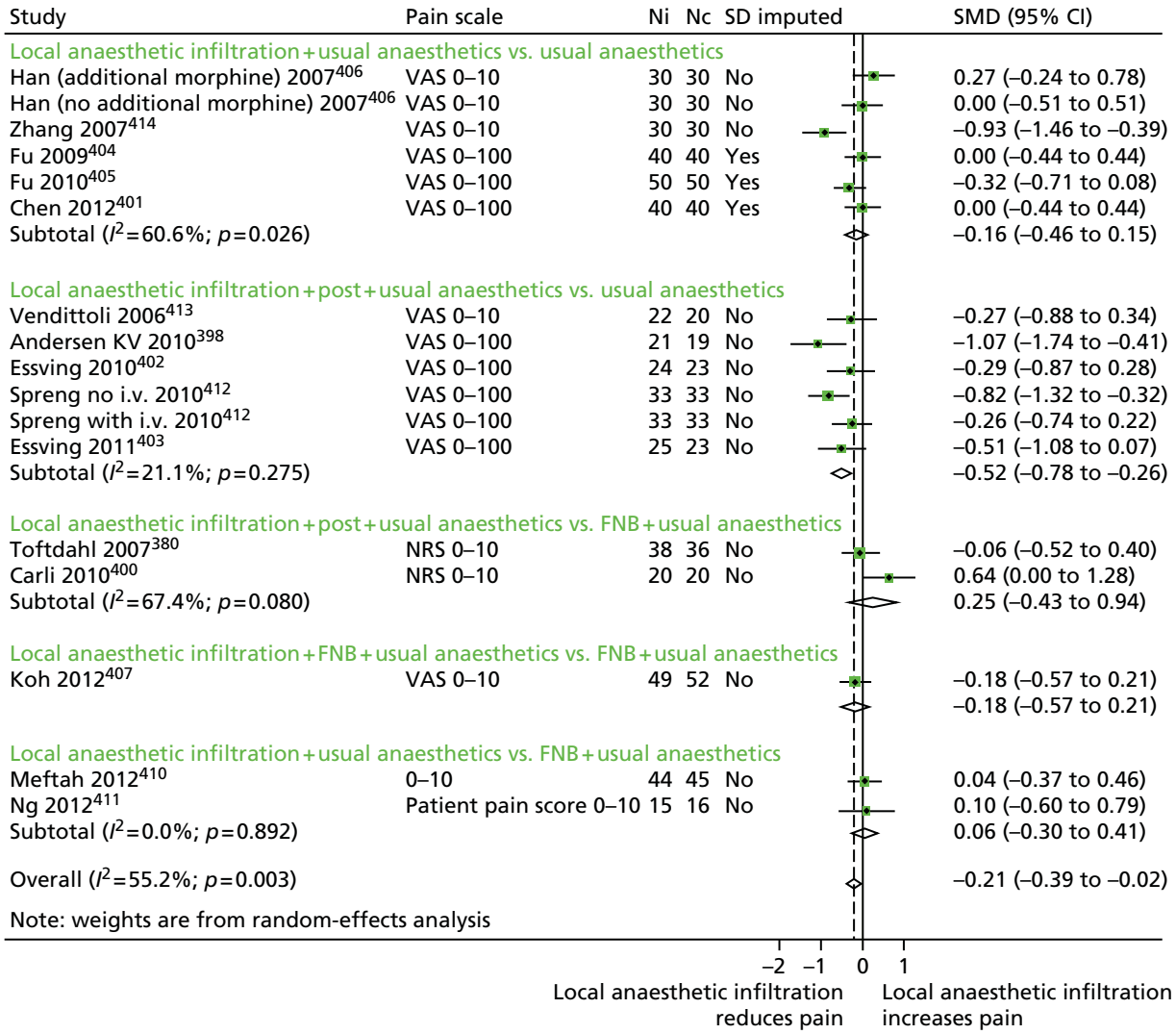


FIGURE 26 Total knee replacement: 48-hour VAS pain score at rest and during activity by local anaesthetic infiltration grouping. SMD in pain at 48 hours post surgery. i.v., intravenous; Nc, number in the control group; Ni, number in the intervention group; NRS, numerical response scale. (a) Pain at rest; and (b) pain during activity. (*continued*)

(b)

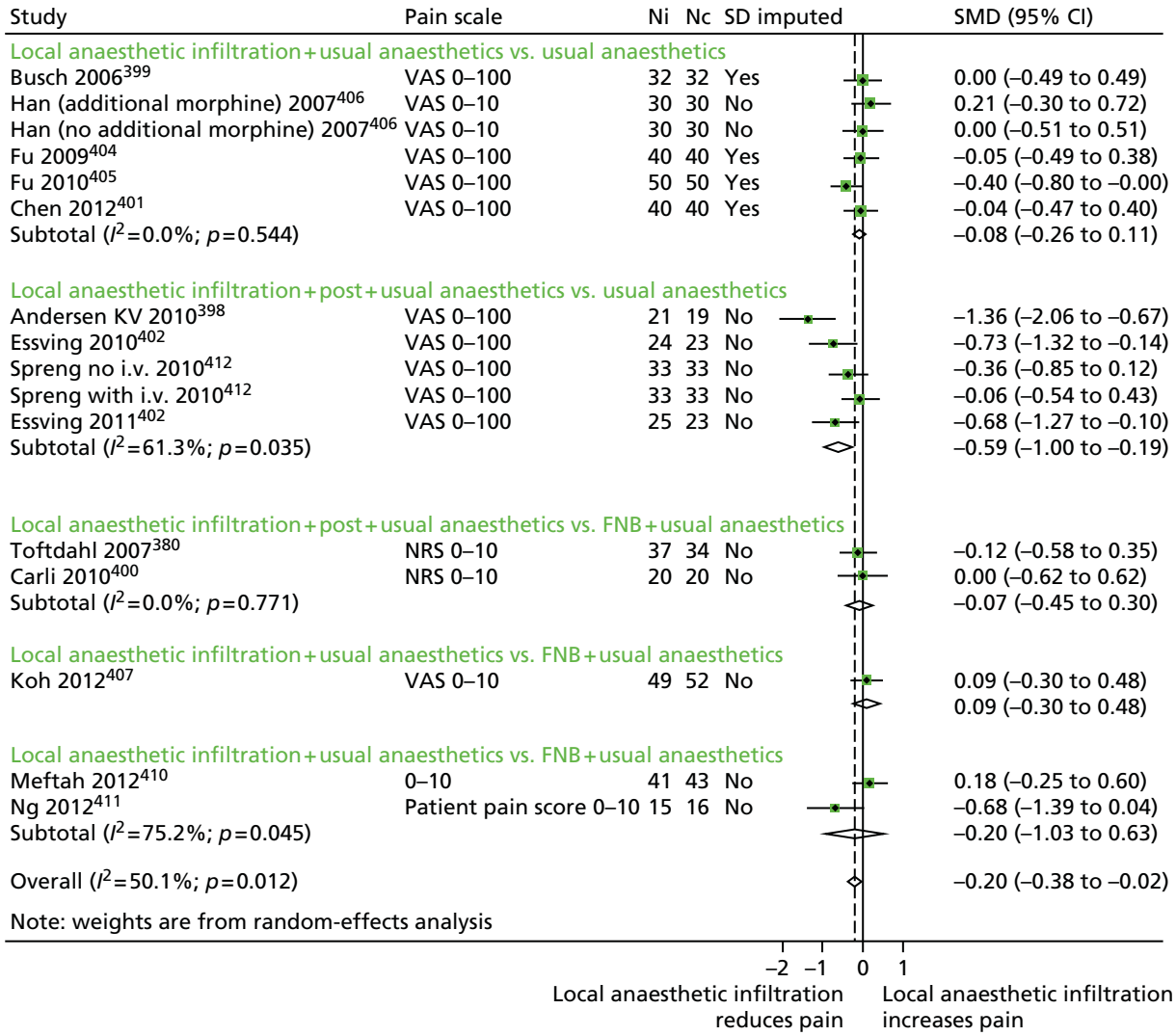


FIGURE 26 Total knee replacement: 48-hour VAS pain score at rest and during activity by local anaesthetic infiltration grouping. SMD in pain at 48 hours post surgery. i.v., intravenous; Nc, number in the control group; Ni, number in the intervention group; NRS, numerical response scale. (a) Pain at rest; and (b) pain during activity.

In four studies, control patients received either an epidural infusion,[381,398,412] or intrathecal morphine.[403] Results of all studies supported a reduction in pain for patients receiving local anaesthetic infiltration compared with epidural or intrathecal morphine.

Opioid consumption

In all four studies reporting opioid consumption, this was reduced by 35–40% in the local anaesthetic infiltration group with no analgesia.[399,401,404,405] In three studies with additional post-closure analgesia opioid consumption was 32–52% lower than in the control groups.[402,403,413]

In six studies for which the control group or both groups received FNB, there was little difference in opioid consumption between randomised groups.[380,386,397,400,407,408]

In four studies for which patients receiving local anaesthetic infiltration with further post-closure analgesia were compared with patients receiving epidural anaesthesia, there was no consistent difference between groups.[381,398,412]

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Mobilisation

A range of mobilisation outcomes were reported in 19 studies.[380,381,386,398,400–410,412,413] Differences in outcome measures precluded meta-analysis.

In three studies, the time to achieve a straight leg raise was reduced by 44–50%,[401,404,405] and in one study three times as many intervention patients could achieve a straight leg raise on the first postoperative day as controls.[386] In two studies in which FNB was given to all patients, the benefit for local anaesthetic infiltration was statistically significant; more patients receiving local anaesthetic infiltration were able to achieve a straight leg raise during the first postoperative day.[407,408]

In four out of five studies, patients receiving local anaesthetic infiltration achieved better knee flexion.[405,406,409,413] Four studies reported ambulation as part of discharge-readiness criteria.[398,402,403,410] These criteria were met earlier in intervention patients in three studies,[398,402,403] but were similar in one study in which control patients received a FNB.[410]

Times to achieve diverse walking goals were reported in six studies.[380,381,400,408,412] In three studies, improvements were evident in intervention patients that received epidural analgesia[381] or FNB compared with control groups.[380,400] Marginal improvements in walking outcomes for intervention patients compared with controls were reported in three studies.[408,412]

One study each showed that intervention patients could get out of bed earlier than controls receiving epidural analgesia,[381] and that the ability to hold quadriceps tension was improved compared with those receiving FNB.[380]

Length of hospital stay

Data on length of hospital stay were available for eight studies in which patients were randomised to local anaesthetic infiltration or control. Results are summarised in *Table 37* and *Figure 27*. There was some evidence that length of hospital stay was reduced in patients receiving local anaesthetic infiltration and additional post-closure delivery (B) by 1.0 day on average (95% CI 0.2 to 1.8 days; $p = 0.012$) compared with controls. In the one study (A) with no post-closure analgesia component, there was no difference in length of hospital stay.

In three studies for which the comparison group received FNB,[380,400,410] there was no suggestion of a difference in length of hospital stay. In one study in which all randomised patients received a FNB the length of hospital stay was about 1.5 days shorter in the control patients who also received an additional sciatic nerve block.[409]

Complications

Based on 11 reported events in 1439 patients, the odds of a major complication after TKR in patients receiving local anaesthetic infiltration compared with controls was 1.17 (95% CI 0.35 to 3.86; $p = 0.80$). Three deep infections were reported: two in the intervention group[380,398] and one in the control group[412] (Peto's OR 1.85, 95% CI 0.19 to 17.83; $p = 0.59$). All infections occurred in patients receiving a catheter although in control patients nothing was injected through it.

Excluding one study in which intervention patients received additional morphine,[406] the incidence of vomiting was lower in patients receiving local anaesthetic infiltration groups than in controls in eight studies (548 patients) with data (Peto's OR 0.56, 95% CI 0.39 to 0.80).[401–406,412] Rates were similar whether or not additional analgesia was delivered through a catheter or injection. There was minor heterogeneity between studies.

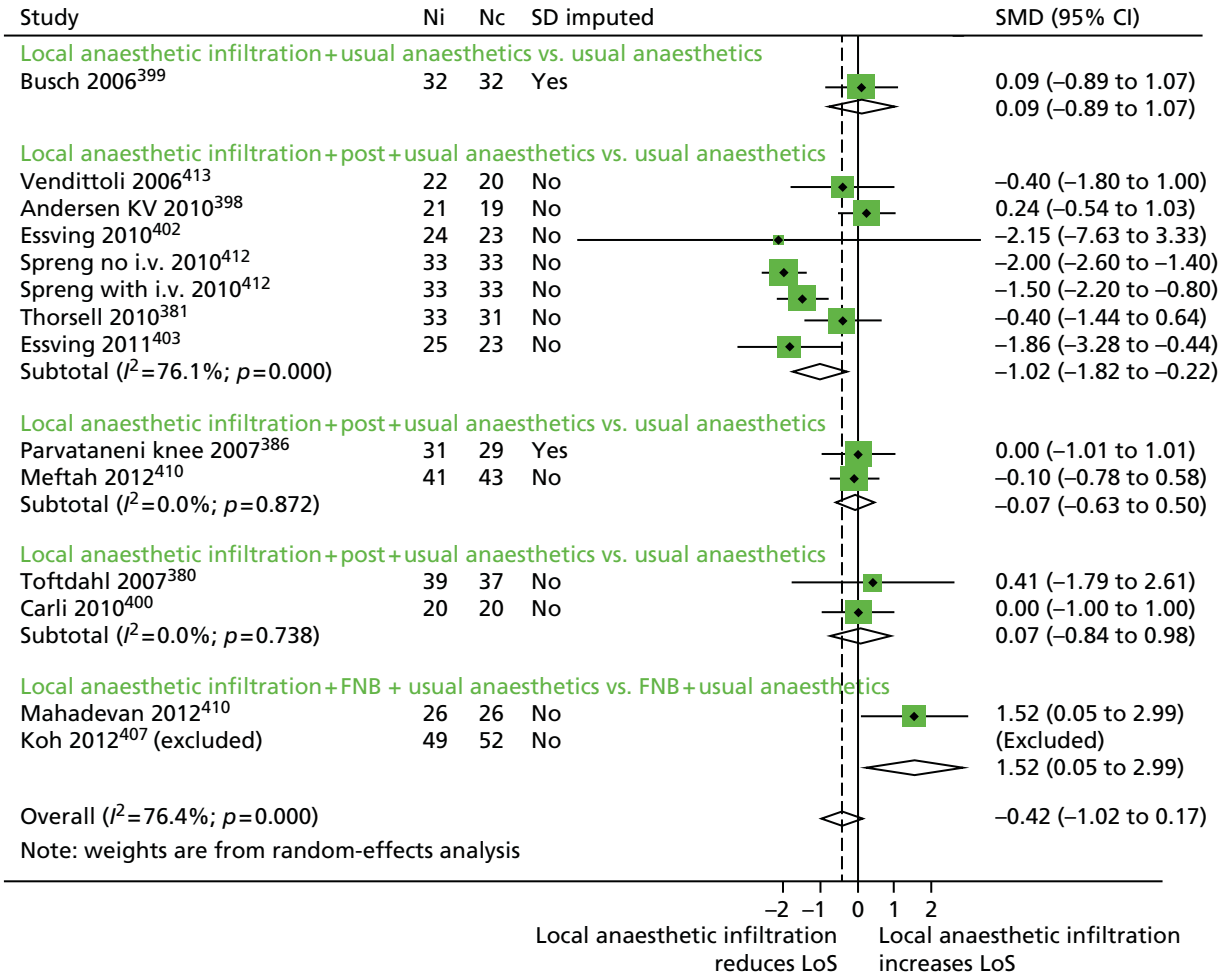


FIGURE 27 Total knee replacement: length of hospital stay by local anaesthetic infiltration grouping. Weighted mean differences in days. i.v., intravenous; LoS, length of stay; Nc, number in the control group; Ni, number in the intervention group.

Long-term outcomes

Five studies reported long-term patient outcomes measured at 6 weeks[399,400] or 3 months.[386,402,403] Busch and colleagues[399] found a non-significant difference in mean VAS pain scores at 6 weeks favouring the intervention group. Parvataneni and colleagues[386] reported comparable pain scores between groups at the 3-month follow-up. In the studies of Essving and colleagues,[402,403] there were no differences between median OKS at 3 months.

In a study comparing different approaches to perioperative pain control, Carli and colleagues[400] reported an improved WOMAC score after 6 weeks in the control group who received FNB compared with the local anaesthetic infiltration group.

Discussion

Our results indicate that in patients with total hip and knee replacement, those receiving local anaesthetic infiltration experience less pain after 24 hours at rest and after 48 hours during activity than controls. For patients with THR, the reduction in pain was, on average, about 35% at rest at 24 hours and 28% at 48 hours during activity when compared with no infiltration analgesia or placebo. For patients with TKR, the estimated average reduction of pain was 26% at rest at 24 hours and 16% at 48 hours during activity for local anaesthetic infiltration when compared with no infiltration analgesia or placebo. In patients receiving TKR, inclusion of the non-steroidal anti-inflammatory agent ketorolac in the infiltrate seemed to enhance postoperative pain relief.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Local anaesthetic infiltration was associated with 0.83 and 0.87 fewer days in hospital for patients with THR and knee replacement, respectively, reduced opioid consumption, earlier mobilisation and fewer complications. The improvement in pain control and shorter hospital stay was greatest for patients receiving additional post-wound closure analgesia. However, this should be weighed against a suggestion of a higher risk of deep infection when delivered through an active catheter. Six infections occurred in 505 patients who received an active catheter (1.19%), compared with eight infections in all 2348 patients randomised (0.34%). Regarding other serious post-surgical complications, there was little evidence of differences between randomised groups.

In studies in patients with TKR comparing local anaesthetic infiltration against FNB, or using a FNB in both groups, there was no benefit for local anaesthetic infiltration. FNB is a well-established method of providing analgesia after TKR and is associated with reduced opioid requirement and, therefore, a reduction in the undesirable side effects of opiates, such as nausea and vomiting. However, after a FNB, there is decreased quadriceps function for a time and an increased risk of falls.[415,416]

Our finding that mobilisation was consistently achieved earlier in patients receiving local anaesthetic infiltration may be a consequence of the reduced requirement for opioids, which may have contributed to the shorter average hospital stay. Opioid medication represents a key strategy in the management of post-surgical pain but its use can delay mobilisation and rehabilitation.[417] The majority of studies were concerned only with improving short-term outcomes, with only one study reporting outcomes beyond 3 months.[389] However, acute postoperative pain is an important risk factor for long-term pain[418,419] and deserves appropriate consideration in future studies of perioperative pain control.

Our study evaluated the clinical effectiveness of local anaesthetic infiltration interventions and has a number of limitations. We noted a range of analgesia regimens, with different studies making different comparisons, particularly for TKR. Although meta-analyses performed were enhanced by extensive contact with authors, imputation was required for some measures of variability. The skewed nature of the hospital length of stay outcome required transformation of outcomes under assumptions of a log-normal distribution.[382] For opioid consumption and mobilisation outcomes, there was insufficient consistency in measures reported to conduct anything but a systematic narrative overview.

Conclusion

Our systematic review shows that local anaesthetic infiltration is effective in reducing short-term pain after TKR and THR when compared with no infiltration. It is enhanced with the addition of post-closure analgesia, although this needs to be considered in light of the infection risks associated with catheters.[420] In TKR, there may be no additional benefit if a FNB has already been sited.

The effect of local anaesthetic wound infiltration on chronic pain after total hip and knee replacement: APEX randomised controlled trials

Background

The need to evaluate the effectiveness of perioperative local anaesthetic infiltration in reducing long-term pain after joint replacement in appropriately powered RCTs is recognised.[421] The other components of the multimodal anaesthesia regimen were based on recommendations from the European Society of Regional Anaesthesia and Pain Therapy, PROcedure SPECific postoperative pain managemenT (PROSPECT), (procedure specific postoperative pain management) guidelines and, in patients receiving TKR, included FNB.[422]

Aim

The aim of these two single-centre double-blind RCTs was to determine if using local anaesthetic infiltration, in addition to the standard anaesthetic regimen at the AOC, is clinically effective and cost-effective at reducing joint pain at 1 year after THR and TKR.

Patients and methods

The trials are registered as an International Standardised RCT (96095682). The protocol for the APEX trials was published in *BMC Musculoskeletal Disorders*.[365] The trials were approved by Southampton and South West Hampshire Research Ethics Committee B (09/H0504/94) and registered as a Clinical Trial of an Investigational Medicinal Product with the Medicine and Healthcare Regulatory Authority (18524/0215/001-0001) and EudraCT (2009-013817-93). The trials were overseen by a Data Monitoring Committee and Trial Steering Committee, which regularly reviewed safety data and monitored trial conduct. A Consolidated Standards of Reporting Trials (CONSORT) checklist is included in *Appendix 10*.

Patient recruitment

Patients were posted information about the study after they were listed for a joint replacement at the AOC. Eligible patients were then approached for recruitment by a research nurse when they attended a pre-operative assessment clinic. All participants provided informed written consent. Inclusion criteria included being listed for a primary THR or primary TKR for osteoarthritis and being willing and able to provide fully informed consent. Exclusion criteria included (1) any medical comorbidity that precludes spinal anaesthesia, regional blocks or the use of strong analgesics postoperatively, (2) severe dementia or psychiatric illness such that the patient was unable to complete the questionnaires or provide informed consent, (3) listed for simultaneous bilateral joint replacement, (4) having been in the APEX trial for a previous joint replacement and (5) being unable to understand English because not all the questionnaires have been translated and validated into other languages. In order to explore the problem of ascertainment bias (the patients enrolled in the trial not being representative of those undergoing arthroplasty), anonymised demographic data were recorded for all eligible patients.

Randomisation

Prior to surgery, patients were randomised to the standard care or the intervention group using an online computer-generated code (provided by the Bristol Randomised Trials Collaboration). Randomisation was stratified by operation site (THR/TKR) and minimised by baseline pain severity and surgical approach. The results of randomisation were concealed from the surgeons and anaesthetists until the beginning of the operation list so that knowledge of randomisation could not affect any clinical decisions they may have made. Trial participants and research nurses were blinded to the treatment allocation throughout the trial.

Intervention: total hip replacement

Standard care group

The standard anaesthetic care for THR patients was a spinal anaesthetic with 3 ml of 0.5% plain bupivacaine placed at the L3–4 or L4–5 interspace. Intraoperatively, the patient was either awake, sedated or under a light general anaesthetic. If there was intraoperative discomfort, then rescue analgesia in the form of intravenous (i.v.) fentanyl was titrated to effect. All participants were given 1 g of i.v. paracetamol 30 minutes before the end of the operation. In the recovery area immediately post operation, patients received (if no contraindications were present) 400 mg of ibuprofen administered orally. A patient-controlled analgesia (PCA) device was started containing 1 mg/ml morphine, a 1-mg bolus dose and a 5-minute lockout. If, on awakening, the patient was in pain with a rating of > 50 mm on a 100-mm pain VAS, a morphine bolus up to 0.2 mg/kg was administered as rescue analgesia. Each day during their hospital stay patients received a visit from a pain specialist nurse. Postoperative analgesia consisted of oral or i.v. paracetamol every 6 hours and, if no contraindications were present, 400 mg of oral ibuprofen every 8 hours. When the PCA was no longer needed, 30–60 mg of oral codeine phosphate every 6 hours, 50–100 mg of tramadol every 6 hours and 10–20 mg of morphine sulphate (Oramorph®, Boehringer Ingelheim) were prescribed as rescue analgesia.

Intervention group

The intervention group received the same anaesthetic and analgesic regime as the standard care group, plus an intraoperative local anaesthetic wound infiltration. The local anaesthetic mixture consisted of 60 ml of 0.25% bupivacaine with 1 in 200,000 adrenaline. If the patient weighed < 60 kg or was particularly

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

frail, the volume of injectate was reduced to 50 ml, or lower if necessary. The surgeon injected the anaesthetic mixture into the joint capsule and short external rotators, fascia, fat and subcutaneous tissue.

Intervention: total knee replacement

Standard care group

In line with evidence-based guidance from PROSPECT, standard care consisted of a FNB and a spinal or general anaesthetic, depending on patient factors.[422] postoperative analgesia was provided as necessary and recorded.

Intervention group

The intervention group received the same anaesthetic regime, plus an intraoperative local anaesthetic infiltration, which consisted of 60 ml of 0.25% bupivacaine with 1 in 200,000 adrenaline. The local anaesthetic mixture was injected directly into the posterior capsule (25 ml), medial and lateral capsule (10 ml), fascia and muscle (10 ml) and subcutaneous tissues (15 ml), prior to wound closure.

Assessment times

Assessments are conducted pre-operatively, daily during the hospital stay and then at 3, 6 and 12 months postoperatively. Outcomes were assessed using self-report questionnaires, joint examinations, radiograph analysis, pressure algometry and extraction of data from hospital records.

Primary outcome measure

The primary outcome measure was the self-completed WOMAC pain scale[114] at 12 months postoperatively. The five-item WOMAC pain scale is a widely used and validated measure of pain severity when performing daily activities. The questionnaire was completed with reference to the operated hip or knee. Scores were transformed onto a 0–100 scale, with lower scores indicating more severe pain.

Secondary outcome measures

Secondary outcomes were collected during the postoperative inpatient stay and at 3, 6 and 12 months postoperatively. Pain severity on admission to, and discharge from, the post-surgical recovery ward was rated on a 4-point Likert-type scale (none to severe pain). Pain severity for the remainder of the day of surgery was rated every 4 hours on a 0–10 scale (best to worst). On postoperative days 1–3, patients rated the severity of night pain, pain on movement and pain at rest on a 100-mm VAS. Satisfaction with pain relief and the occurrence of nausea and vomiting were also recorded daily during the inpatient stay. Length of hospital stay and postoperative analgesia use were extracted from medical records. At 3, 6 and 12 months postoperatively, patients completed the WOMAC function and Stiffness subscales[114] and the Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP).[280] The painDETECT questionnaire,[283] a measure of neuropathic pain, was completed at 12 months postoperatively.

Pressure pain thresholds of the volar forearm were measured pre-operatively, at discharge from hospital and 12 months postoperatively using an algometer. Data on medical and surgical complications were recorded from hospital records during the inpatient stay, by a telephone call to patients at 3 months and by a comprehensive joint assessment by a research nurse at 12 months postoperatively. Cost-effectiveness was assessed through data on health services resource use collected from hospital records and patient self-report questionnaires. Preference-based HRQoL was measured by administering the European Quality of Life-5 Dimensions 3-Level version (EQ-5D-3L)[278] at baseline and at all follow-up points. This provides a single index score for each patient's health state profile.

Details of medical and surgical adverse events were recorded throughout the trial through review of medical records, self-report by patients and assessment by a research nurse.

Potential prognostic factors

Measures of possible effect modifiers included sociodemographic factors, Functional Comorbidity Index,[279] Kellgren and Lawrence osteoarthritis grading scheme,[423] HADS,[281] Pain Self-Efficacy questionnaire,[275] Illness Perceptions Questionnaire-Revised[282] and Brief COPE.[276] Any imbalance between trial arms in factors that might influence the perception of pain and pattern of recovery was considered in sensitivity analyses.

Sample size calculation

A sample size of 300 patients in each trial provided 90% power to detect a difference of 0.5 SDs on the WOMAC pain scale with a two-sided 1% significance level, allowing for a 20% dropout rate. Previous research suggests SDs of around 17 on the WOMAC pain scale before surgery.[424] Hence, a difference between the treatment groups of 0.5 SDs equates to a difference of approximately 8–9 units on the WOMAC pain scale, which represents a minimally perceptible clinical improvement.[425]

Statistical analysis

The hip and knee trials were analysed separately, undertaken in Stata 13.1, and reported in accordance with CONSORT guidelines.

Primary analyses

Following a predefined analysis plan agreed with the Trial Steering Committee,[365] we used linear regressions to estimate between-group differences in mean WOMAC pain scores at 12 months postoperatively, adjusted for pre-operative WOMAC pain scores and surgical approach. All patients in their original assigned groups with available primary outcome data (THR, $n = 281$; TKR, $n = 273$) were included in the primary analyses [intention-to-treat complete cases (ITT-CC)].

Sensitivity analyses

Analyses were repeated on all the randomised 322 patients with THR and 316 patients with TKR using multiple imputation technique by chained equations (20 imputations for the THR trial, 25 imputations for the TKR trial) stratified by randomisation arm to handle missing outcomes [intention-to-treat imputed (ITT-imputed)].[426] The analyses were also conducted on a per-protocol basis, excluding participants who did not receive their allocated intervention or did not have a primary outcome (participants who opted out, died or were lost to follow-up). Per-protocol analyses included 266 patients with THR and 259 patients with TKR [per protocol complete cases (PP)].

In addition, any potential imbalance in patients baseline characteristics were controlled for in the ITT-CC, ITT-imputed and PP analyses.

Post hoc analyses

To explore the impact of potential ceiling effect in the WOMAC pain score on the primary analyses, that is the robustness of the linear regression coefficient standard errors, CIs and *p*-values (via violations of the assumptions of homoscedasticity and normality), we conducted two further sensitivity analyses. First, we investigated transformations of WOMAC pain scores to model the primary outcomes as continuous variables in the linear regressions. Second, the scores were then modelled as a categorical variable using published threshold definitions [severe/extreme (0–50), moderate (51–75), mild (76–99), no (100) pain],[49] and partial proportional odds regressions.[427] These categories relate to the original ordinal WOMAC pain scale (e.g. a patient who reports no pain for every item will score 100, and a patient who reports mild pain on all the items will score 75, etc.).

Secondary analyses

Drug intake, length of hospitalisation and patients' complications after surgery were compared by treatment arm with the use of chi-squared or Fisher exact tests for categorical variables, *t*-tests or Wilcoxon Mann–Whitney *U*-tests for continuous variables. All analyses were performed on complete cases (patients with available outcome information) and the proportion of missing data is reported for each of these variables for information only.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Investigations of pain scores on days 1–3 after the operation were conducted using linear mixed models to account for repeated measurements within participants[339] and using adequate transformation of the outcomes when required. The effect of the intervention on WOMAC pain scores at 3 months and 6 months post operation was also modelled using a mixed linear regression.

Period-specific intervention effects were modelled with interaction terms between the intervention and the assessment day/period parameters. The choice of modelling the raw or transformed continuous scores was based on the normality of the distribution of residuals assessed in a linear regression. When no suitable transformation was identified, the outcome was categorised and modelled with a non-linear regression.

For the THR trial, ICOAP and WOMAC Stiffness scores at 12 months post operation were dichotomised and modelled with a Poisson modified regression with robust variance estimation, a preferable approach to logistic regression when the outcome of interest has a high prevalence.[428] Investigations of the intervention effects on these outcomes at 3 and 6 months were conducted with an extension of this model accounting for the clustering of outcomes by patients.[429] For the TKR trial, ICOAP and WOMAC stiffness and function scores at 12 months post operation were modelled with linear regression and adequate transformation of the outcomes, when required. Investigations of the intervention effects on these outcomes at 3 and 6 months after surgery were conducted with a linear mixed model.

The WOMAC function scores at 12 months and then at 3 months and 6 months post operation were investigated with linear and linear mixed models in both THR and TKR trials. The painDETECT score at 12 months post operation was dichotomised and modelled with a Poisson modified regression with robust variance estimation in both trials.

The modelling strategy of the secondary outcomes was similar to the one described in the statistical analysis section of the main manuscript using an 'intention-to-treat complete cases' approach (THR, $n = 281$; TKR, $n = 273$), an 'intention-to-treat imputed' approach ($n = 322$ THR patients and $n = 316$ TKR patients) and a per-protocol approach ($n = 266$ THR patients and $n = 259$ TKR patients). Baseline analyses were adjusted for pre-operative WOMAC pain and surgical approach. Imbalanced baseline patients' characteristics were then controlled for.

Results

Total hip replacement

Participants

Between November 2009 and February 2012, 630 eligible patients were approached about the trial. Of these patients, 322 (51%) were recruited and randomised: 163 to the intervention arm and 159 to the standard care arm (*Figure 28*). Primary outcome data were collected from 288 patients (87%). Baseline demographic and clinical characteristics were generally well balanced between the trial arms (*Table 38*). Differences between trial arms in sex, living arrangement and number of comorbidities were adjusted for in the analysis.

Primary outcome

As shown in *Table 39*, the majority of patients in both trial arms had excellent pain relief at 12 months after surgery, with a median WOMAC pain score in the intervention arm of 100 out of 100 (i.e. no pain) and in the standard care arm of 95 out of 100.

As shown in *Table 40*, the primary analysis found some evidence that patients in the intervention group had less pain at 12 months post operation than patients in the standard care group (coefficient 4.74, 95% CI 0.95 to 8.54; $p = 0.015$). This difference remained after further adjustments for baseline imbalances between groups, although it was less apparent in the adjusted intention to treat (ITT) with imputed data and per-protocol analyses.

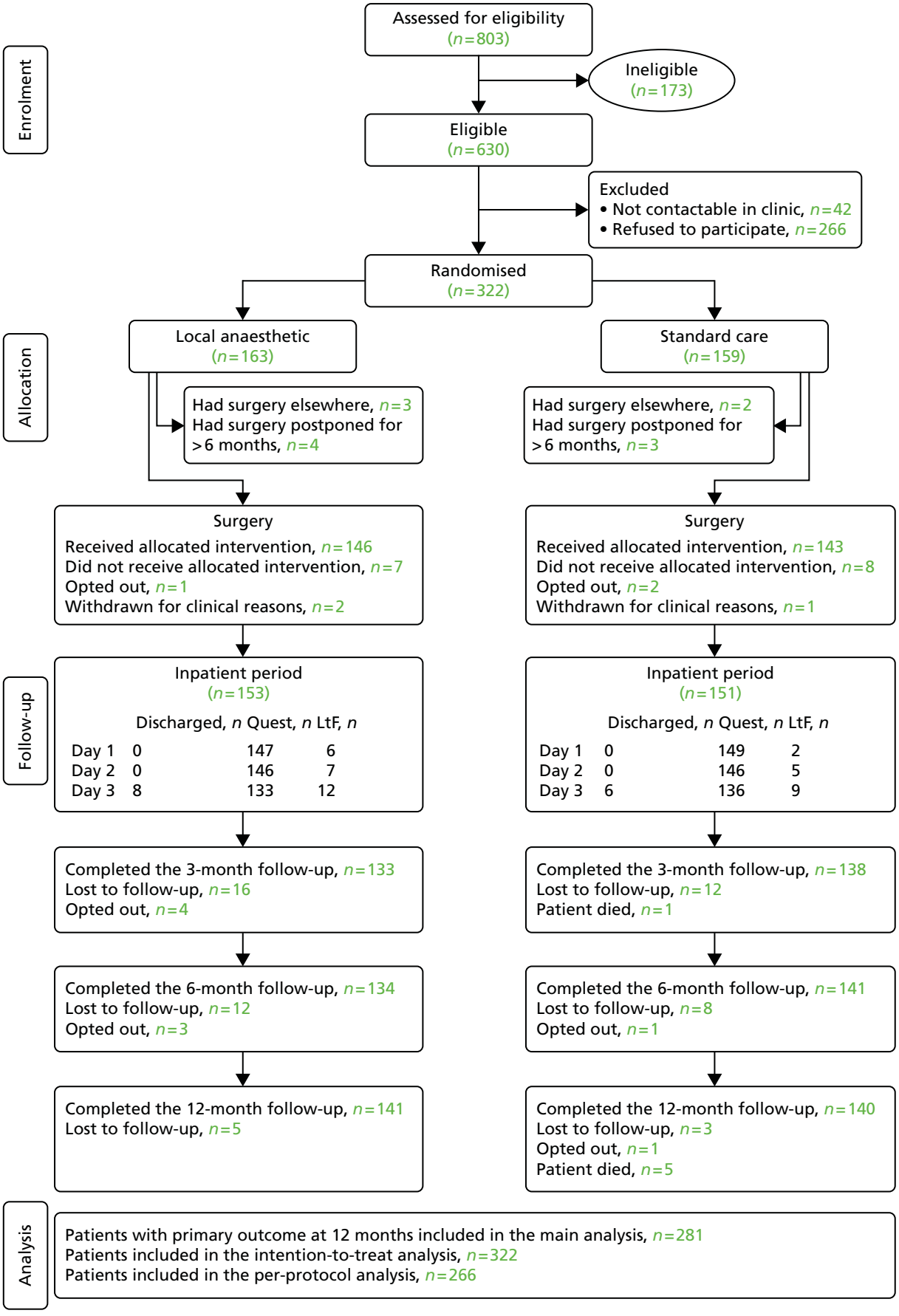


FIGURE 28 Total hip replacement: APEX patient recruitment, randomisation and follow-up. Quest, in patient questionnaire; LtF, lost to follow-up.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 38 Total hip replacement: baseline characteristics of APEX participants by trial arm

Characteristic	Intervention ($n = 163$)	Standard care group ($n = 159$)
Female sex, *n* (%)	86 (53)	103 (65)
Age (years), mean (SD)	66.0 (11.4)	66.4 (10.2)
BMI (kg/m^2), mean (SD)	28.9 (5.6)	29.4 (5.4)
Living arrangement,* n *(%)		
Live with someone	110 (68)	123 (77)
Live alone	43 (26)	32 (20)
Missing	10 (6)	4 (3)
Working status,* n *(%)		
Paid employment/voluntary work	47 (29)	52 (33)
Retired	104 (64)	104 (65)
Missing	12 (7)	3 (2)
Education,* n *(%)		
Compulsory age or before	98 (60)	108 (68)
College	34 (21)	30 (19)
University	20 (12)	17 (11)
Missing	11 (7)	4 (2)
Comorbidities,* n *(%)		
0 to 1	57 (35)	53 (33)
2	48 (30)	36 (23)
3	25 (15)	36 (23)
≥ 4	21 (13)	28 (18)
Missing	12 (7)	6 (4)
Anxiety,* n *(%)		
Definite	26 (16)	31 (19)
Potential	26 (16)	23 (15)
None	100 (61)	100 (63)
Missing	11 (7)	5 (3)
Depression		
Definite, *n* (%)	20 (12)	25 (16)
Potential, *n* (%)	25 (15)	28 (18)
None, *n* (%)	106 (65)	101 (63)
Missing, *n* (%)	12 (7)	5 (3)
Self-efficacy, mean (SD)	35.6 (13.7)	34.2 (13.3)
WOMAC pain, mean (SD)	43.4 (19.0)	41.5 (17.9)
WOMAC function, mean (SD)	43.7 (20.2)	41.2 (17.2)
WOMAC stiffness, mean (SD)	47.4 (24.9)	42.6 (20.7)

TABLE 38 Total hip replacement: baseline characteristics of APEX participants by trial arm (*continued*)

Characteristic	Intervention ($n = 163$)	Standard care group ($n = 159$)
Surgical approach,* n *(%)		
Posterior	151 (93)	147 (92)
Lateral	12 (7)	12 (8)
Kellgren and Lawrence grade,* n *(%)		
< 3	4 (3)	8 (4)
≥ 3	136 (83)	128 (81)
Non-interpretable	12 (7)	12 (8)
Missing	11 (7)	11 (7)

TABLE 39 Total hip replacement: WOMAC pain scores at 12 months after surgery

Outcome	Intervention ($n = 163$)	Standard care ($n = 159$)
WOMAC pain at 12 months *Continuous score, by categorised pain level*		
Median (IQR)	100 (10)	95 (20)
None = 100	72 (44%)	59 (37%)
Mild = 75–100	51 (31%)	53 (33%)
Moderate = 50–75	16 (10%)	16 (10%)
Severe = 0–50	2 (1%)	12 (8%)
Missing data	22 (14%)	19 (12%)

TABLE 40 Total hip replacement: primary analysis of WOMAC pain scores at 12 months after surgery

	ITT-CC		ITT-imputed		PP	
Model	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value
Baseline	4.74 (0.95 to 8.54)	0.015	5.35 (1.33 to 9.34)	0.009	3.81 (–0.02 to 7.63)	0.051
Adjusted	4.31 (0.63 to 7.98)	0.022	4.36 (0.48 to 8.25)	0.028	3.45 (–0.26 to 7.16)	0.068

Baseline model: linear regression – adjusted for baseline pain score and surgical approach. Adjusted model: baseline model + adjustments for sex, living arrangement and number of comorbidities.

As described in the statistical methods, the assumptions of homoscedasticity and normality underlying the use of linear regression, our a priori primary analysis, were violated. Therefore, we performed a further secondary analysis of the primary outcome to test the robustness of the above findings by categorising the WOMAC pain score and using a partial proportional odds model. This method of analysis found similar results (*Table 41*), with evidence that patients in the intervention group were less likely to have severe pain at 12 months post operation than those in the standard care group (OR 10.19, 95% CI 2.10 to 49.55; $p = 0.004$). This finding remained after further adjustments for baseline imbalances between groups and was also observed in the ITT with imputed data and the per-protocol approaches.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 41 Total hip replacement: secondary analysis of WOMAC pain scores at 12 months after surgery

	Baseline model		Adjusted model	
Groups compared	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
(Moderate, mild or none) vs. reference = (severe)				
ITT-CC ($n = 281$)	10.19 (2.10 to 49.55)	0.004	10.78 (2.15 to 54.17)	0.004
ITT-imputed ($n = 322$)	6.81 (1.81 to 25.68)	0.005	6.26 (1.61 to 24.36)	0.008
PP ($n = 266$)	8.93 (1.83 to 43.62)	0.007	9.50 (1.88 to 47.76)	0.006
(Mild or none) vs. reference = (severe or moderate)				
ITT-CC ($n = 281$)	1.72 (0.90 to 3.30)	0.100	1.70 (0.86 to 3.33)	0.125
ITT-imputed ($n = 322$)	1.76 (0.95 to 3.26)	0.073	1.59 (0.84 to 3.02)	0.157
PP ($n = 266$)	1.56 (0.81 to 3.02)	0.186	1.54 (0.77 to 3.05)	0.220
(None) vs. reference = (severe, moderate or mild)				
ITT-CC ($n = 281$)	1.40 (0.89 to 2.25)	0.168	1.35 (0.82 to 2.22)	0.243
ITT-imputed ($n = 322$)	1.42 (0.90 to 2.26)	0.136	1.30 (0.80 to 2.10)	0.290
PP ($n = 266$)	1.31 (0.80 to 2.14)	0.277	1.27 (0.76 to 2.12)	0.363

Baseline model: partial proportional odds model adjusted for baseline pain score and surgical approach. Adjusted model: baseline model + adjustments for sex, living arrangement and number of comorbidities.

Secondary outcomes

Details of the analysis of secondary outcomes are shown in *Table 42* and *Appendices 11–28*. There was no difference in any of the secondary outcomes except that patients in the intervention group reported less pain on postoperative night 2 (coefficient –0.81, 95% CI –1.40 to –0.23; $p = 0.006$) and less neuropathic pain at 12 months post operation (ITT adjusted model: relative risk 0.17, 95% CI 0.03 to 0.82; $p = 0.028$). Post-surgical superficial and deep wound infection rates were similar in the intervention group and standard care group (1.8% vs. 1.9%; $p = 1.000$).

TABLE 42 Total hip replacement: ITT and per-protocol analyses of the effect of the intervention on pain during the inpatient stay

	ITT-CC		ITT-imputed		PP	
Model	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value
Pain over night (square root)						
Day 1						
Baseline model	0.29 (–0.29 to 0.87)	0.325	0.25 (–0.36 to 0.85)	0.419	0.36 (–0.22 to 0.95)	0.223
Adjusted model	0.39 (–0.19 to 0.97)	0.184	0.34 (–0.27 to 0.94)	0.276	0.45 (–0.12 to 1.03)	0.124
Day 2						
Baseline model	–0.81 (–1.40 to 0.23)	0.006	–0.87 (–1.43 to 0.30)	0.003	–0.75 (–1.34 to 0.16)	0.012
Adjusted model	–0.71 (–1.30 to –0.13)	0.016	–0.78 (–1.35 to –0.20)	0.008	–0.66 (–1.25 to –0.08)	0.025
Day 3						
Baseline model	–0.29 (–0.89 to 0.31)	0.347	–0.40 (–0.98 to 0.18)	0.173	–0.09 (–0.70 to 0.51)	0.765
Adjusted model	–0.18 (–0.78 to 0.41)	0.545	–0.31 (–0.89 to 0.27)	0.301	0.01 (–0.59 to 0.60)	0.986

TABLE 42 Total hip replacement: ITT and per-protocol analyses of the effect of the intervention on pain during the inpatient stay (*continued*)

	ITT-CC		ITT-imputed		PP	
Model	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value
Pain at rest (square root)						
Day 1						
Baseline model	0.12 (–0.36 to 0.60)	0.621	0.12 (–0.35 to 0.59)	0.619	0.15 (–0.33 to 0.63)	0.546
Adjusted model	0.19 (–0.28 to 0.66)	0.432	0.17 (–0.30 to 0.65)	0.468	0.21 (–0.27 to 0.68)	0.394
Day 2						
Baseline model	–0.22 (–0.69 to 0.26)	0.373	–0.27 (–0.75 to 0.21)	0.270	–0.05 (–0.53 to 0.43)	0.848
Adjusted model	–0.15 (–0.62 to 0.33)	0.546	–0.21 (–0.70 to 0.27)	0.381	0.01 (–0.46 to 0.49)	0.962
Day 3						
Baseline model	–0.34 (–0.83 to 0.15)	0.171	–0.45 (–0.92 to 0.02)	0.062	–0.21 (–0.71 to 0.28)	0.391
Adjusted model	–0.27 (–0.75 to 0.22)	0.282	–0.39 (–0.86 to 0.08)	0.108	–0.15 (–0.64 to 0.33)	0.545
Pain on movement						
Day 1						
Baseline model	1.52 (–3.90 to 6.95)	0.582	1.25 (–4.20 to 6.69)	0.653	1.26 (–4.21 to 6.74)	0.651
Adjusted model	2.01 (–3.46 to 7.48)	0.471	1.52 (–4.02 to 7.05)	0.591	1.88 (–3.62 to 7.38)	0.503
Day 2						
Baseline model	1.57 (–3.88 to 7.02)	0.573	1.66 (–3.79 to 7.12)	0.549	2.07 (–3.44 to 7.57)	0.462
Adjusted model	2.07 (–3.43 to 7.56)	0.461	1.93 (–3.61 to 7.48)	0.494	2.69 (–2.83 to 8.21)	0.339
Day 3						
Baseline model	0.01 (–5.56 to 5.58)	0.997	–0.47 (–5.88 to 4.95)	0.866	0.27 (–5.35 to 5.89)	0.925
Adjusted model	0.54 (–5.07 to 6.16)	0.849	–0.16 (–5.64 to 5.31)	0.954	0.94 (–4.70 to 6.57)	0.745

Baseline model: linear mixed model adjusted for baseline pain score and surgical approach. Adjusted model: baseline model + adjustments for sex, living arrangement, number of comorbidities and self-efficacy.

Total knee replacement

Participants

Between November 2009 and February 2012, 585 eligible patients were approached to take part in the trial. Of these patients, 316 (54%) were recruited and randomised: 157 to the intervention arm and 159 to the standard care arm (*Figure 29*). Primary outcome data were collected from 273 patients (86%). Baseline demographic and clinical characteristics were generally well balanced between the trial arms (*Table 43*). Differences between trial arms in working status, number of comorbidities, anxiety and depression were adjusted for in the analysis.

Primary outcome

The majority of patients in both trial arms had good pain relief at 12 months after surgery, with a median WOMAC pain score in the intervention group of 90 (IQR 30) and in the standard care group of 85 (IQR 35) (*Table 44*).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

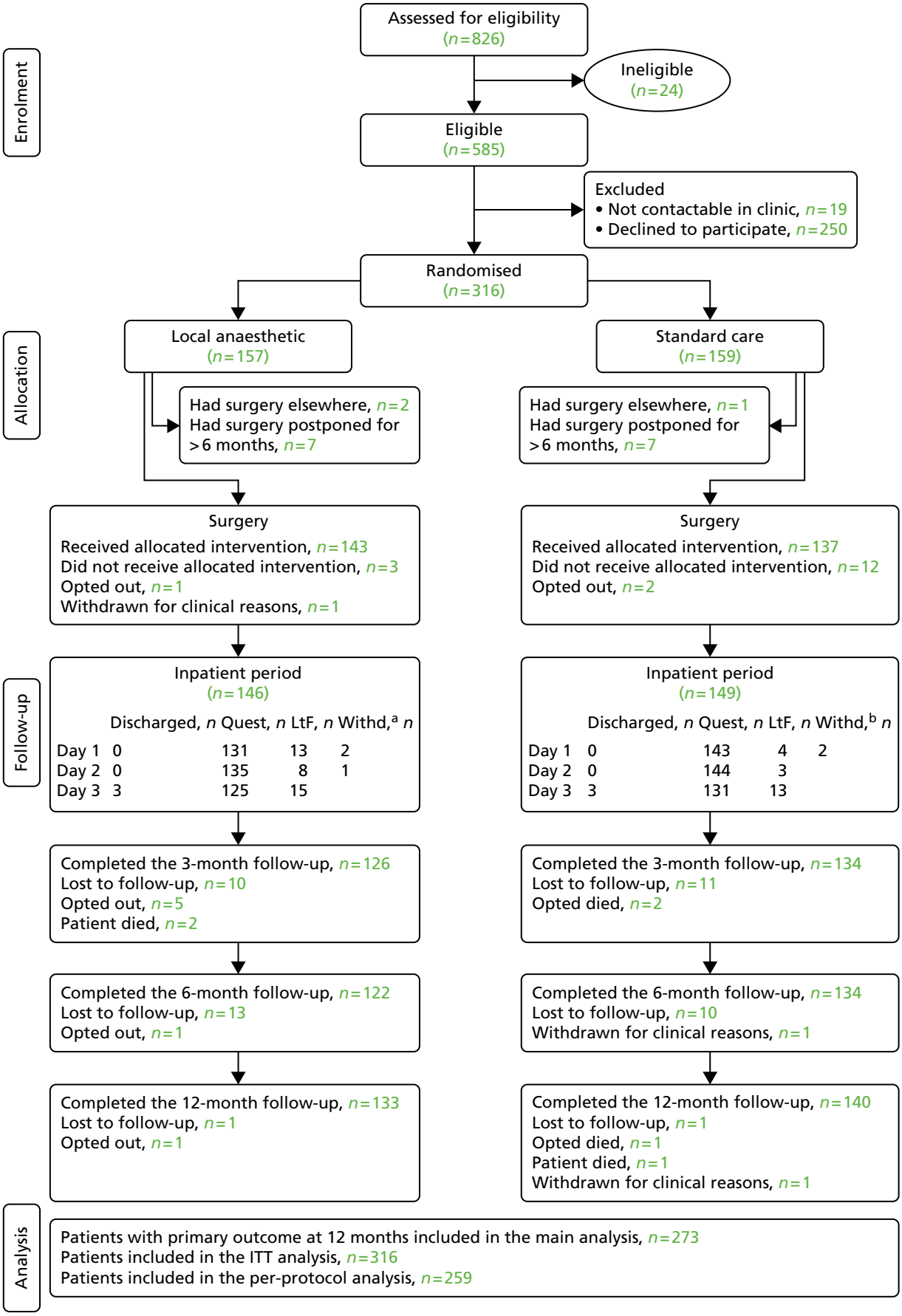


FIGURE 29 Total knee replacement: APEX patient recruitment, randomisation and follow-up. LtF, lost to follow-up; Quest, in patient questionnaire. a, Withdrawn: one patient died, two opted out during the inpatient period; b, withdrawn: one patient was withdrawn for clinical reasons, one opted out during the inpatient period.

TABLE 43 Total knee replacement: baseline characteristics of APEX participants by trial arm

Characteristic	Intervention group ($n = 157$)	Standard care group ($n = 159$)
Female sex, *n* (%)	81 (52)	86 (54)
Age (years), mean (SD)	69.5 (9.4)	68.7 (7.9)
BMI (kg/m^2), mean (SD)	32.4 (6.5)	32.8 (6.5)
Living arrangement,* n *(%)		
Live with someone	112 (71)	103 (65)
Live alone	41 (26)	44 (28)
Missing	4 (3)	12 (7)
Working status,* n *(%)		
Paid employment/voluntary work	41 (26)	27 (17)
Retired	111 (71)	117 (74)
Missing	5 (3)	15 (9)
Education,* n *(%)		
Compulsory age or before	115 (73)	109 (69)
College	26 (17)	25 (16)
University	9 (6)	10 (6)
Missing	7 (4)	15 (9)
Comorbidities,* n *(%)		
0 to 1	46 (29)	39 (24)
2	30 (19)	41 (26)
3	36 (23)	25 (16)
≥ 4	38 (24)	43 (27)
Missing	7 (5)	11 (7)
Anxiety,* n *(%)		
Definite	33 (21)	18 (11)
Potential	24 (15)	32 (20)
None	93 (59)	99 (62)
Missing	7 (5)	10 (6)
Depression		
Definite, *n* (%)	30 (19)	16 (10)
Potential, *n* (%)	29 (19)	30 (19)
None, *n* (%)	91 (58)	104 (65)
Missing, *n* (%)	7 (4)	9 (6)
Self-efficacy, mean (SD)	36.0 (13.4)	37.3 (12.0)
WOMAC pain, mean (SD)	42.5 (17.3)	42.4 (16.1)
WOMAC function, mean (SD)	46.1 (17.7)	46.0 (17.9)
WOMAC stiffness, mean (SD)	41.9 (21.0)	41.1 (19.4)

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 43 Total knee replacement: baseline characteristics of APEX participants by trial arm (*continued*)

Characteristic	Intervention group ($n = 157$)	Standard care group ($n = 159$)
Surgical approach*, n *(%)		
Medial parapatellar	122 (78)	125 (79)
Subvastus	35 (22)	34 (21)
Kellgren and Lawrence grade*, n *(%)		
< 3	133 (84)	133 (84)
≥ 3	1 (1)	3 (2)
Non-interpretable	1 (1)	5 (3)
Missing	22 (14)	18 (11)

TABLE 44 Total knee replacement: WOMAC pain scores at 12 months after surgery

	Continuous score, by categorised pain level	
Outcome	Intervention ($n = 157$)	Standard care ($n = 159$)
WOMAC pain at 12 months		
Median (IQR)	90 (30)	85 (35)
None = 100	45 (29%)	36 (23%)
Mild = 75–100	44 (28%)	44 (28%)
Moderate = 50–75	29 (18%)	42 (26%)
Severe = 0–50	15 (10%)	18 (11%)
Missing data	24 (15%)	19 (12%)

The primary analysis revealed that there was no evidence that pain severity at 12 months after surgery was different between the intervention and standard care group (ITT-CC coefficient 3.83, 95% CI –0.83 to 8.49; $p = 0.107$; *Table 45*). This finding was consistently observed in the different approaches.

Similar to the THR trial, the assumptions of the linear regression were violated. The partial odds model also revealed no difference in pain severity between the two groups with the exception that the per-protocol and ITT-CC analysis showed some evidence that the intervention reduced the number of patients with severe to moderate pain (*Table 46*).

TABLE 45 Total knee replacement: primary analysis of WOMAC pain scores at 12 months after surgery

	ITT-CC		ITT-imputed		PP	
Model	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value
Baseline	3.83 (–0.83 to 8.49)	0.107	3.33 (–1.21 to 7.88)	0.146	4.21 (–0.66 to 9.09)	0.090
Adjusted	4.14 (–0.51 to 8.80)	0.081	4.16 (–0.37 to 8.69)	0.082	4.60 (–0.28 to 9.50)	0.064

Baseline model: linear regression – adjusted for baseline pain score and surgical approach. Adjusted model: baseline model + adjustments for working status, number of comorbidities, depression and anxiety.

TABLE 46 Total knee replacement: secondary analysis of WOMAC pain scores at 12 months after surgery

	Baseline model		Adjusted model	
Groups compared	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
(Moderate, mild or none) vs. reference = (severe)				
ITT-CC ($n = 273$)	1.28 (0.60 to 2.72)	0.515	1.27 (0.58 to 2.78)	0.543
ITT-imputed ($n = 316$)	1.28 (0.63 to 2.61)	0.497	1.34 (0.64 to 2.81)	0.444
PP ($n = 259$)	1.28 (0.60 to 2.72)	0.515	1.29 (0.59 to 2.81)	0.527
(Mild or none) vs. reference = (severe or moderate)				
ITT-CC ($n = 273$)	1.61 (0.96 to 2.71)	0.071	1.77 (1.02 to 3.07)	0.042
ITT-imputed ($n = 316$)	1.48 (0.89 to 2.48)	0.131	1.65 (0.95 to 2.86)	0.077
PP ($n = 259$)	1.75 (1.03 to 2.97)	0.039	1.94 (1.11 to 3.42)	0.021
(None) vs. reference = (severe, moderate or mild)				
ITT-CC ($n = 273$)	1.41 (0.82 to 2.43)	0.216	1.55 (0.87 to 2.75)	0.135
ITT-imputed ($n = 316$)	1.39 (0.82 to 2.35)	0.227	1.54 (0.88 to 2.69)	0.133
PP ($n = 259$)	1.48 (0.85 to 2.59)	0.168	1.64 (0.91 to 2.67)	0.099

Baseline model: partial proportional odds model adjusted for baseline pain score and surgical approach. THR adjusted model: baseline model + adjustments for sex, living arrangement and number of comorbidities. TKR adjusted model: baseline model + adjustments for working status, number of comorbidities, depression and anxiety.

Secondary outcomes

Details of the analysis of secondary outcomes can be found in *Table 47* and *Appendices 11–28*. There was some evidence that patients in the intervention group had fewer drugs administered on the recovery ward (98 vs. 118; $p = 0.010$) and reported less vomiting (26% vs. 39%; $p = 0.025$) and nausea (58% vs. 85%; $p = 0.005$) on postoperative day 1. There was no difference in any of the other secondary outcomes. Post-surgical superficial and deep wound infection rates were similar in the intervention group and standard care group (3.2% vs. 1.9%; $p = 0.500$).

Comparison of the results of the hip and knee trial

Table 48 presents the effect of the intervention when all the participants of the THR and TKR trials are combined. The results are adjusted for pre-operative WOMAC pain scores, surgical approach and surgical site (hip or knee). Patients in the intervention group had a higher mean WOMAC score at 12 months after surgery than those in the standard care group (ITT-CC, between-group difference in mean WOMAC at 12 months: 4.10, 95% CI 1.08 to 7.12; $p = 0.008$; *Table 48*). This finding was consistently observed in the different approaches.

The intervention effect observed in the hip patients was then contrasted with the intervention effect observed in the knee using an interaction term between the intervention effect (intervention or standard care) and site of surgery (hip or knee) in the above model. Despite the statistical significant effect observed in the hip group (ITT-CC, MD: 4.74; $p = 0.015$; see *Table 40*) and the non-significant effect observed in the knee group (ITT-CC, MD: 3.83; $p = 0.107$; see *Table 45*), these two effects were not statistically different (ITT-CC: $p = 0.904$; ITT-imputed: $p = 0.657$; and P: $p = 0.682$).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 47 Total knee replacement: ITT and per-protocol analyses of the effect of the intervention on pain during the inpatient stay

	ITT-CC		ITT-imputed		PP	
Model	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value
Pain over night						
Day 1						
Baseline model	3.81 (–3.07 to 10.69)	0.278	4.12 (–2.87 to 11.12)	0.248	5.46 (–1.50 to 12.41)	0.124
Adjusted model	3.75 (–3.08 to 10.58)	0.282	3.70 (–3.21 to 10.62)	0.294	5.43 (–1.47 to 12.33)	0.123
Day 2						
Baseline model	2.30 (–4.49 to 9.10)	0.506	2.39 (–4.47 to 9.25)	0.494	2.35 (–4.52 to 9.21)	0.503
Adjusted model	2.20 (–4.54 to 8.95)	0.522	1.97 (–4.85 to 8.80)	0.571	2.26 (–4.56 to 9.08)	0.516
Day 3						
Baseline model	–3.55 (–10.58 to 3.49)	0.323	–2.13 (–9.14 to 4.89)	0.552	–3.77 (–10.87 to 3.33)	0.298
Adjusted model	–3.94 (–10.92 to 3.04)	0.269	–2.54 (–9.50 to 4.41)	0.473	–4.13 (–11.18 to 2.91)	0.250
Pain at rest						
Day 1						
Baseline model	–2.53 (–7.62 to 2.56)	0.330	–2.39 (–7.74 to 2.95)	0.379	–1.89 (–7.12 to 3.34)	0.478
Adjusted model	–2.49 (–7.46 to 2.49)	0.327	–2.37 (–7.67 to 2.93)	0.380	–1.70 (–6.82 to 3.41)	0.514
Day 2						
Baseline model	2.48 (–2.58 to 7.54)	0.337	2.56 (–2.70 to 7.83)	0.339	2.22 (–2.98 to 7.42)	0.402
Adjusted model	2.52 (–2.42 to 7.46)	0.318	2.59 (–2.58 to 7.76)	0.325	2.41 (–2.67 to 7.50)	0.352
Day 3						
Baseline model	0.63 (–4.56 to 5.83)	0.811	0.73 (–4.47 to 5.94)	0.782	0.06 (–5.27 to 5.38)	0.983
Adjusted model	0.54 (–4.53 to 5.62)	0.833	0.76 (–4.33 to 5.85)	0.769	0.12 (–5.08 to 5.33)	0.963
Pain on movement						
Day 1						
Baseline model	–1.08 (–6.64 to 4.47)	0.702	–1.06 (–6.88 to 4.77)	0.721	–0.69 (–6.41 to 5.03)	0.814
Adjusted model	–1.12 (–6.66 to 4.41)	0.690	–0.98 (–6.90 to 4.93)	0.744	–0.73 (–6.42 to 4.96)	0.802
Day 2						
Baseline model	0.68 (–4.84 to 6.20)	0.809	0.79 (–4.85 to 6.42)	0.784	0.66 (–5.03 to 6.35)	0.820
Adjusted model	0.64 (–4.87 to 6.15)	0.818	0.86 (–4.86 to 6.58)	0.768	0.62 (–5.04 to 6.28)	0.830
Day 3						
Baseline model	1.00 (–4.65 to 6.65)	0.729	1.07 (–4.86 to 6.99)	0.724	0.58 (–5.23 to 6.39)	0.845
Adjusted model	0.90 (–4.75 to 6.53)	0.753	1.14 (–4.82 to 7.11)	0.706	0.49 (–5.29 to 6.27)	0.868

Baseline model: linear mixed model adjusted for baseline pain score and surgical approach. Adjusted model: baseline model + adjustments for working status, number of comorbidities, depression and anxiety.

TABLE 48 Combined analysis of WOMAC pain scores at 12 months for THR and TKR participants: linear regression

	ITT-CC		ITT-imputed		PP	
Intervention effect	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value
Effect	4.10 (1.08 to 7.12)	0.008	4.28 (1.19 to 7.36)	0.007	3.89 (0.77 to 7.00)	0.014

Discussion

These are the first reported RCTs powered to investigate the clinical effectiveness of local anaesthetic infiltration at reducing chronic pain at 12 months after THR and TKR. Administering local anaesthetic infiltration is easy and quick, with no increased morbidity or hospital stay. Our trials found evidence that local anaesthetic wound infiltration can reduce pain severity at 12 months after THR, but not TKR. The reasons for the observed difference in the effectiveness of the intervention in TKR and THR patients are unclear and require further research, but one contributing factor could be the use of FNB in both arms of the TKR trial.

Strengths of these trials include the long-term postoperative follow-up, the use of robust and validated outcome measures to assess pain, good rates of data collection for the primary outcome measure and use of an independent allocation system and blinding to minimise bias. Our sample population is representative of the population undergoing THR and TKR as a whole with a similar disease profile, sex mix and age range as reported by the National Joint Registry for England and Wales,[3] and other national registries;[430] thus, we believe our results to be generalisable. However, our trials do have weaknesses and it is important to note that the number of patients with severe chronic post-surgical pain in the THR trial was small, generating wide 95% CIs for the ORs in the secondary analysis of the primary outcome. These risks should be interpreted with caution. It is also important to keep in mind that the trials were not powered for the analyses of the primary outcome as categorical variables or to detect differences in treatment effect for the secondary outcomes. This may explain the lack of strong evidence for an intervention effect on acute postoperative pain in the two trials.

For many patients, THR and TKR are effective treatments for painful osteoarthritis, and additional interventions to improve pain relief are not required. However, a sizeable proportion of people report chronic post-surgical pain.[18] The findings of this trial suggest that local anaesthetic infiltration is beneficial for decreasing long-term pain in THR patients but not in TKR patients. In addition, we found some evidence that the intervention may reduce neuropathic pain at 12 months after THR, indicating that infiltration may benefit those patients experiencing severe and/or neuropathic pain in the long term, both of which can be difficult to treat once established.[431] Given that approximately 80,000 THR operations are performed annually in England, Wales and Northern Ireland,[3] and 7–23% of patients are likely to develop severe chronic post-surgical pain,[18] our findings suggest that routine use of local anaesthetic infiltration has the potential to improve pain outcomes for between 4600 and 15,300 patients every year in the NHS.

Conclusion

The double-blind APEX RCTs provide evidence that administering local anaesthetic infiltration before wound closure reduces chronic post-surgical pain at 1 year after THR. This suggests that the routine use of infiltration would be beneficial in improving long-term pain relief for THR patients. Findings from our TKR trial suggest that local anaesthetic infiltration would have little long-term benefit for TKR patients. However, it must be noted that the majority of patients had good or excellent long-term pain relief after both hip and knee replacement, regardless of whether they were randomised to local anaesthetic infiltration or not.

The cost-effectiveness of local anaesthetic wound infiltration on chronic pain after lower limb joint replacement: APEX randomised controlled trials

Introduction

The APEX economic evaluation assessed the cost-effectiveness of local anaesthetic wound infiltration in patients receiving (1) TKR and (2) THR, compared with usual care, at 1 year post surgery, from a NHS and PSS perspective. We also collected data allowing for a future economic evaluation from a societal perspective.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Methods

Resource use identification and collection

Collection of resource-use data was identical for both the hip and the knee trials. Resources used during the initial inpatient stay for joint replacement and subsequent inpatient stays and outpatient visits at Southmead Hospital during the 12 months of follow-up were extracted from medical records onto study designed proformas. Initial inpatient resource use included operating theatre time, perioperative local anaesthetic infiltration in the intervention group, time spent in recovery and number of days admitted to a ward after surgery. After initial hospital discharge, inpatient and outpatient resource-use data collected included the duration and reason for visit, ward details of inpatient admissions including day-case admissions, accident and emergency visits, and outpatient visits and specialty clinics attended during the 12-month follow-up period.

Use of PSS and other NHS resources was collected using patient-completed questionnaires, sent by post at 3, 6 and 12 months' follow-up. Patient-reported data included secondary care visits at other hospitals; community-based health-care visits including GP, practice nurse, district nurse, community physiotherapist and OT contacts; medication use; and use of PSS, such as food at home and home care worker services, contacts with social workers, equipment provided to patients and changes made to patients' homes during the follow-up period. We further collected private expenses, such as travel expenses, prescription costs, over-the-counter medications, privately paid equipment, changes made to the patient's home, the burden of informal care and productivity losses through the collection of time-off work and leisure activities, and help from friends and relatives to allow for further future economic work.

We gave patients resource-use logs at hospital discharge at 3 and 6 months in order to facilitate their completion of these questionnaires.[432] Both the logs and the questionnaires were tailored to the type of joint replacement. Examples of the 3-month resource-use questionnaire and log are available online on the Data Instruments for Resource Use Measurement (DIRUM) database.[433,434]

Valuation of resource use

Resources used during the initial hospital stay were valued using a microcosting approach, using unit costs obtained from the North Bristol Trust finance department. Estimates for time spent in theatre and recovery and admissions to hospital wards included staff time, overheads, consumables and medications. Unit costs for the local anaesthetic infiltration injection were provided by the Management and Procurement Department at Southmead Hospital.

Hospital resources used during the follow-up period were macrocosted and valued using Department of Health Reference costs[435] for specialty outpatient clinic and tariffs for inpatient admissions. When tariffs could not be derived because of insufficient information, inpatient admissions were microcosted using the number of nights spent in the ward and a day ward cost estimate from the North Bristol Trust finance department.

Community-based resources and PSS were valued using Curtis's *Unit Costs of Health and Social Care*.[436] Equipment and changes to patients' homes, such as dressing aids, furniture raisers, walking aids and chair lifts, were financed by social services, but provided to patients – on loan – through OTs and physiotherapists at Southmead Hospital. We assumed a 2-year life period for all equipment and valued it as the fraction of equipment cost proportional to the duration of patient use. Unit costs were obtained from equipment suppliers to Southmead Hospital or online sources from other suppliers when procurement costs were not available.

Economic outcome measured

The primary health outcome for the APEX economic evaluation was the quality-adjusted life-year (QALY). A QALY is a measure of disease burden that weights survival by QoL. This generic measure allows for direct clinical effectiveness and cost-effectiveness comparisons between interventions across all patient groups and health conditions. NICE guidelines provide recommendations for the UK's societal willingness to pay for one QALY gained (section 6.3, Decision-Making[86]) which allows for inferences about the absolute cost-effectiveness of interventions to be made. QALYs for the APEX trial were derived using the EQ-5D-3L questionnaire.[437] APEX patients completed the EQ-5D-3L at baseline, and at the 3-, 6- and 12-month follow-ups. The EQ-5D-3L questionnaire is a simple and quick tool developed by health economists to measure generic HRQoL with the purpose of estimating QALYs. It comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has three levels: no problems, some problems or severe problems. Each of the possible 243 health states has been assigned a quality weight (utility) through a valuation survey of a sample of the UK population.

The preference-based quality weights are measured on a scale anchored at zero for death and 1 for the best imaginable health. Negative values for 'health states worse than death' are also possible.[438] The scale has cardinal properties, for example spending 1 year in a health state with a quality weight of 0.5 is equivalent to spending 6 months in perfect health (quality weight equal to 1). QALYs within APEX were derived for each trial arm, attributing the quality weights from the UK population to the patients' answers to the EQ-5D-3L questionnaire,[439] at baseline (pre-operative), and at the 3-, 6- and 12-month follow-ups. QALYs were then estimated using the area under the curve approach, which assumed a linear change between time points.[440]

Data analysis

The economic evaluations in relation to total hip and TKR were conducted as two separate analyses; however, the same methodology was used for both analyses. The primary analysis for both of these evaluations was an ITT analysis and took a NHS and PSS perspective, in line with NICE guidelines.[86] Costs and QALYs were not discounted because of the 1-year duration of follow-up. All costs are reported in 2012–13 prices.

Costs were estimated by multiplying units of resource use by its unit cost (*Table 49*).

The total cost for each individual patient for each of the 17 resource-use categories was calculated as the sum of the cost of the resource-use items. All available data were used to calculate means and SDs for resource use and costs for each category by trial arm. This enables comparisons between trial arms of absolute resource use and costs to aid decision-making. The cost categories were then grouped into initial inpatient stay costs, secondary care costs during the follow-up period, community-based health-care costs including medication, and PSS costs. The total cost for each individual patient for these four groups as well as total NHS costs and total NHS and PSS costs were calculated as above.

Mean and SDs for QALYS were calculated for each arm of the two trials.

Incremental costs for the four main cost groupings, and QALY differences between arms, were then estimated using ordinary least squares (OLS) regression, with robust standard errors adjusting for the APEX trial treatment group allocation and minimisation variables: baseline WOMAC pain score and surgical approach (see *Equation 1*). QALYs were further adjusted for baseline utility imbalances (see *Equation 2*).[443]

Equation 1 for costs:

$$\text{Cost}_{ijk} = \beta_{0j} + \beta_{1j} \times \text{Treatment group} + \beta_{2j} \times \text{Baseline pain score} + \beta_{3j} \times \text{Surgical approach} + e_{ij}. \quad (1)$$

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 49 Unit costs for total hip and knee replacement resource use

Resource use	Unit cost	Assumption	Source
Initial inpatient admission			
Theatre (per minute)	£14.22	Includes implant cost, staff time, overheads, consumables, facilities	Mr Michael Iwasiuk, North Bristol NHS Trust Finance Department, 2014, personal communication
Injection of local anaesthesia infiltration	£2.00	Box of bupivacaine with adrenaline 0.25%/1 in 200,000 is £20.00. One box contains 10 ampoules	Mrs Helen Wright, North Bristol NHS Trust Finance Department, 2014, personal communication
Recovery (per minute)	£3.84	Includes staff time with overheads, consumables, facilities and medications administered during stay. Base cost per minute	Mr Michael Iwasiuk, North Bristol NHS Trust Finance Department, 2014, personal communication
Day in general orthopaedics ward: Frome, Severn, Kennett and Critical Care Unit	£311	Includes staff time with overheads, consumables, facilities and medications administered during stay. Base cost per day	Mr Michael Iwasiuk, North Bristol NHS Trust Finance Department, 2014, personal communication
Day in other orthopaedics ward: Chew	£250	Includes staff time with overheads, consumables, facilities and medications administered during stay. Base cost per day	Mr Michael Iwasiuk, North Bristol NHS Trust Finance Department, 2014, personal communication
Day in high-dependency unit	£1356	Includes staff time with overheads, consumables, facilities and medications administered during stay. Base cost per day	Mr Michael Iwasiuk, North Bristol NHS Trust Finance Department, 2014, personal communication
Inpatient admissions following discharge from initial surgery			
Revision surgery: TKR	£9439	HB22 A Major Knee Procedures for Non-Trauma, with Major CC	NHS Reference Costs 2012–13: Non elective Long Stay[435]
Revision surgery: THR	£8890	HB12 A Major Hip Procedures for Non-Trauma, with Major CC	NHS Reference Costs 2012–13: Non elective Long Stay[435]
Manipulation under anaesthetic: TKR	£2044	HB24C Minor Knee Procedures for Non-Trauma, Category 2, without CC	NHS Reference Costs 2012–13: Non elective Long Stay[435]
Infections	£4124	Infections of Bones or Joints, with CC Score 5–8	NHS Reference Costs 2012–13: Non elective Long Stay[435]
Day case procedures: TKR	£655	Day case: HB29Z Minimal Knee Procedures for Non-Trauma	NHS Reference Costs 2012–13: Non elective Day Case[435]
Day case procedures: THR	£788	Day case: HB19Z Minimal Hip Procedures for Non-Trauma	NHS Reference Costs 2012–13: Non elective Day Case[435]
Nights in hospital for other admissions	£311	Unit cost based on SMH cost per night in general orthopaedics ward	North Bristol NHS Trust Finance department
A&E and outpatient visits			
A&E	£117	Average of all accident and emergency visits	NHS Reference Costs 2012–13: Outpatient appointments: 180 Accident and Emergency[435]
Trauma and orthopaedics: consultant led	£102	Non-admitted face-to-face attendance, follow-up, consultant led	NHS Reference Costs 2012–13: Outpatient appointments: 110 Trauma and Orthopaedics[435]
Trauma and orthopaedics: non-consultant led	£90	Non-admitted face-to-face attendance, follow-up, non-consultant led	NHS Reference Costs 2012–13: Outpatient appointments: 110 Trauma and Orthopaedics[435]
Physiotherapy: non-consultant led	£39	Non-admitted face-to-face attendance, follow-up, non-consultant led	NHS Reference Costs 2012–13: Outpatient appointments: 650 Physiotherapy[435]

TABLE 49 Unit costs for total hip and knee replacement resource use (*continued*)

Resource use	Unit cost	Assumption	Source
General medicine: consultant led	£145	Non-admitted face-to-face attendance, follow-up, consultant led	NHS Reference Costs 2012–13: Outpatient appointments: 300 General Medicine[435]
Neurology: consultant led	£157	Non-admitted face-to-face attendance, follow-up, consultant led	NHS Reference Costs 2012–13: Outpatient appointments: 400 Neurology[435]
Respiratory: consultant led	£137	Non-admitted face-to-face attendance, first appointment, consultant Led	NHS Reference Costs 2012–13: Outpatient appointments: 340 Respiratory Medicine[435]
Pain management: consultant led	£136	Non-admitted face-to-face attendance, follow-up, consultant led	NHS Reference Costs 2012–13: Outpatient appointments: 191 Pain management[435]
Vascular: consultant led	£133	Non-admitted face-to-face attendance, follow-up, consultant led	NHS Reference Costs 2012–13: Outpatient appointments: 107 Vascular surgery[435]
Dermatology: consultant led	£95	Non-admitted face-to-face attendance, follow-up, consultant led	NHS Reference Costs 2012–13: Outpatient appointments: 330 Dermatology[435]
Haematology: consultant led	£209	Non-admitted face-to-face attendance, follow-up, consultant led	NHS Reference Costs 2012–13: Outpatient appointments: 303 Clinical Haematology[435]
Community-based health services			
GP surgery visit	£45	Base cost per patient contact with GP with qualifications, including direct care staff costs, lasting 11.7 minutes	PSSRU 2013: 10.8b General practitioner[441]
GP home visit	£114	Base cost per out of surgery visit with GP with qualifications, including direct care staff costs, lasting 23.4 minutes	PSSRU 2013: 10.8b General practitioner[441]
Phoned GP for advice	£27	Base cost per telephone consultation with GP with qualifications, including direct care staff costs, lasting 7.1 minutes	PSSRU 2013: 10.8b General practitioner[441]
GP practice nurse visit	£13.43	Based on 15.5 minutes per surgery consultation using the base cost (£52) of 1 hour of face-to-face contact with GP nurse with qualifications	PSSRU 2013: 10.6 Nurse (GP practice)[441]
Phoned GP practice nurse for advice	£4	Based on 6 minutes of GP nurse time using the base cost (£40) of 1 hour of GP nurse time with qualifications	PSSRU 2013: 10.6 Nurse (GP practice)[441]
Repeat prescription (without seeing doctor)	£11.40	Based on 3 minutes of GP time, using the base cost of 1 minute GP patient contact time (£3.80), with qualifications, including direct care staff costs	PSSRU 2013: 10.8b General practitioner[441]
District nurse	£18.08	Based on the assumption that the duration of a DN visit is the same as GP nurse visit (15.5 minutes) and using the base cost of 1 hour of community nurse visit (£70) with qualifications including travel	PSSRU 2013: 10.1 Community nurse[441]
OT at home/GP surgery/clinic	£17	Based on 30 minutes contact using the base cost (£34) of 1 hour of OT contact with qualifications	PSSRU 2013: 9.2 NHS community OT[441]

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 49 Unit costs for total hip and knee replacement resource use (*continued*)

Resource use	Unit cost	Assumption	Source
Community physiotherapist at home/GP surgery/clinic	£17	Based on 30 minutes contact using the base cost (£34) of 1 hour of physiotherapist contact with qualifications	PSSRU 2013: 9.1 Community physiotherapist
Prescriptions costs per consultation	£44.64	Prescription costs per consultation (net ingredient cost)	PSSRU 2013:10.8b General practitioner
Social services			
Home care worker (home help) provided by social services	£24	Based on 1 hour of face-to-face weekday contact for independent sector home care provided for social services	PSSRU 2013: 11.6
Food at home service (meals on wheels)	£3.14	Based on one meal a day using the meals on wheels average weekly cost (2012/13) of £44, assuming two meals per day, 7 days a week	PSSRU 2013: 8.1.1 Community care package for older people: very low cost
Social worker visits	£113	Based on a 30-minute visit using the base cost (£226) of 1 hour of face-to-face contact of social worker with qualifications	PSSRU 2013: 11.2 Social worker (adult services)
Social worker telephone calls	£39.50	Based on a 30-minute telephone call using a base cost (£79) 1 hour of client related work of a social worker with qualifications	PSSRU 2013: 11.2 Social worker (adult services)
Home changes and equipment provided by social services		All unit costs for home changes and equipment are based on 3-month loan period, assuming a 24 months life span	
Toilet seat or toilet raiser	£1.80	Cost of equipment £14	NRS price – equipment provider for Southmead Hospital (Mrs Catherine Hale, Head of Occupational Therapy at North Bristol NHS Trust, 2014, personal communication)
Dressing aids: socks, shoes, etc.	£1.25	Cost of equipment £10	NRS price – equipment provider for Southmead Hospital (Mrs Catherine Hale, Head of Occupational Therapy at North Bristol NHS Trust, 2014, personal communication)
Furniture raisers	£2.48	Cost of equipment £20	NRS price – equipment provider for Southmead Hospital (Mrs Catherine Hale, Head of Occupational Therapy at North Bristol NHS Trust, 2014, personal communication)
Perching stool	£6.00	Cost of equipment £48	NRS price – equipment provider for Southmead Hospital (Mrs Catherine Hale, Head of Occupational Therapy at North Bristol NHS Trust, 2014, personal communication)
Walker or trolley	£7.50	Cost of equipment £60	NRS price – equipment provider for Southmead Hospital (Mrs Catherine Hale, Head of Occupational Therapy at North Bristol NHS Trust, 2014, personal communication)

TABLE 49 Unit costs for total hip and knee replacement resource use (*continued*)

Resource use	Unit cost	Assumption	Source
Crutches	£3.75	Cost of equipment £30	NRS price – equipment provider for Southmead Hospital (Mrs Catherine Hale, Head of Occupational Therapy at North Bristol NHS Trust, 2014, personal communication)
Commode	£5.69	Cost of equipment £46	NRS price – equipment provider for Southmead Hospital (Mrs Catherine Hale, Head of Occupational Therapy at North Bristol NHS Trust, 2014, personal communication)
Rails and hand grips	£2.85	Cost of equipment £23	NRS price – equipment provider for Southmead Hospital (Mrs Catherine Hale, Head of Occupational Therapy at North Bristol NHS Trust, 2014, personal communication)
Bath boards	£3.00	Cost of equipment £24	NRS price – equipment provider for Southmead Hospital (Mrs Catherine Hale, Head of Occupational Therapy at North Bristol NHS Trust, 2014, personal communication)
Hospital bed at home	£59.88	Cost of equipment £479	Google (Google Inc., Mountain View, CA, USA) search for procurement prices (cheaper range)
Bath lift	£44.75	Cost of equipment £358	Google search for procurement prices (cheaper range)
Chair and stair lift	£125.00	Cost of equipment £1000	Google search for procurement prices (cheaper range)

A&E, accident and emergency; NRS, numerical response scale.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Equation 2 for QALYs:

$$\text{QALY}_{ij} = \gamma_{1j} + \gamma_{1j} \times \text{Treatment group} + \gamma_{2j} \times \text{Baseline utility} + \gamma_{3j} \times \text{Baseline pain score} + \gamma_{4j} \times \text{Surgical approach} + \mu_{ij}, \quad (2)$$

where i = individual patient, j = surgery: TKR or THR, k = cost category, and error terms e_{ijk} and μ_{ijk} are heteroskedasticity consistent (or robust) standard errors.[442] Baseline WOMAC pain score and surgical approach are the two variables used in the minimisation process for randomisation in both APEX trials.

Missing cost and QALY data were imputed using White's chained equations for multiple imputation[426] and Royston's 'ice' command in Stata 13,[444] to generate 20 complete data sets. This method uses regression techniques to estimate missing values, based on the values of available data. The 17 cost categories and four EQ-5D utility scores (baseline and three follow-up time points) were imputed jointly, by treatment group allocation, adjusting for trial minimisation variables and patient baseline characteristics [age, sex, BMI and dichotomous variables for education level (high vs. medium or low) and marital status (single vs. married or other)]. The imputation model was run for the hip and knee trial data separately and used predictive mean matching by trial arm. This avoided unrealistic utility scores or cost values. QALYs and grouped cost categories were then recalculated using the imputed values and incremental costs and QALYs with imputed data were then re-estimated using the models in *Equations 1* and *2*. A decision was made prior to the analysis that if the missing data were > 30%, then the primary analysis results would be based on the imputed data.

The incremental costs and QALYs for both trials were then examined for dominance, that is, when one of the arms cost less but had improved outcome compared with the other arm. If no arm was dominant then incremental cost-effectiveness ratios were estimated.

Incremental net monetary benefit (INMB) statistics for a range of societal willingness-to-pay thresholds were estimated. The net monetary benefit statistic is estimated by multiplying the QALY gained by the societal willingness to pay for QALY gained (λ) and then deducting the cost difference between the intervention and the control arm (see *Equation 3*).

Equation 3 for the INMB:

$$\text{INMB}_{\text{of LAI in relation to control}} = (\text{QALY}_{\text{LAI}} - \text{QALY}_{\text{control}}) \times \lambda - (\text{COST}_{\text{LAI}} - \text{COST}_{\text{control}}), \quad (3)$$

where LAI is the local anaesthetic infiltration arm and λ is the societal willingness to pay for a QALY threshold.

The INMB statistic quantifies whether or not society is willing to pay for incremental cost of providing the intervention. Positive INMB statistics indicate a cost-effective intervention, whereby society is willing to pay more for the health gain than the intervention costs, for a given willingness to pay threshold. We used the thresholds (λ) of £10,000 per QALY and NICE recommended £20,000 and £30,000 per QALY[86] to estimate INMB statistics. In order to account for the uncertainty around the economic results, bootstrapped confidence intervals (BCIs) with 1000 replications were estimated for the adjusted costs, QALYs and the three INMB statistics. We further plotted bootstrapped cost and QALY estimates in cost-effectiveness planes. Cost-effectiveness acceptability curves (CEACs) illustrate the probability of the intervention being cost-effective, given a range of societal willingness-to-pay thresholds. All analyses were conducted using Stata 13.

Results

Tables 50 and *51* show the mean resource use and costs in total hip and total knee by trial arm.

Available case categorical resource use and costs

For both total hip and knee replacement, the available case results do not suggest that administering local wound infiltration analgesia perioperatively increases operation time in theatre; however, local anaesthetic infiltration may reduce time in recovery by about 10 minutes. For THR, during the initial inpatient stay, the mean number of days spent in the ward was the same (5.2 days) for both trial arms. However, for TKR, the intervention arm had 5.9 mean number of ward days compared with 5.2 in the control arm.

TABLE 50 Mean resource use and cost by APEX trial arm for THRs (available cases)

	Intervention ($N = 163$)					Control ($N = 159$)				
Resource	*n*	Mean resource use	SD	Mean cost (£)	SD (£)	*n*	Mean resource use	SD	Mean cost (£)	SD (£)
Initial inpatient stay										
Theatre time (minutes)	148	99	29	1407	411	147	101	31.6	1441	449
Recovery time (minutes)	143	103	65	397	251	144	113	77.4	435	297
Days in wards	153	5.2	3.3	1597	1516	154	5.2	2.8	1553	886
Secondary care after initial discharge										
Inpatient admissions after initial discharge[a]	115	–	–	341	1847	122	–	–	101	554
Orthopaedics appointments	142	1.96	1.2	199	121	146	1.97	1.4	201	138
Physiotherapy appointments	142	0.19	0.8	7	32	146	0.23	0.8	9	30
A&E visits	142	0.06	0.4	7	46	146	0.04	0.3	5	30
Other appointments	142	0.04	0.3	5	37	146	0.04	0.3	7	59
Community-based resources										
GP contacts	107	1.90	3.3	61	113	108	2.66	4.5	83	145
Nurse contacts	110	1.60	4.1	25	70	114	1.24	2.7	18	41
OT contacts	113	0.04	0.4	1	7	116	0.08	0.5	1	8
Community physiotherapist contacts	109	0.25	1.1	4	19	113	0.58	1.8	10	30
Prescriptions at GP consultation	108	0.72	1.3	32	60	111	1.13	2.0	50	87
Total NHS cost	**94**			**3768**	**1534**	**90**			**3818**	**1086**
PSS										
Home care worker (hours)	139	1.11	8.1	27	195	144	5.36	56.3	129	1351
Meals (food at home services)	137	2.76	24.0	9	75	138	0.00	0.0	0	0
Contacts with social worker	138	0.05	0.5	4	36	144	0.13	1.1	7	59
Home changes[a]	161	–	–	1	3	158	–	–	2	5
Total NHS + PSS cost	**90**			**3828**	**1618**	**88**			**3999**	**2088**

A&E, accident and emergency.
a The category combines different types of resource use; therefore, an overall mean could not be calculated.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 51 Mean resource use and cost per trial arm in TKR (available cases)

	Intervention ($N = 157$)					Control ($N = 159$)				
Resource	*n*	Mean resource use	SD	Mean cost (£)	SD (£)	*n*	Mean resource use	SD	Mean cost (£)	SD (£)
Initial inpatient stay										
Theatre time (minutes)	142	102	32	1449	453	145	103	32.9	1461	469
Recovery time (minutes)	140	94	44	359	169	136	104	69.1	398	265
Days in wards	147	5.9	3.9	1789	1224	149	5.2	2.9	1586	1034
Secondary care after initial discharge										
Inpatient admissions after initial discharge[a]	103	–	–	104	533	110	–	–	296	907
Orthopaedics appointments	128	2.06	1.5	209	149	137	1.99	1.4	202	143
Physiotherapy appointments	128	0.44	2.1	17	82	137	0.40	1.3	16	50
A&E visits	128	0.16	0.7	18	84	137	0.18	1.2	20	145
Other appointments	128	0.00				137	0.03	0.2	4	34
Community-based resources										
GP contacts	85	2.65	4.3	84	151	102	3.83	5.7	122	212
Nurse contacts	90	0.98	1.4	14	22	104	1.09	2.7	16	43
OT contacts	95	0.28	1.1	5	19	105	0.25	1.3	4	22
Community physiotherapist contacts	90	1.03	2.7	18	45	107	1.29	3.5	22	60
Prescriptions at GP consultation (GP practice)	87	1.30	2.7	58	121	105	1.74	3.7	78	165
Total NHS cost	**72**			**3862**	**1310**	**82**			**4239**	**1803**
PSS										
Home care worker (hours)	135	1.17	12.9	28	310	136	1.24	14.4	30	346
Meals (food at home services)	132	0.14	1.6	0	5	129	0.11	1.2	0	4
Contacts with social worker	133	0.11	1.1	4	45	134	0.14	1.6	7	84
Home changes[a]	157	–	–	3	13	158	–	–	1	4
Total NHS + PSS cost	**72**			**3868**	**1309**	**79**			**4276**	**2076**

A&E, accident and emergency.
a The category combines different types of resource use; therefore, an overall mean could not be calculated.

In both THR and TKR, the intervention group seemed to have less community-based resource use, particularly in relation to GP contacts, than the control group.

For TKR, there were lower costs owing to hospital readmission for patients in the intervention group, whereas the reverse was true for patients receiving THR.

Personal Social Services costs contributed minorly to the overall costs of delivering treatment for both types of joint replacement.

All cost drivers for these trials display high variability, with large SDs around the categorical mean cost estimates.

Complete case costs

In the THR trial, 90 out of the 163 (55%) patients in the intervention arm and 88 out of the 159 (55%) patients in the control arm had complete NHS and PSS cost data. In the TKR trial, the corresponding figures were 72 out of 157 (46%) for the intervention arm and 79 out of 159 (50%) for the control arm patients. For the complete case analysis total unadjusted mean NHS and mean NHS + PSS cost were lower in the intervention group than in the control group for the two types of joint replacement.

Tables 52 and *53* report the economic evaluation results and differences between arms in outcomes with BCIs and totals by cost categories.

In both the THR and the TKR analyses, differences in the imputed and adjusted NHS and NHS + PSS costs between the arms indicated that patients in the intervention group had lower mean costs than those in the control arm at 1 year.

TABLE 52 Total hip replacement: differences in costs and outcomes between APEX randomised groups

Outcome or cost	Difference (intervention – control)			
	n	Mean	95% CI	*p*-value
QALYs				
QALY gain: available cases (unadjusted)	216	0.071	0.018 to 0.124	
QALY gain: available cases (adjusted)[a]	216	0.064	0.018 to 0.110	0.007
QALY gain: imputed data (adjusted)[b]	322	0.056	0.015 to 0.097	0.008
Cost (£)				
Initial inpatient stay				
Total of inpatient stay: available cases (unadjusted)	274	–127	–367 to 114	
Total of inpatient stay: available cases (adjusted)[c]	273	–123	–364 to 118	0.32
Total of inpatient stay: imputed data (adjusted)[b]	322	–24	–345 to 297	0.88
Secondary care after initial discharge				
Inpatient admissions after initial discharge: available cases (unadjusted)	237	240	–115 to 595	
Inpatient admissions after initial discharge: available cases (adjusted)[c]	236	251	–114 to 617	0.18
Inpatient admissions after initial discharge: imputed data (adjusted)[b]	322	63	–308 to 434	0.74
Total outpatient visits: available cases (unadjusted)	288	–4	–39 to 30	
Total outpatient visits: available cases (adjusted)[c]	287	–2	–36 to 32	0.92
Total outpatient visits with: imputed data (adjusted)[b]	322	2	–36 to 39	0.94
Total secondary care cost after initial discharge: available cases (unadjusted)	232	239	–138 to 617	
Total secondary care cost after initial discharge: available cases (adjusted)[c]	231	251	–136 to 639	0.2
Total secondary care cost after initial discharge: imputed data (adjusted)[b]	322	64	–314 to 443	0.74
Community-based resources				
Total community-based costs: available cases (unadjusted)	209	–25	–82 to 31	
Total community-based costs: available cases (adjusted)[c]	209	–23	–79 to 33	0.41
Total community-based costs: imputed data (adjusted)[b]	322	–47	–116 to 22	0.18
Total NHS cost: available cases (unadjusted)	184	–50	–436 to 335	
Total NHS cost: available cases (adjusted)[c]	184	–43	–427 to 341	0.83
Total NHS cost: imputed data (adjusted)[b]	322	–7	–535 to 521	0.98

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 52 Total hip replacement: differences in costs and outcomes between APEX randomised groups (*continued*)

Outcome or cost	Difference (intervention – control)			
	n	Mean	95% CI	*p*-value
PSS				
Total PSS: available cases (unadjusted)	264	–100	–343 to 142	
Total PSS: available cases (adjusted)[c]	263	–83	–289 to 123	0.43
Total PSS: imputed data (adjusted)[b]	322	–167	–421 to 88	0.2
Total NHS + PSS cost: available cases (unadjusted)	178	–170	–724 to 383	
Total NHS + PSS cost: available cases (adjusted)[c]	178	–151	–680 to 377	0.57
Total NHS + PSS cost: imputed data (adjusted)[b]	322	–173	–762 to 415	0.56
RESULTS				
Mean QALY gain (adjusted, bootstrapped)[b]	322	0.056	0.020 to 0.092	0.002
Mean NHS + PSS cost difference (£) (adjusted, bootstrapped)[b]	322	–173	–658 to 312	0.480
INMB statistic: λ = £10,000 (adjusted, bootstrapped)[b]	322	£729	£62 to £1397	0.032
INMB statistic: λ = £20,000 (adjusted, bootstrapped)[b]	322	£1285	£329 to £2242	0.009
INMB statistic: λ = £30,000 (adjusted, bootstrapped)[b]	322	£1841	£559 to £3122	0.005

λ, societal willingness-to-pay threshold.
a Adjusted for baseline utility and minimisation variables.
b Adjusted for minimisation variables (and baseline utility for QALYs), Number of multiple imputation sets = 20, BCIs with 1000 replications.
c Adjusted for minimisation variables.

TABLE 53 Total knee replacement: differences in costs and outcomes between APEX randomised groups

Outcome or cost	Difference (intervention – control)			
	n	Mean	95% CI	*p*-value
Outcome				
QALY gain: available cases (unadjusted)	201	0.015	–0.045 to 0.075	
QALY gain: available cases (adjusted)[a]	201	0.010	–0.039 to 0.060	0.68
QALY gain: imputed data (adjusted)[b]	316	0.012	–0.035 to 0.058	0.62
Cost (£)				
Initial inpatient stay				
Total of inpatient stay: available cases (unadjusted)	268	76	–215 to 367	
Total of inpatient stay: available cases (adjusted)[c]	268	89	–194 to 371	0.54
Total of inpatient stay: imputed data (adjusted)[b]	316	179	–119 to 476	0.24
Secondary care after initial discharge				
Inpatient admissions after initial discharge: available cases (unadjusted)	213	–191	–391 to 8	
Inpatient admissions after initial discharge: available cases (adjusted)[c]	213	–170	–365 to 24	0.086
Inpatient admissions after initial discharge: imputed data (adjusted)[b]	316	–278	–517 to –38	0.024
Total outpatient visits: available cases (unadjusted)	265	2	–46 to 50	
Total outpatient visits: available cases (adjusted)[c]	265	2	–47 to 52	0.92

TABLE 53 Total knee replacement: differences in costs and outcomes between APEX randomised groups (*continued*)

Outcome or cost	Difference (intervention – control)			
	n	Mean	95% CI	*p*-value
Total outpatient visits with: imputed data (adjusted)[b]	316	15	–38 to 68	0.57
Total secondary care cost after initial discharge: available cases (unadjusted)	203	–194	–423 to 36	
Total secondary care cost after initial discharge: available cases (adjusted)[c]	203	–165	–391 to 61	0.15
Total secondary care cost after initial discharge: imputed data (adjusted)[b]	316	–263	–516 to –9	0.043
Community-based resources				
Total community-based costs: available cases (unadjusted)	177	–69	–176 to 37	
Total community-based costs: available cases (adjusted)[c]	177	–65	–181 to 50	0.27
Total community-based costs: imputed data (adjusted)[b]	316	–51	–153 to 51	0.32
Total NHS cost: available cases (unadjusted)	154	–377	–875 to 121	
Total NHS cost: available cases (adjusted)[c]	154	–281	–761 to 200	0.25
Total NHS cost: imputed data (adjusted)[b]	316	–135	–559 to 289	0.53
PSS				
Total PSS: available cases (unadjusted)	259	–4	–95 to 86	
Total PSS: available cases (adjusted)[c]	259	–4	–95 to 87	0.93
Total PSS: imputed data (adjusted)[b]	316	4	–138 to 145	0.96
Total NHS + PSS cost: available cases (unadjusted)	151	–408	–962 to 146	
Total NHS + PSS cost: available cases (adjusted)[c]	151	–329	–851 to 193	0.21
Total NHS + PSS cost – imputed data (adjusted)[b]	316	–131	–595 to 332	0.58
Results				
Mean QALY gain (adjusted, bootstrapped)[b]	316	0.013	–0.027 to 0.052	0.530
Mean NHS + PSS cost difference (£) (adjusted, bootstrapped)[b]	316	–131	–501 to £239	0.490
INMB statistic: λ = £10,000 (adjusted, bootstrapped)[b]	316	£258	–£362 to £879	0.410
INMB statistic: λ = £20,000 (adjusted, bootstrapped)[b]	316	£386	–£585 to £1356	0.440
INMB statistic: λ = £30,000 (adjusted, bootstrapped)[b]	316	£513	–£832 to £1857	0.450

λ, societal willingness-to-pay threshold.
a Adjusted for baseline utility and minimisation variables (baseline WOMAC pain score and surgical approach).
b Adjusted for minimisation variables (and baseline utility for QALYs), M = 20 multiple imputation sets, BCIs with 1000 replications.
c Adjusted for minimisation variables (baseline WOMAC pain score and surgical approach).

For THR, differences between the arms in terms of NHS costs were very minor (–£7). In the intervention group, the mean cost per patient was £24 lower for the initial inpatient stay (95% BCI –£345 to £297; $p = 0.88$), £47 lower for community-based health-care costs (95% BCI –£116 to £22; $p = 0.18$) and £63 more for readmission costs (95% BCI –£308 to £434; $p = 0.74$) when compared with the control group. Mean PSS costs were lower in the intervention group by £167 per patient (95% BCI –£421 to £88; $p = 0.2$). This meant that the combined PSS + NHS mean cost per patient was £173 lower in the intervention group (95% BCI –£762 to £415; $p = 0.56$).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

In contrast, for the intervention group receiving TKR, mean cost per patient for the initial inpatient stay was greater by £179 (95% BCI –£119 to £476; $p = 0.24$) and the mean cost per patient of readmissions was lower by £278 (95% BCI –£517 to –£38; $p = 0.024$). This meant an overall lower combined PSS + NHS mean cost of £131 per patient in the intervention group (95% BCI –£595 to £332; $p = 0.58$) compared with the control group.

For patients receiving THR, the adjusted and imputed 0.056 incremental QALY gain per patient (95% BCI 0.02 to 0.09; $p = 0.002$) for the intervention group was markedly higher than for those in the control group. This corresponded to patients in the intervention arm spending on average an estimated 20 more days in 'perfect health' than patients in the control arm. For the TKR patients, the estimated health benefit for the intervention arm was also positive but the findings were more uncertain, with a mean of 0.012 QALYs gained per patient and wider CIs crossing the null (95% BCI –0.027 to 0.052 QALYs; $p = 0.53$).

The cost and QALY results indicate that local anaesthetic infiltration is the dominant treatment option, that is, it is cost-saving and more effective than current clinical practice for both THR and TKR surgery.

The INMB statistics in relation to the THR study were positive, even at the more stringent willingness-to-pay threshold of £10,000 per QALY, resulting in a mean INMB of £729 (95% BCI £62 to £1397; $p = 0.032$). In the TKR analysis, our findings also indicate positive INMB statistics at all willingness-to-pay thresholds, but smaller absolute value statistics and more uncertainty around these estimates, with all BCIs crossing the null. *Figures 30* and *31* plot the 1000 replications of the adjusted bootstrapped incremental cost-effectiveness estimates for THR and TKR in the cost-effectiveness plane and the corresponding CEACs.

Our findings are depicted in the cost-effectiveness planes for THR and TKR, with most estimates falling within the south-east quadrant of dominant strategies, more notably so for THR than for TKR. The CEAC shows the uncertainty around the economic results, with a probability of local anaesthetic infiltration being cost-effective in TKR only slightly > 60% at the £10,000 and £20,000 threshold, whereas the probability of it being cost-effective is > 99% in THR at £20,000 per QALY and > 96% at £10,000 per QALY.

Discussion

Our findings suggest that administering local anaesthetic infiltration before wound closure is a cost-effective treatment option, compared with current clinical analgesia regimens in joint replacement surgery. These findings are supported in THR surgery with large positive INMB statistics for the willingness-to-pay thresholds of £10,000, £20,000 and £30,000 and a probability of being cost-effective of > 96% at the lowest threshold. There is no statistical evidence for the positive INMB statistics for TKR surgery, the probability of being cost-effective is only slightly > 60% at £10,000 and £20,000, although results point to local anaesthetic infiltration being the dominant treatment option in both surgeries. Considering results from a NHS perspective only, the cost differences in favour of the intervention arm are greater for TKR than for THR.

Our study has limitations. The economic evaluation was carried out alongside the two APEX RCTs, which were powered to detect a difference in the primary clinical outcome between arms but not in the cost-effectiveness outcomes. Secondary economic analyses to include private expenses and productivity losses incurred during the follow-up period of these trials are planned but have not yet been conducted. Methodological uncertainties need to be explored in sensitivity analyses. For example, in the THR trial, PSS cost differences favouring the intervention arm were driven mainly by one control patient requiring many hours of home care provision. Excluding this patient would potentially lead to a decrease in net monetary benefits. Our bootstrapping methods will have under-represented the uncertainty of our results with smaller CIs; sensitivity analysis on multiple imputation and bootstrapping techniques would address this. Collection of resource-use data, particularly community-based resources and use of PSS, relied on patient-reported data from postal questionnaires completed at three follow-up points. This led to a substantial number of missing data and imputation was therefore needed. The imputed value estimates varied substantially from available case estimates. Such methodological uncertainties need also to be explored in sensitivity analyses.

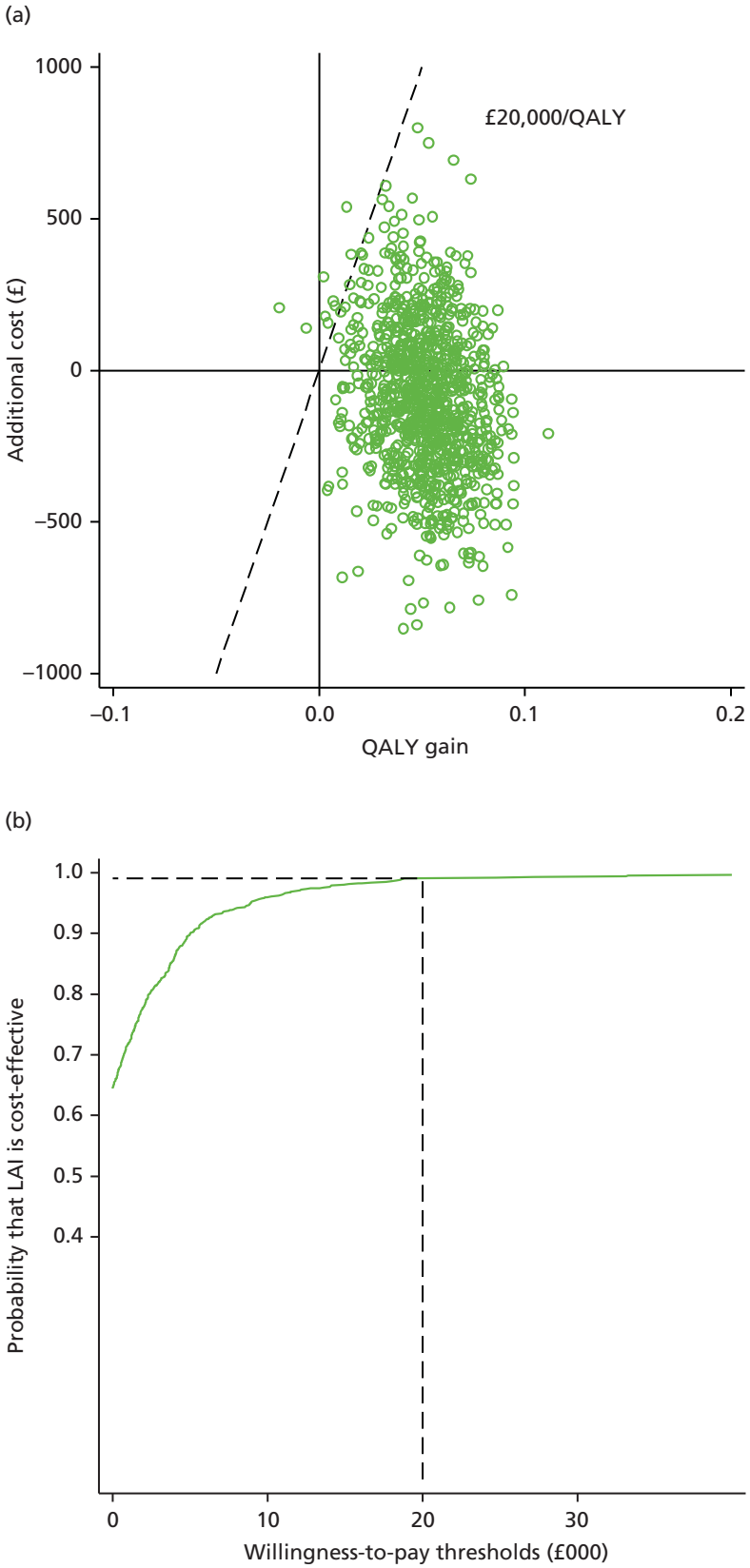


FIGURE 30 APEX cost-effectiveness plane and CEAC for THR. (a) Cost-effectiveness plane; and (b) CEAC. LAI, local anaesthetic infiltration.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

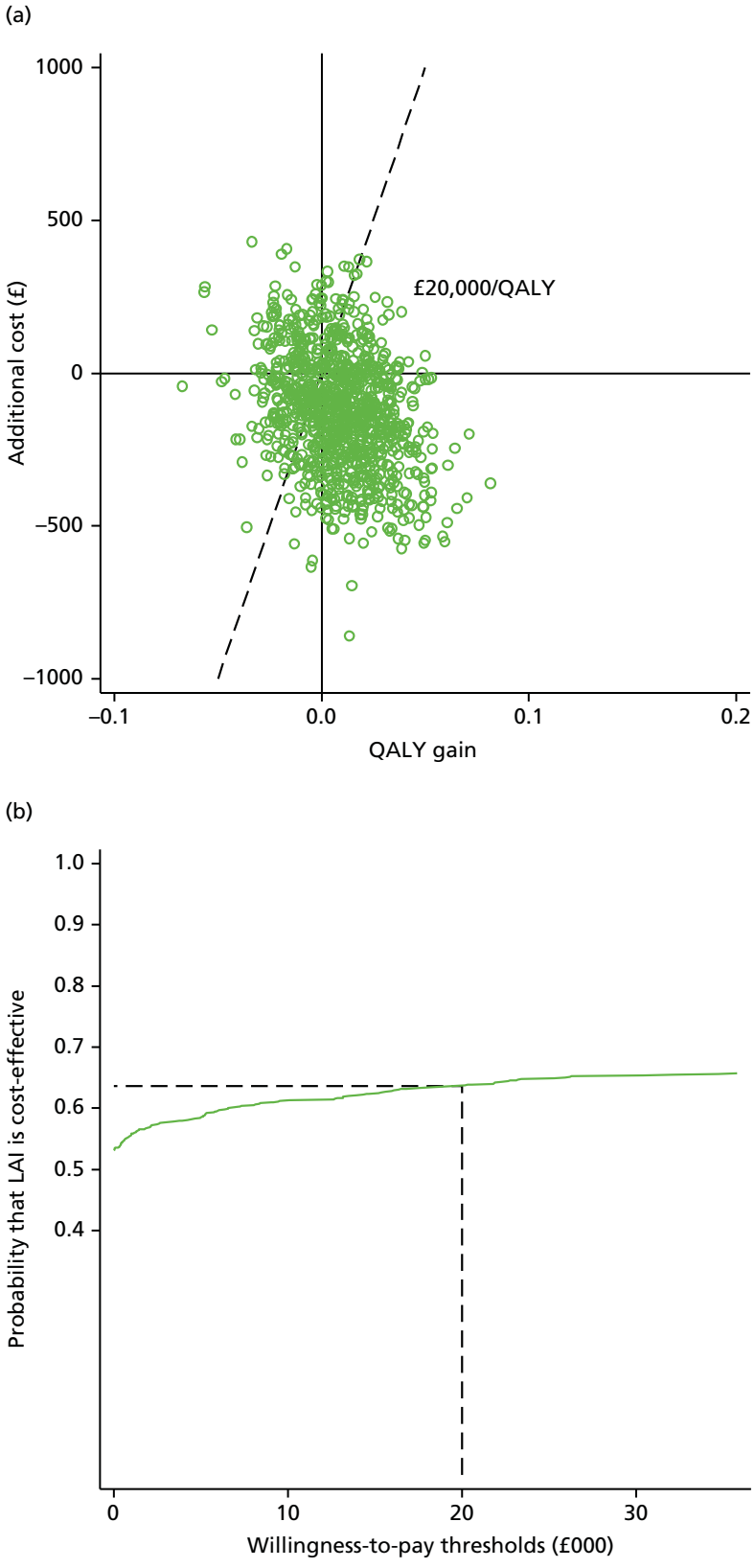


FIGURE 31 APEX cost-effectiveness plane and CEAC for TKR. (a) Cost-effectiveness plane; and (b) CEAC. LAI, local anaesthetic infiltration.

Conclusion

The addition of local anaesthetic infiltration to the usual analgesia regimen from the perspective of the NHS and PSS is a cost-effective treatment option in primary THR. Given that the intervention was dominant, any uncertainty addressed through future analyses is unlikely to alter the intervention being cost-effective at current NICE thresholds. Our findings also indicate positive health benefits and cost savings in TKR, but with considerably more uncertainty around the cost-effectiveness result. Therefore, there is less evidence in favour of adopting local anaesthetic infiltration before wound closure in routine clinical practice for patients receiving TKR surgery.

Evaluation of patient recruitment

Sound recruitment processes are critical to the success of RCTs and ethical conduct mandates informed decision-making by participants. How trial information is explained is vital but communication and training can be inadequate.

In the early stages of the APEX RCTs, recruitment interviews between research nurses and potential participants were recorded and transcribed and used as the basis of a peer-review intervention to improve trial processes and recruitment. This study describes how this process we have named Internal Peer review for Recruitment Training in Trials (InterPReTiT)[368] was developed and used to address the training needs of nurses recruiting to the APEX RCTs.

The aim of this study was to discuss the potential benefits, effectiveness and acceptability of this process as a universal method of training recruiters to trials. The discussion is informed by examination of the review forms the nurses completed over 3 months from 2009 to 2010 when they listened to audio-recordings of their recruitment interviews and by qualitative evaluation of the audio-recordings of the nurses' discussions of these reviews.

Methods

Ethics approval was gained to record recruitment interviews to allow the peer-review process. The recruiting team consisted of four nurses working in clinical research roles. Before starting recruitment, the recruiting team familiarised themselves with the APEX trial protocols and research literature regarding best practice for trial recruitment.

Role-play was used to rehearse presenting study information using an interactive style. When recruitment began, the nurses gained consent from potential participants to audio-record using a digital recorder. It was explained to potential participants that the recruitment interview was being recorded for training purposes. Two potential participants declined to be recorded. In total, 53 recruitment interviews were recorded, including four interviews with individuals who declined trial participation.

Team members listened to their own, as well as their colleagues', recruitment interviews and reviewed them using a standardised checklist to identify whether or not the trial aims, the trial arms, equipoise, trial involvement, voluntary participation, blinding and randomisation had been adequately explained. Free-text space was included to record patients' questions, requests for extra information/clarification and any notable reactions. A roster ensured a different reviewer for each member of the team each week and meetings of the team were scheduled to discuss the reviews. The recruiting team met five times over a 12-week period during pilot phase of the trial.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

The recruiting team completed 50 feedback forms, covering 35 recruitment interviews. Recruitment interviews were selected to be reviewed by more than one nurse because they were of particular interest. These included recruitment interviews for which potential participants ultimately declined trial participation and recruitment interviews when communicating the information had been challenging. When the first reviewer thought that a recruitment interview provided an example of good practice, it was recommended to the whole team to review.

Analysis

The findings presented derive from audio-recordings of three out of five peer-review meetings and from the review forms.

Review forms were scrutinised for instances of where the recruiting nurse had failed to convey items of trial information. When one recruitment interview was reviewed by more than one nurse, the review forms were compared to assess concordance across reviewers, both of the checklist items and of the free-text comments. Three out of the five review meetings were audio-recorded with the consent of the recruiting nurses and used in the evaluation. The first meeting was not recorded as we did not immediately recognise the value of doing so. The fifth meeting was not recorded as it had already been agreed at the previous meeting that the training process was complete. No outstanding concerns or uncertainties remained and the nurses now felt confident in their recruitment practice. Only two nurses attended the fifth meeting and nothing new arose from the discussion.

The three audio recordings of the review meetings were transcribed verbatim and analysed using Framework methodology.[445] This accommodates both predetermined themes and themes that arise inductively from the data. Each transcript was read and reread and then coded in duplicate so that salient content was integrated into the coding framework. The review forms were scrutinised for instances where the recruiting nurse had failed to convey one or more items of trial information and the free-text comments were integrated into the coding framework. The coding framework was developed from a review of the literature regarding recruitment difficulties for RCTs and from the need to check the content and delivery of trial information during the recruitment interviews. Certain codes including equipoise, understanding of randomisation and specific information about the trial process were included as predetermined themes in the coding framework. New codes arising from the data were added to these and amalgamated into a final overarching framework. New codes derived from the data, included the role of relatives and managing those who wished to decline.

The data were initially coded by one researcher who is a recruiting nurse who has qualitative research experience and also training in counselling skills. A second researcher who is an experienced qualitative researcher with a social and behavioural science background independently double coded the transcripts and no additional codes were identified.

Results

A flow diagram summarising the peer-review process in the APEX trials is shown in *Figure 32*.

In the interviews that were reviewed by more than one nurse ($n = 7$), the inter-rater concordance was between 78% and 100% (mean 97%). There was universal agreement over which interviews demonstrated good practice and those which did not.

Interview durations ranged from 6 to 30 minutes, with a mean of 12.4 minutes. Review meetings lasted from 40 to 60 minutes.

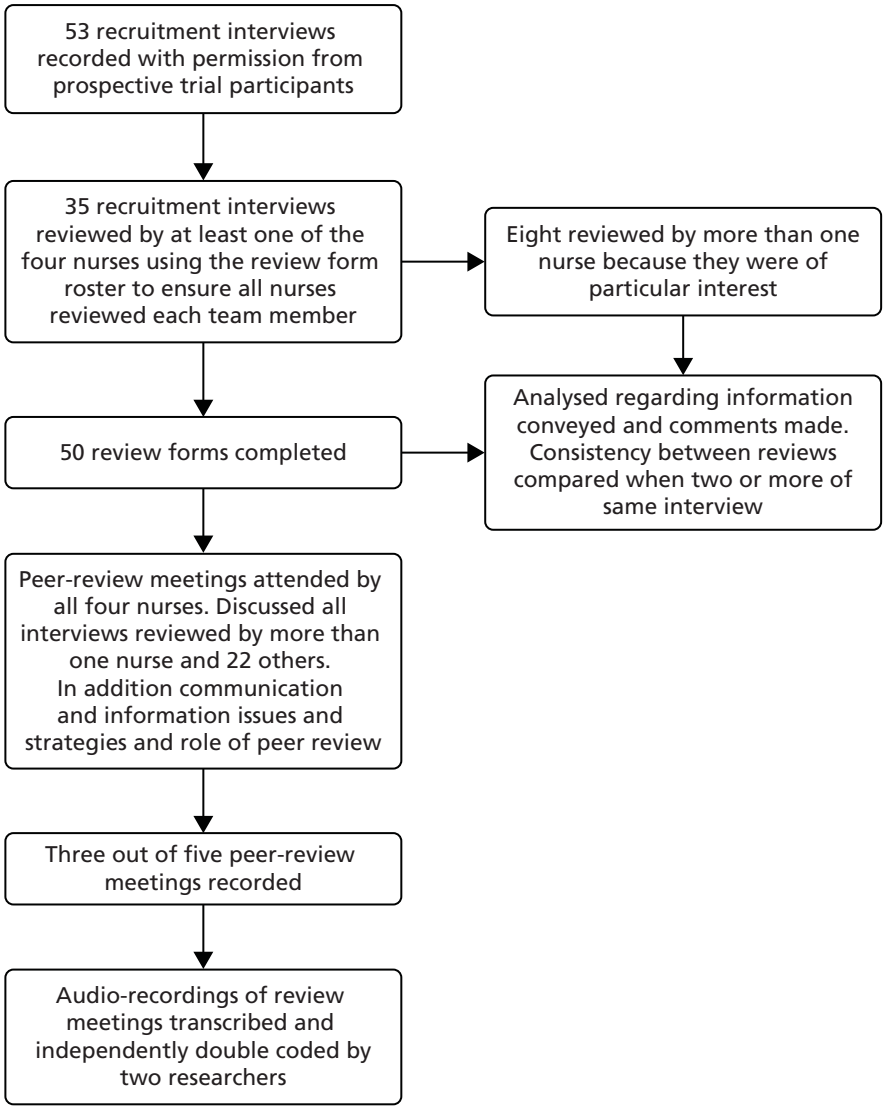


FIGURE 32 The peer-review process and evaluation.

Five main themes were identified from the qualitative analysis: provision of information, flexible communication of information, verifying participant understanding, ensuring voluntary participation and recruiters' perceptions of the peer-review process. The results presented outline each theme and direct changes made to the design and conduct of the APEX trials as a consequence of the findings. Supporting data are presented in *Table 54*.

Provision of information

To ensure that participants' consent is fully informed, it is essential that trial information is conveyed accurately and consistently and in a manner that is clearly understood by potential participants. The analysis identified both faults in the communication of trial information and participants misunderstanding information.

From comparing recruitment interviews, the nurses identified that the information they were conveying regarding anaesthesia was not consistent between recruiters. It became apparent that the study protocol was unclear regarding how the standard anaesthetic technique for patients undergoing THR differed from that for patients undergoing TKR. Consequently, the diagram used to explain the different anaesthetic techniques to potential participants was incorrect regarding standard anaesthetic care (see *Table 54*, section A, quotation 1).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 54 Quotations from research nurse meetings

Section A: provision of information		
1	RN1 second meeting	*She was given the message that whether or not she had a spinal was nothing to do with the study whereas what we've now found out is that if they're a hip and they cannot have a spinal they can't be in the study so if anyone who is for a hip is saying clearly I don't want a spinal then they shouldn't be recruited*
2	RN3 second meeting	*From reading the information sheet, she hadn't grasped the trial because she didn't think she was going to get an anaesthetic, she thought she was just going to get a local by the sounds of what she asked*
3	RN4 third meeting	*I think people are reading [the anaesthetic leaflet] and really taking a lot of notice of that and then maybe not giving perhaps quite so much attention to the information sheet*
4	RN1 third meeting	*The major benefit is that [the peer-review process] has made us all clarify exactly what the anaesthetic options are*
Section B: flexible communication of information		
5	RN2 second meeting	*Patients are very different and you do have to tailor it and you try and make it conversational so it's not so stilted and so artificial*
6	RN4 third meeting	*Most people have dental experience and it's a good one to use, isn't it, because people have that understanding*
7	RN3 second meeting	*If you have a planned kind of set routine to your patter, you know that you're potentially going to cover every point but then if you make it fresh for each patient you might miss something*
8	RN1 second meeting	*I was . . . trying to keep in my head what I was trying to say and keep it clear and get to the end of it so you kind of override what the patient wants to say*
9	RN2 second meeting	*When it's more participant led . . . you perhaps don't give everything but you've still had a good consenting process, . . . they're reassured and they actually understand it . . . and that's come back that . . . they've got it*
Section C: verifying participant understanding		
10	RN4 second meeting	*I found myself just repeating things just because I wasn't really getting any feedback from her at all. And I found it really difficult because . . . there wasn't really any verbal or any other sort of communication from them*
11	RN1 second meeting	*It's checking comprehension isn't it, which is different to asking if they've got any questions, because they might not have questions but they might have completely the wrong idea of the trial*
12	RN3 second meeting	*The patient told you their understanding of the study and you gap-filled . . . you could actually tell . . . from listening to it that she understood the study and she was consenting because she knew what was going to happen*
13	RN2 second meeting	*I think it's doing that delicately without patronising. It's sort of open questions but I know I find it difficult . . . how to get it from them, without patronising them or . . . putting them on the spot*
Section D: ensuring voluntary participation		
14	RN2 third meeting	*I've said to a guy 'you're not quite sure or perhaps this isn't for you' and they've leapt on that with you know, enthusiasm, 'yes, that's quite right' you know, and that having given them that door they're out and down the corridor*
15	RN1 fourth meeting	*I thought . . . how we can break this up a bit more so that we get a bit more from her and make it possible for her to say no*
16	RN4 second meeting	*It is difficult because she had a daughter with her . . . You don't know if she's agreeing because, yes OK she is happy or is she agreeing because her daughter thinks it is a good idea?*
17	RN3 fourth meeting	*And it also shows . . . with the husband interjecting so much, how much it's not just the patient you need to win over but the relative with them*

TABLE 54 Quotations from research nurse meetings (*continued*)

Section E: recruiters' perceptions of the peer-review process		
18	RN4 second meeting	*I just don't feel very comfortable with tape-recording. I think it is a good way to learn . . . I think it does highlight your own strengths and weaknesses which is a good thing*
19	RN3 second meeting	*I was a bit like cringe . . . Oh my god, we're going to record, we're going to record and I'm slightly better with it now, but I can see the value of it and the learning experience from it*
20	RN4 second meeting	*I think once we knew that it was going to remain within this group that made me feel a bit more comfortable*
21	RN2 third meeting	*You want people to feel comfortable so that you can constructively say things about other people, you can reflect on yourself*
22	RN1, RN2, RN4 third meeting	*But it helps to increase trust, doesn't it? In that we are all kind of working the same way* *Reassurance as well, isn't it* *I think it's brought us together more as a team*
23	RN2 third meeting	*You are more aware of reflecting on was that good, was that bad, why wasn't it? . . . I think with any new study you develop your pattern and you often get stuck in that pattern. I think with this, I have definitely changed mine . . . and put things differently which I wouldn't have done otherwise*
24	RN4 third meeting	*Wouldn't you feel if you move onto another study that you'd want to do this*

RN, research nurse.

In addition, it became apparent that the description of the different anaesthetic techniques in the participant information sheet was frequently misunderstood and that many patients feared they might only receive a local anaesthetic during surgery (see *Table 54*, section A, quotation 2). This was partly because a separate information booklet about spinal anaesthesia produced by the Royal College of Anaesthetists in the UK was included with the study information. This deterred some participants from considering participation (see *Table 54*, section A, quotation 3).

Impact on trial design

A substantial amendment was submitted to the ethics committee to amend the participant information sheet, clarifying that the intervention anaesthetic was additional to the current standard anaesthetic. The explanatory diagram used in recruitment was amended to reflect the correct anaesthetic information. The protocol was also amended to remove the booklet about spinal anaesthesia from the study information pack sent to potential participants. Information routinely provided to patients receiving standard care did not include this booklet. The nurses were satisfied that they had now achieved clarity regarding the anaesthetic options (see *Table 54*, section A, quotation 4).

Flexible communication of information

The nurses recognised that ensuring information needs were properly met required a flexible, interactive, conversational style tailored to each patient, while still conveying standardised information (see *Table 54*, section B, quotation 5). Different ways of conveying key concepts were explored and the whole group subsequently adopted ones that were felt to be the most effective at communicating the concept because they drew on experiences familiar to the participant, for example explaining the intervention anaesthetic by likening it to the local anaesthetic used for dental work (see *Table 54*, section B, quotation 6).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

In the early stages of recruitment, the recruiting nurses identified difficulty conveying all the necessary information while also making the recruitment interviews interactive and tailored to individual communication needs (see *Table 54*, section B, quotations 7 and 8). However, the nurses agreed that presenting all the information at once, using a script, made it harder for patients to comprehend and express questions or concerns and was less likely to elicit evidence of understanding (see *Table 54*, section B, quotation 9).

Impact on trial design

To allow for an interactive, tailored approach to engage participants and address their concerns and information needs, while still ensuring that all the information was conveyed, the use of a checklist instead of script was adopted.

Verifying patient understanding

In order to gain evidence that consent was informed, the nurses needed to stimulate sufficient interaction to address all potential concerns and questions and to confirm understanding. However, some patients were less responsive or did not ask questions (see *Table 54*, section C, quotations 10 and 11). Recruitment interviews were critiqued regarding helpful and unhelpful techniques to overcome this, such as using open questions, encouraging patients to interrupt, asking what understanding patients had of the study and asking them to summarise what the recruiting nurse had told them. The strategic use of open questions facilitated a participant-centred interaction in which potential gaps in understanding could be explored. However, the task of checking understanding needed to be accomplished respectfully and sensitively (see *Table 54*, section C, quotations 12 and 13).

Impact on trial design

Different ways of checking participants' understanding were discussed and subsequently all the recruiters began by asking the potential participant what they had understood about the study from what they had read in the information leaflet. This conferred the advantages of confirming whether or not the patient had read the information leaflet, clarifying how much information they understood and recalled, and inviting the patient to take an active part in the discussion of the trial information from the outset.

Ensuring voluntary participation

Sometimes it was difficult to gauge potential participants' understanding of the trial and whether or not they were genuinely willing to participate. The nurses realised that some patients may have difficulty in freely discussing their potential participation owing to anxiety about their intended operation, being out of their own environment and feeling somewhat intimidated by professional roles, or might simply find it difficult to say no. Sensitivity to both verbal and non-verbal cues prompted nurses to create opportunities for potential participants to decline (see *Table 54*, section D, quotations 14 and 15).

The role of participants' relatives was also discussed as their presence could complicate assessment of truly informed consent. Relatives were often helpful in facilitating the patient to understand key trial information, but sometimes took it on themselves to decide about study involvement on behalf of the patient and had their own questions and concerns that needed addressing (see *Table 54*, section D, quotations 16 and 17). The nurses identified the need to deal respectfully with relatives' questions and opinions while at the same time maintaining the focus on the potential participant's wishes.

Recruitment interviews that ended without consent were felt to be particularly useful in the peer-review process because they provided an opportunity to review whether or not the recruiting nurse might have achieved a different result if the interaction had been managed differently or communication conveyed in a different way. They also provided an opportunity to evaluate the appropriate level of encouragement to participate and to check that if potential participants were reluctant to participate this was respected and handled appropriately. Reviewing these interactions provided an excellent opportunity to discuss the potential tension between maximising recruitment and ensuring that consent was truly voluntary and fully informed. The nurses were reassured that patients were being recruited appropriately and not subject to undue persuasion.

Recruiters' perceptions of the peer-review process

The recruiting nurses also reflected on their experience of the peer-review process. Initially they were apprehensive about recording and hearing their own recruitment interviews, but recognised the potential benefits (see *Table 54*, section E, quotations 18 and 19). There was anxiety about feeling judged or being considered less effective than colleagues, but seeing it as a mutual learning experience contained within the nurse team helped to overcome reservations and was important to enable open discussion (see *Table 54*, section E, quotations 20 and 21).

Important perceived benefits of the peer-review process were reassurance about individual and team practice and increased team cohesion (see *Table 54*, section E, quotation 22). Other benefits included reflection on personal practice, which prompted changes in individual conduct of recruitment interviews (see *Table 54*, section E, quotation 23). Overall, the process was felt to be a valuable learning tool because it facilitated reflection and learning from others' practice in a supportive and reassuring environment. All felt that overall practice and safeguards in recruitment were enhanced and that they would want to repeat this process in subsequent trials (see *Table 54*, section E, quotation 24).

Discussion

As recruitment to RCTs is pivotal to their success,[446] it is crucial to equip recruiters adequately for their important role. In addition to a sound knowledge of protocol and ethical principles, those involved in recruitment require good interpersonal communication skills to respond flexibly to the specific information and comprehension needs of individual participants and to identify their concerns. Previous qualitative analysis of recordings of recruitment interviews[447] has highlighted the need to improve communication techniques, in particular adequately explaining equipoise and the process of randomisation, in order to ensure fully informed consent. Acquisition of these skills has been identified as a key area to address to optimise recruitment,[447,448] but there is as yet no reproducible process that has been demonstrated to be both effective and acceptable in a range of trials.

We have drawn on prior work conducted in the Prostate Testing for Cancer and Treatment (ProtecT) study, which sought to improve trial processes and recruitment to a multisite RCT using a variety of approaches, including using a peer-review process in which senior staff from one site reviewed the practice of another site.[449] Further work focused on using qualitative analysis of recruitment interviews, followed by feedback to recruiting staff in other trials to see if it could be used to improve recruitment.[450] However, difficulties relating to both logistics and acceptability limited effectiveness. de Salis and colleagues[450] found that, because the analysis and feedback process had not been included in the initial study protocol of the trials, they were faced with governance issues which made it very difficult to implement peer review quickly enough to make a difference in trials currently under way.[450] They also found it difficult to get all members of the study team on board and to commit to the process, concluding that it was important to build it into the study protocol at the trial design stage. In addition, reluctance among recruiting nurses to take part in recording recruitment interviews that would be listened to and scrutinised by researchers outside the study team seriously hampered the process.

We aimed to overcome these difficulties. First, the initial APEX trial protocol specified that recordings of the recruitment interviews would be analysed during the pilot phase in order to ensure consistency of trial recruitment and assist with training needs of the study recruitment staff and this was included in all research governance applications. Embedding the peer-review process in the trial design from the outset ensured that all members of staff recruited to deliver the trial were made aware that recording recruitment interviews would be standard practice. Building this process into the protocol also means that the time and costs needed to conduct the peer-review process can be factored in when writing grant applications. Study performance gains, such as increased recruitment and acceptance of randomisation may potentially outweigh the cost of staff time to complete the process, but this needs to be formally evaluated in future work. In our study, the total time taken to listen to the recordings and complete review forms was 10.33 hours, based on an average of 12.42 minutes per recording and a total of 50 recruitment interviews reviewed. The total nurse time spent in review meetings was approximately 16 hours. Not all the

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

interviews that were recorded were reviewed but having a good sample size allowed the purposive selection of interviews that were of particular value for the training process, because they provided examples of good practice, had been particularly challenging, or demonstrated the need for additional clarification about aspects of the trial. Furthermore, the length of time needed to complete the training process was not predetermined and the meetings concluded when consensus was reached among the nurses that no new learning was likely to be achieved and each felt competent in their recruitment practice. The period of time required for training is likely to differ according to the complexity of the trial and the intervention, and the experience of the recruiting nurses, but sufficient time needs to be given for at least two cycles of reviewing, evaluating and sharing practice, implementing new techniques or adjusting practice, and re-evaluating. Sufficient interviews need to be recorded to capture a good variety of interviews and circumstances and of participant interactions and responses.

Second, whereas de Salis and colleagues[450] had been hampered by recruiting nurses' reluctance to record recruitment interviews, we circumvented the nurses' apprehension that others might scrutinise and appraise them by confining the peer review to the recruiting nurses. In addition, making the peer review exclusive to the recruiting nurse team enhanced team cohesion by helping to build trust and foster working relationships, benefiting both communication and efficiency.

Qualitative methods were used to evaluate the intervention from the points of view of both effectiveness and acceptability to the recruiting nurses. Effectiveness, in terms of benefits for the recruitment process, was evident in several areas. First, adherence to the protocol was improved. As a result of peer review, the recruiters increased their knowledge of the trial design, identified areas of the protocol that were ambiguous and clarified the eligibility criteria. Second, a barrier to recruitment was identified in the information that patients received prior to meeting the recruiting nurse and was subsequently addressed. Third, use of a checklist during review of recruitment recordings improved the consistency and completeness of information given verbally to potential participants. It would have been difficult to identify these issues using other quality control methods[449] and, without this structured process during the initial pilot phase, problems may have continued for some time. Fourth, compliance with good clinical practice was enhanced by developing strategies to check participant understanding of trial information and key concepts, ensuring equipoise and gaining better evidence of informed voluntary consent, all of which can impact on trial recruitment and retention.[451] A formal trial of our methods could provide additional important evidence regarding effectiveness, as in this case we had no comparator and were unable to determine whether or not the intervention made a difference to recruitment rates. In future evaluations it would also be valuable to gain consent to analyse the recruitment interviews to unpack the processes at work and to directly compare patients' and recruiting nurses' perspectives of the same interview.

The acceptability of recruitment training by means of peer review was evident in the qualitative data. Our evaluation provided similar findings to other studies involving other health professionals and different contexts. Those involved in peer review as a training method often experience initial apprehension but later conclude that it is both supportive and valuable for improving practice.[452] Once initial apprehension was overcome, the recruiting nurses considered peer review to have been a very productive and acceptable training method. Each nurse within the team benefited from individual feedback and the opportunity to learn from other members of the team, which contributed to professional development in a way that was clearly recognised. Consideration needs to be given to how peer review is facilitated so that group members feel safe enough to share examples of practice that they feel are suboptimal.[453] The requisite skills and knowledge also need to be available to the group, either from the facilitator or from within the group as a whole.[452] In our case, one member had previous training in group facilitation and communication skills and others had extensive experience of trial recruitment.

Implications for nurses recruiting patients into clinical trials

Nurses recruiting to trials require additional training because they must obtain consent for an intervention that is administered for reasons other than anticipated benefit to the individual patient. Recruitment training should address both generic and study-specific skills as 'each RCT has a unique – and uniquely

complex – recruitment pathway and its own set of issues that need to be resolved'.[450] Although training those responsible for recruitment to a RCT is a crucial part of the set-up phase of a trial, it is often not done in a structured way. Our intervention provided a constructive forum to compare and critique ways of conveying the study information and become skilled at clearly articulating the trial design, which is vital to maximising recruitment.[454] From this process, we developed a set of recruitment competencies, specific to the APEX trial, that were then used in conjunction with the peer-review training method to train new members of the nurse recruiting team in a structured way. This was an important step towards formalising and evaluating recruitment training and in creating a process that could be applied to other trials. As a result of this work, the NHS sponsoring organisation adopted the principle of assessing the competencies of nurses recruiting to RCTs, creating a two-part competency framework based on the competencies developed in this study. The first part consists of generic competencies related to International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice principles. The second part consists of competencies specific to the individual trial, which must be specified and assessed by the principal investigator (PI) in order to delegate responsibility for recruitment to suitably experienced and qualified recruiters.

Conclusions

Sharing experience of recruitment and formal comparison of recruitment interviews in a creative and supportive environment can lead to the identification of best practice, improved communication skills and early awareness of issues and problems which might otherwise have an impact on recruitment for much longer.

Views and experiences of trial participation and use of analgesics

In addition to our longitudinal qualitative research focusing on experience of patients undergoing hip and knee replacement, we also conducted qualitative research with patients and health-care professionals who were involved in the APEX trials. This qualitative study aimed to describe and explore the experience of health-care professionals who were involved in the trials and patients' experience of participation. The qualitative research with patients also aimed to explore patients' experiences of joint replacement, with a focus on surgery and medication. Using qualitative methods in the context of controlled trials has long been advocated[455] and such methods are valuable to improve understanding of the experiences of patients receiving, and staff delivering, a trial and intervention.[456,457]

Background

Involvement in clinical trials

Previous research has highlighted weakness in the present orthopaedic literature, as studies are being given poor ratings in independent meta-analyses and the American Academy of Orthopaedic Surgeons evidence-based clinical guidelines.[458,459] This has led to a growing emphasis on the importance of orthopaedic evidence through higher-quality RCTs.[460]

The success of a RCT is dependent on adequate recruitment and retention of patients within a timely manner. It has been suggested that 50% of RCTs fail to recruit their planned number of participants,[451] which can undermine the power the study, lead to sampling bias and limit generalisability of results. Little is known about why patients may be motivated to take part in trials, or their experiences of taking part. Understanding these can be integral to successful recruitment and retention.[461] Trial success is equally dependent on the engagement of a large multidisciplinary clinical team and involves effective communication and attention to the study protocol. Less is known about clinical staff members' experiences of trial involvement. Exploring the views of health-care professionals involved in a delivering RCTs and patients' participating in the same trials enables the identification of factors that may enhance understanding of how to best deliver RCTs in orthopaedics.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Attitudes to analgesics

Patients living with osteoarthritis use medication including paracetamol, non-steroidal anti-inflammatory drugs and opioid medication to manage their condition.[26,27,462,463] Research has provided insights into how people living with osteoarthritis feel about and use pain relief, highlighting the complexity of adherence to these medications.[26,27] In addition, although persistent pain is the key indication for total hip or knee replacement, the need for pain management continues after surgery.[464,465] Over half of patients undergoing total hip or knee replacement report moderate to severe pain on the first day after surgery.[70] Chronic post-surgical pain is also common, with 10–34% of TKR patients and 7–23% of THR patients reporting long-term pain after their operation.[18] The pain associated with both osteoarthritis and total hip or knee replacement confirms the need for patients to receive appropriate intervention at all stages of the illness trajectory. Therefore, it is important to learn how undergoing total hip or knee replacement affects existing attitudes and behaviours with regard to pain medications.

Methods

Sampling and recruitment

During recruitment to the APEX trials, patients were asked if they were willing to be contacted about taking part in a qualitative interview. From those who agreed to contact we identified a sample of men and women who were a range of ages and comprised a balance of THR and TKR patients. The programme's qualitative researcher telephoned individuals in this sample and asked if they were still interested in taking part in a qualitative interview. Of the 26 people contacted, 25 agreed to see the researcher to discuss study participation and interview; however, one of these subsequently withdrew from APEX and was no longer eligible to take part. Interviews were also conducted with a range of health-care professionals involved in the APEX trial. Health-care professionals were purposely sampled to include those involved in pre-assessment, surgery and recovery phase of the trial and contacted by telephone or e-mail. Fifteen health-care professionals took part in interviews. The samples are described at the start of *Results*, below. Data collection proceeded in parallel with analysis and continued until data saturation was reached such that no new insights were being achieved by the end of data collection.[255]

Data collection

All participants provided their written, informed consent immediately prior to interview. Interview topic guides were used, informed by the literature. Patients were asked to describe their decision-making regarding trial participation, understanding and experience of the trial. In addition, patients were asked about their views on, and experience of, pain and pain relief as a way of contextualising their experiences of trial participation. Health-care professionals were asked to talk about their views and experiences of trial involvement.

Interviews with patients were conducted 2–4 weeks after surgery in participants' own homes between April 2010 and January 2011 and lasted between 45 and 120 minutes. Health-care professional interviews were undertaken in hospital premises between March 2011 and June 2012 and lasted between 19 and 40 minutes. The research team comprised qualitative methodologists with backgrounds in social and behavioural sciences.

Data analysis

Interviews were audio-recorded, transcribed and anonymised. Interview transcripts were checked for accuracy and then imported into ATLAS.ti qualitative data analysis software, which aids the management and indexing of qualitative data. Analysis began shortly after data collection started and was ongoing and iterative. Thematic analysis,[257] utilising a data-driven inductive approach,[466] was used to scrutinise the data in order to identify and analyse patterns and themes of particular salience for participants and across the data set using constant comparison techniques.[467] Transcripts from patients and health-care professionals were analysed separately and, using an inductive approach, we assigned codes to all of the data. We developed a coding framework, which was refined as analysis progressed. The research team grouped the codes and coded material into superordinate themes by identifying connections between the codes and

data.[259] To ensure robust analysis a subset of transcripts was independently double coded by other members of the research team and compared, any discrepancies were discussed within the research team and resolved in order to ensure robust analysis. We did not analyse the patient data according to the group allocation of participants within the randomised trial. This is because this nested qualitative study aimed to explore beliefs and behaviour relating to pain around the time of surgery and trial involvement. The trials aimed to study impact of additional analgesia on outcome at 12 months after surgery.

Results

The 24 patients who participated were 11 men and 13 women, aged 26–92 years. Fourteen were in the trial to undergo hip replacement and 10 were in the trial for knee replacement (*Table 55*). The 15 health-care professionals consisted of four men and 11 women, aged 28–56 years. They comprised three pre-operative clinical nurses, four ward nurses, four orthopaedic surgeons, two anaesthetists and two ward managers. We have not provided a table of participating health-care professionals so anonymity is not compromised. Patients were assigned pseudo initials and health-care professionals were assigned a number with their job role listed when we provide illustrative quotations.

TABLE 55 Views and experiences of trial participation and use of analgesics: patient characteristics

Pseudonym	Age (years)	Sex	Operated joint
Mrs A	73	Female	Hip
Mrs B	65	Female	Hip
Mrs C	72	Female	Knee
Mr D	72	Male	Knee
Mrs E	79	Female	Hip
Mr F	67	Male	Hip
Mrs G	59	Female	Hip
Mrs H	73	Female	Hip
Mr I	53	Male	Knee
Mrs J	64	Female	Knee
Mrs K	63	Female	Knee
Mrs L	46	Female	Knee
Mr M	50	Male	Hip
Mr N	45	Male	Hip
Mrs O	52	Female	Hip
Mrs P	76	Female	Knee
Mr Q	75	Male	Hip
Mr R	26	Male	Hip
Mr S	76	Male	Knee
Mr T	74	Male	Hip
Mrs U	71	Female	Knee
Mr V	66	Male	Knee
Mr W	92	Male	Hip
Mrs X	77	Female	Hip

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Findings from the interviews with health-care professionals

Health-care professionals views on trial involvement

Clinical staff said that they were happy to be involved in a trial that they understood as important, relevant to patient experiences and central to the clinical staff members' professional practice (*Table 56*).

Staff weighed up the perceived benefits and costs of being involved in the trial. Some clinical staff reported initial concerns relating to expectations of the research staff, the possibility of an increased workload and the logistics of recruiting patients in a busy clinic. These initial concerns were alleviated once they learned more about the study, with many commenting that they appreciated that the trial had been designed to have minimal impact on, and normalised into, their daily clinical practice (*Table 57*).

Clinical staff noted that the research nurses played a central support role in clarifying procedural details and their flexibility in smoothing out any initial issues and reducing any burden of the trial on clinical staff was appreciated and welcomed (*Table 58*).

TABLE 56 Health-care professionals' views on trial involvement

Health-care professional	Quotation
S8, senior nurse	*I think it's really valuable because the more you can help people with pain, you know, it's really - I think that's one thing that the patients are frightened of, isn't it, when they have surgery with anybody? I would be. . . . So, you know, the advances in pain relief and making sure they're relatively pain-free, has got to be good*
S9, trainee nurse practitioner	*That's really good. Because I mean that comes – you know, that rolls into what we're doing as well, to what you're doing, and everything is just contributing towards trying to keep the patient pain-free for longer, and to get them more mobile, and to get them out back into their own home, which is good*
S10, surgeon	*I thought that it was a good idea to give a little local anaesthetic, you know, so the patient um, they're more comfortable when they wake up um and er the body gets time to acclimatise, so to speak, to the pain, rather than they wake up in serious pain. . . . I've never thought about doing an objective assessment, you know, um, you know, as qualitative as this*

TABLE 57 Health-care professionals' views about benefits and costs of trial involvement

Health-care professional	Quotation
S2, ward nurse	*It was a little bit worrying and we'd think, 'Oh gosh, you know, we're all being watched.' [Laughs.] You know, because you do think, oh research, are people going to be coming in, and are they going to be asking lots of questions? And I suppose sometimes there is a fear there of thinking, 'Oh my gosh, you know, what is going to be expected?'*
S7, pre-operation clinic manager	*Well it's just like part of what happens now*
S14, consultant anaesthetist	*No I have no problem, I mean it's a great opportunity to contribute to research . . . So there's not much that we have to do there. OK, we had to just do a standardised anaesthetic and fill in the form, so I think you didn't ask for too much*
S12, consultant anaesthetist	*I thought it was going to be OK because essentially it was using the same anaesthetic that we were already using for the knee, um for our primary knee replacements. So I didn't think it would have much impact on what I did, in terms of the anaesthetic, so I was quite happy to go along with it*

TABLE 58 Role of research nurses

Health-care professional	Quotation
S5, ward manager	*Seeing someone every day is good. You know they are going to come up, if there's any issues. Um. . . . So I think that's worked well that they're very visible*
S6, ward manager	*We haven't really asked for as much help as they [research nurses] have offered. They have been here and given us a lot of information and they have again been offering staff any support they can possibly think of and um you know whether it was to do with filling out the forms or where we put the forms after we have completed them. You know what sort of support we need to give the patients. So yes they've been excellent really*

Health professionals' views of patient benefit from trial participation

During the interview, some ward staff also commented on the benefits that they thought patients achieved by participating in a trial. These included patients gaining a better understanding of their situation through completing study questionnaires, an increased sense of security as patients felt that they received additional monitoring and satisfaction from involvement in health research (*Table 59*).

Findings from the interviews with patients

Trial participation

Benefiting others Patients reported several different reasons for trial participation. Altruistic reasons focusing on benefit to society were common; patients viewed their participation in trials as contributing to advancement of scientific knowledge. In addition, patients expressed gratitude to unknown members of previous generations who had participated in research that had contributed to improvements in medical care that they were currently receiving. This motivated them to participate in research to help future generations (*Table 60*).

Perceived benefits and costs of trial participation Patients weighed up potential risks and benefits of trial participation and were motivated to take part in the trial if they saw few negative consequences in relation to being randomised to either of the trial arms. Patients said that APEX was seen as a low-risk trial to participate in owing to being randomised to standard care or standard care plus additional treatment. Patients did not feel like they would be 'losing out on anything' (Mrs L). The requirements of the trials in terms of data collection were not seen as a burden to the majority of patients. They considered the data collection methods and length of follow-up to be clear, acceptable and undemanding (*Table 61*).

TABLE 59 Health-care professionals' perceptions of patients' trial participation

Health-care professional	Quotation
S2, ward nurse	*Oh they like it, because they're involved. They feel like they're involved and they're participating in a trial, 'I'm doing a study, I'm helping them do a study, looking at how we're going to help patients in pain.' So yeah, most – well all of them seem to be pleased about being on the trial*
S3, senior ward nurse	*I think it's [trial participation] probably given the patients a lot more support and security maybe understanding in their own pain relief and to know they are being followed through as well*
S6, ward manager	*I think most of them [patients] seem very laid back about it. They have expressed absolutely no worries about it whatsoever and they seem very well informed. My feeling is that they probably think it's quite exciting*

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 60 Altruistic and reciprocal reasons for patient trial participation

Health-care professional	Quotation
Mrs B	*Well I just thought that anything that might help people in the future. You know if people don't do things like that [then] improvements might take place but probably a lot more slowly. I think that it's a good thing to do for the benefit of people who are having operations in the future really that's why*
Mrs G	*I think, well unless you have guinea pigs how do you know how things are going to work? Yeah you don't know if you were one of the people that got the stuff or if you were one of the people that didn't but unless you have people to talk to and to find out about things how do you know? You're never going to learn*
Mrs Q	*My attitude to that is things they know now somebody has done that in the past so if they learn more it's going to be valuable to people in the future. I'm all for that. . . . Years ago they used to cut peoples legs off with saws, they've moved on quite a bit from that haven't they*

TABLE 61 Patients' trial participation decision-making

Health-care professional	Quotation
Mrs L	*I thought well it's not as though it's going to be a new drug what you're testing on her, it's only going to be anaesthetic but it's only going to be a trial if it works or it didn't work. I mean it's not as though I'm going to lose anything if it doesn't work. I thought if it does work then I've gained a lot so it's not as though it's going to be a new drug you're trying out if it's only anaesthetic. So I thought well yeah, if it's going to help me with the pain afterwards then yeah*
Mrs K	*It's all self explanatory isn't it really, no I don't think so no, I understood and knew what it all entailed like. I mean it doesn't really entail much apart from a few forms*
Mrs E	*Yeah, I thought, 'Well, somebody got to do it', I mean, all these things take time, and someone's got to do it, and I thought, 'Well, I don't mind, I won't be doing anything when I come home'. [Laughs.] Yeah, it'd be an interest anyway*
Mr M	*What harm can it do? I am sitting at home so I might as well, better than doing a crossword*

Potential personal benefits Patents were additionally motivated to participate in the trial by the hope that they may also have personal benefit from trial participation. Trial involvement brought with it the chance that patients might obtain the latest medical care, possibly receiving medical treatment that is not routinely available. Patients described the potential benefit of receiving more anaesthetic if they had been randomised into the intervention arm of the trial, while also demonstrating a good understanding of the process and the need for randomisation and blinding (*Table 62*).

TABLE 62 Patients' perceived potential physical benefits of trial participation

Health-care professional	Quotation
Mrs P	*When she said they would inject into the scar before they send it up I thought 'oh lovely a bit more pain, less pain' [yes], but I don't know whether I had it done so I suppose it is in my mind. I might have had it I don't know*
Mrs X	*I just thought what a good thing um, you know, to have that extra help at that time, er to relieve pain, you know. So I thought it – yeah, I said to my daughter, 'No, I will do that, because I think it's really good'*

Patients also reported a range of psychological benefits of trial participation. Patients described that a potential personal benefit from trial participation could be from increased surveillance by the researcher team. Even though trial participation may not directly improve their situation, the extra monitoring reassured patients. Patients also thought that completion of the questionnaires may have helped them to consider and better understand their pain and outcomes and helped quantity the patients' pain experience (*Table 63*).

Pain relief medication Patients who took part in the qualitative study nested within the APEX trials also reflected on their use of pain relief medication pre-surgery, during their hospital stay and while recovering from their operation at home. The analysis of the data relating to pain relief medication identified two superordinate themes relating to use of pain relief over these periods: shifting acceptability, and necessity and value. We also found that behaviour and beliefs relating to pain relief medication were influenced by external factors that are described after the two themes.

Summaries of patients' experiences at different time points in their journeys through joint replacement are illustrated in *Figure 33* and are summarised in *Box 19*. We present a description of the themes that describe how and why patients made their decisions about pain relief.

*Shifting acceptability (*Table 64*)* Patients' decisions about use of pain relief medication were influenced by their beliefs about the acceptability of medication use. This changed over time, with short-term use seen as acceptable but longer-term use seen as not acceptable. Patients' willingness to use pain relief medication changed from their time before surgery, during their time in hospital and subsequently on their return home. Immediately after surgery, patients thought that recovery in the acute postoperative phase was time-limited and they started to reduce their use of pain medication. This was directly related to their wish to return to a situation of some normality in which they limited their use of pain relief. As time passed, long-term use was no longer acceptable. Decisions about medication use were also influenced by other factors including the acceptability of using pain medication compared with living with pain and associated limitations, concerns about side effects and beliefs about 'light' non-prescription medications compared with 'heavy' prescription medications.

TABLE 63 Patients' perceived psychological benefits of trial participation

Health-care professional	Quotation
Mr M	*I think for a certain degree that I had some scepticism to a degree in my own mind that if there is a what if it went wrong, somebody else is looking from another corner at me, it may help to decipher why, when, where, what how it went wrong*
Mrs P	*Oh my pain going down? Yes because you don't think do you. You think everyday 'oh it is the same, oh I wish it would hurry up oh it is still there'. But it wasn't you could tell and as like when I get up in the morning and I would go to the toilet, have my wash and come back in and then I would sit and fill it and I would think 'oh it is a lot better today'*

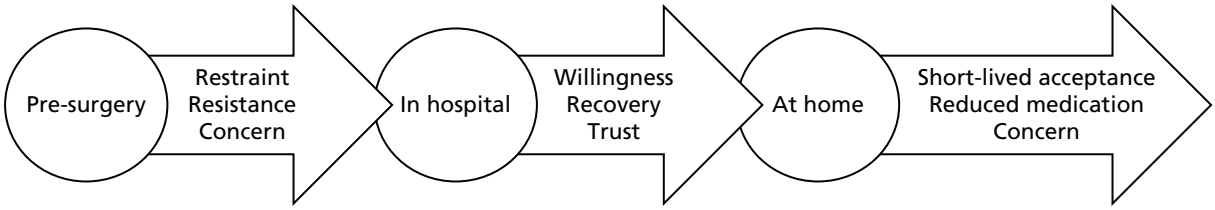


FIGURE 33 Summary of patients' pain relief experiences over the total hip or knee replacement journey.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

BOX 19 Summary of patterns of pain relief use over the total hip or knee replacement journey

Patterns of pain relief use during the pre-operative period

- Patients were living with chronic pain.
- Patients had access to non-prescription medication and prescriptions for stronger pain relief.
- However, use of pain relief medication was avoided and restricted.

I would take very, very rarely and only when the pain was unbearable . . . I could go a month or six weeks without because I don't like taking tablets.

Mr N

Patterns of pain relief use during the hospital stay

- Patients were faced with the threat of acute postoperative pain.
- Many changed their use of pain relief during this period.
- They were motivated and more willing to take full and regular doses of pain medication.

But I felt that I needed that, by golly that was needed without a doubt and I used to have one eye on the clock . . . especially as things started to wear off.

Mr M

Patterns of pain relief use while recovering at home

- After discharge, patients initially took their medications as they had done in hospital.
- However, within a few days of coming home, they returned to their pre-surgical pattern of medication use.
- Patients cut back on their use of pain medication whether or not they were still in pain.

I was on regular medication [when I came home after total hip or knee replacement], I was obediently taking it, accepting my bag of drugs that I came out with thinking, maybe I won't need all of that, but I did, and I went back to the GP, I did get some of the prescription replenished. But since then I've dropped the lower level medication down considerably.

Mrs O

TABLE 64 Shifting acceptability

Health-care professional	Quotation
Mrs O	*So over a sort of time scale, means to an end, I'm very compliant. But it's the long-term aspect that I'm so defiant about. . . . I'm fine around accepting it when it's short-term, short-term issue, and it's, it's deemed with a current problem. I can handle it then, yeah it's becoming a long-term reliance that frightens me*
Mrs P	*I don't like this feeling. . . . I would rather put up with the pain than be feeling nauseous because it is a horrible feeling. . . . So I have cut down to one now. I have got to stop because they are not doing me any good. They are stopping the pain but they are not making me eat*
Mrs O	*I was very, very reluctant to get on that, on that track as far as the heavier duty medication was concerned. So I was managing with over-the-counter stuff really. . . . I suppose you always needed to know that you had a margin to, to operate with. I don't know, yeah letting yourself down*

*Necessity and value (*Table 65*)* Patients described beliefs about the necessity and value of medication to help them manage their changing pain experience. Use of medication was in part a moral decision, based on notions about when it was right to take analgesia. Although many talked of experiencing chronic pain before their operation, most did not think the pain was 'bad enough' to justify use of pain relief medication. Patients first waited to see if they could manage without use of pain relief and only took it as a last resort to enable them to 'live' and function with pain. However, patients also reported that the intensity of pain and discomfort that they experienced immediately after surgery outweighed their concerns about certain medications, resulting in increased pain relief medication use. This view that medication was needed to facilitate coping with pain caused by surgery also influenced their decisions about medication in their early recovery period after discharge. Taking regular pain relief after their operation was also recognised by patients as an imperative component of their recovery process, an outlook that served to over-ride any long-held negative attitudes towards analgesia. Patients' thoughts about the value of pain medication were also balanced against the intensity of their pain in the weeks after their operation. At 2–4 weeks post surgery, some patients had stopped taking pain medication. They explained that this was because they were no longer experiencing what they considered to be significant pain and, therefore, saw no real value or continued benefit in doing so.

*External influence on behaviour and beliefs (*Table 66*)* Narratives illustrated the central role that health-care professionals can have in influencing patients' views on and use of pain relief during their journey through total hip or knee replacement. Before patients had their operation, consultations with health-care professionals were useful in encouraging them to increase the effectiveness of their self-management by moving from 'light' pain relief to the 'heavier' prescription-only drugs. The influence of health-care professionals in patients' use of pain relief increased when they went into hospital to have their operation. It was then that most no longer held firm to their long-standing beliefs about the acceptability, necessity and value of pain relief when 'experts' were directly on hand to provide pain management.

TABLE 65 Necessity and value

Health-care professional	Quotation
Mrs C	*I felt well see if I could go around without taking them. . . . You know if you can manage without the tablets*
Mrs G	*And you can't tell when the shooting pain's going to come anyway so what was the point?*
Mr M	Interviewer: *And how did you feel when you woke up?* Mr M: *Rough, bloody rough, yes really rough, not right, and I was on a drip that I could control* [PCA: morphine] *but it was timed but I had to press the button to get any more, and it went to 2 minutes and 39 seconds because I counted 37, 39, yes, because I wanted that extra . . . I was a bit worried, especially with morphine, of becoming addicted to morphine because I have heard stories about people who are but I am fine*
Mrs X	*When I was in hospital, yes. And I had to struggle to get out of bed and, and take myself to the toilet. So in order to fortify myself, I had to, I knew I would have to take those painkillers, you see*
Mrs E	*I felt, 'Oh, I don't know what the pain's about, so I'll take . . . come off of them and see', but I haven't had any pain since. Touch wood. And then the next day, I thought, 'I'm coming off this sickness one as well, because why am I taking it if I'm not being sick now'. So I came off that as well. So all I'm taking is my blood pressure tablets and two aspirin, that's all I'm taking now*

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 66 External influences

Health-care professional	Quotation
Mrs H	Pre-surgery
	I was only taking paracetamol, four times a day, two four times a day. And then my doctor said 'well you ought to be taking ibuprofen that will get the inflammation down' so I was taking ibuprofen
Mr N	In hospital
	Always coming round with your tablets . . . and on their little rounds and anything from a couple of tablets at a time to about eight. You could have had a right cocktail sometimes. . . . I took whatever they gave me because . . . I, they know what they're doing. I wouldn't have dreamt of not taking any of them because it's tried and tested so I had all the belief in it
Mr N	At home
	Interviewer: *So all the painkillers you've been taking since your operation, was that something that was discussed with you?*
	Mr N: *Yes. They explained what benefits . . . and obviously I've had to lower my guard on my tablet intake . . . and I go with the experience and knowledge of people telling me*

Instead, they put their faith in health-care professionals to provide them with only those medications that were essential to help with their recovery. Accounts also revealed the heightened influence of health-care professionals over the ways in which patients used pain relief after their surgery. For example, the influence they had over decisions to carry on regularly using pain medications during their initial period of recovery at home.

Discussion

Trial involvement

Both patients and health-care professionals reported that their initial interest in APEX was a result of the trial being perceived as an important area of research that was highly relevant to the patients' experience of surgery. The data demonstrate the importance of addressing a question of substantial interest, relevance and value to health-care professionals and patients to get 'buy-in' from all. In addition, revealing the need to produce clear trial information for both patients' and health-care professionals to explain the rational and importance of the RCT.

Patients and health-care professionals both stated weighing of perceived benefits and costs associated with involvement in APEX. The data demonstrate the need for minimal personal burden when undertaking a trial.[468] For health-care professionals, this was achieved by employing research nurses to ensure that the trial had minimal impact on daily clinical practice and also to be available to clarify procedural details to ensure the protocol was adhered to. Patients thought that participation in the trial had minimum costs to them and they felt that the possibility of randomisation to either trial arm, and the requirements of data collection, were acceptable. A limitation of the study is that we only captured the views of patients who agreed to take part in the trials and we were unable to speak with patients who declined to take part.

Patients motivations for trial involvement are multifaceted and complex,[469] and include a range of personal and social elements.[470] Patients often stated altruistic reasons and expressed the desire to help others by contributing to the furthering of clinical knowledge.[471] However, only a minority of patients stated purely altruistic reasons, with many reporting a range of perceived physical and psychological benefits.[461] It is therefore vital during recruitment that time is spent on identifying and dispelling expectations that might not be met by the RCT.

Pain relief medication

Attitudes to pain relief medication are dynamic. Undergoing total hip or knee replacement has the potential to temporarily alter an individual's view of the acceptability, necessity and value of pain relief medication. This alteration is related to views about the cause of pain (pain from intervention vs. pain from chronic condition) and interactions with health-care professionals. However, once initial recovery from surgery has begun, long-standing beliefs about the appropriate use of analgesia in the management of pain may again take prominence.

Health-care professionals appeared to exert considerable influence on patients' beliefs about the essential nature of pain medication during the hospital stay. Although there is notable contact with health-care professionals during this period, in the pre-surgical period this contact is less frequent. After surgery, patients are discharged from hospital with pain medications, but contact with health-care professionals may be minimal, which means that contact before surgery might be particularly important. It was clear from this study that interactions between health-care professionals can provide crucial opportunities to discuss pain management. During these interactions, health-care professionals may wish to consider challenging or reinforcing patients' beliefs about pain relief medication with a view to ensuring that patients' pain is as well managed as possible.

Local anaesthetic anaesthesia: overall discussion and conclusions

Perioperative care should include appropriate multimodal anaesthesia supported by evidence from adequately powered RCTs. Systematic review identified 36 RCTs evaluating local anaesthetic infiltration in patients receiving THR and TKR. Few reported long-term post-surgical follow-up. Local anaesthetic infiltration was effective in reducing short-term pain when compared with no infiltration. Clinical effectiveness was enhanced with the addition of post-closure analgesia through drains that had been sited intraoperatively. However, there was some evidence to suggest that this was associated with an increased risk of infection. In patients receiving TKR, there was no evidence of additional benefit if a FNB had already been sited. FNBs affect knee extension and could delay postoperative mobilisation. Therefore, we need to compare local anaesthetic infiltration with FNB to see which is most effective and which allows earlier mobilisation and discharge.

In the APEX RCTs, local anaesthetic infiltration was associated with reduced long-term pain 1 year after THR. Findings in patients receiving TKR provided no strong evidence that local anaesthetic infiltration reduced long-term pain in addition to that provided by FNB. From the perspective of the NHS and PSS, local anaesthetic infiltration is a cost-effective treatment option in primary THR but evidence supporting its use in TKR was less strong.

Patients' views on pain medication are dynamic and change in the perioperative period when they have more clinician contact and perceive a necessity to take analgesic to treat surgical pain. After surgery, clinician contact diminishes and patients tend to revert to traditional and long-standing beliefs about pain medication. The attitudes of patients to pain and pain medication throughout the patient journey need to be explored more fully, particularly with regard to whether or not patients' needs are being addressed prior to surgery, and for those who have long-term pain.

In addition to the clinical results from the trial, we have learned valuable lessons about the running of trials from our qualitative work with patients, clinicians and researchers. Patients are willing to participate in a trial if they feel the question being addressed is important, if the participation burden is low and if there is a perceived or possible benefit for them. Clinicians are willing to participate if the appointment of research staff does not result in the trial impinging on clinical time.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Chapter 7 Exploring and understanding pain in the context of hip and knee replacement: a cohort study

Parts of this chapter have been reproduced from Wylde and colleagues[472] © 2015 Wlyde V, Sayers A, Lenguerrand E, Gooberman-Hill, Pyke M, Beswick AD, *et al.* Preoperative widespread pain sensitization and chronic pain after hip and knee replacement: a cohort analysis. *Pain* 2015;**156**:47–54 and from Sayers and colleagues[473] © 2016 The Authors. Arthritis Care & Research published by Wiley Periodicals, Inc. on behalf of the American College of Rheumatology. This is an open access article under the terms of the TODO: click through URL Creative Commons Attribution-Non Commercial-No Derivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

Abstract

Background

The wealth of data collected in the APEX RCTs provided the opportunity for further analyses as a cohort study.

Methods

The APEX cohort study included 322 patients receiving a THR and 316 patients receiving a TKR. Radiographic measures of osteoarthritis severity were correlated with pre-operative WOMAC pain and function. Associations between measures of pain over time were explored. The association between pain and widespread pain sensitivity, measured using quantitative sensory testing (QST), was investigated.

Results

There was no relationship between the degree of radiographic damage and pain or function in patients waiting for THR. In patients waiting for TKR, those with the least severe radiographic damage reported more severe pain and poorer function.

Long-term pain after THR was predominantly associated with pain at rest during the pre-operative and acute postoperative period. In contrast, long-term pain after TKR was predominantly associated with the severity of pain on movement during the pre-operative period.

Pre-operative widespread pain sensitivity was not associated with change in pain severity from pre-operatively to 12 months postoperatively in patients with total hip or knee replacement.

Conclusions

There was an inverse association between radiographic severity of osteoarthritis and pain and function in patients waiting for TKR but no association in THR. Different pain characteristics predicted long-term pain in total hip and knee replacement. Pre-operative widespread pain sensitivity did not predict the amount of pain relief that patients experienced after joint replacement.

Background

As described in *Chapter 6*, between 2009 and 2012 322 patients undergoing THR and 316 undergoing TKR were recruited into the APEX trials.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

The main purpose of the APEX trials was to assess the relationships between perioperative pain and patient outcomes at 12 months. However, the study also provides us with a large cohort of patients having hip and knee joint replacement surgery and the opportunity to investigate the associations between baseline characteristics, as well as the associations between baseline characteristics and outcomes at 1 year after surgery. The primary focus of these cohort analyses was on pain because we have comprehensive assessments of pre-operative pain, acute postoperative pain and chronic post-surgical pain.

Relationship between structural joint changes and pain and function

Background

Osteoarthritis can be defined on clinical terms, by radiographic evidences of changes, or on the basis of the pathology in the joint. Epidemiological studies of osteoarthritis have generally used radiographic assessment of joint damage to define the disease and the most widely used tool is the Kellgren and Lawrence X-ray grading system.[423]

The relationship between radiographic evidence and pain is generally poor,[474,475] although relatively few data have been published on this relationship in patients with osteoarthritis that is severe enough to result in them having joint replacement, as opposed to population- or service-based cohorts with milder forms of the disease. Furthermore, very few studies have looked at the separate relationships between pain and function and radiographic severity. Some recent data suggest that those patients coming to surgery who have milder radiographic changes respond less well to joint replacement than those with the most severe evidence of joint damage on a radiograph.[476,477]

In the APEX study we have assessed all pre-operative radiographs available, using standard methods, and we are relating radiographic data to pre-operative pain and function data.

Methods

A single observer assessed all radiographs. The observer was a specialist registrar in trauma and orthopaedic surgery who had undergone two training sessions on the specific study research methods with one of the coPIs of the project who has extensive experience with radiographic changes in osteoarthritis. Standard proformas used to report the findings are shown in *Appendices 29* and *30*. After first checking that the radiograph was readable and reporting the presence on any existing implant, the Kellgren and Lawrence score[423] was assessed using standard definitions of the five grades (0–4). We then assessed individual radiographic features (osteophyte, joint space narrowing, subchondral sclerosis and cysts) using the Altman and Gold atlas of individual radiographic features in osteoarthritis.[478] Finally, the pattern of osteoarthritis within the joint was reported. From these data, we then calculated a modified Kellgren and Lawrence grading, as previously reported by Dieppe and colleagues.[479] This divides the two most severe grades (3 and 4) into two subcategories each, based on the amount of joint space narrowing reported and the presence or absence of major subchondral bone remodelling. The purpose of this is to provide a finer differentiation of the severity of radiographic damage in severe osteoarthritis, which, on the traditional Kellgren and Lawrence score, will almost always be grade 3 or 4.

Inter-reader reliability was assessed by the main reader and his mentor assessing 30 random films selected from both the hip and knee cohorts independently, at the end of the study, and the κ-statistic was calculated.

One-way analyses of variance (ANOVAs) were used to analyse the differences between grades of modified Kellgren and Lawrence score WOMAC pain or function means. Tukey post hoc tests were conducted to identify which means differed from each other.

Results

A total of 322 hip patients and 316 knee patients were randomised in the APEX trials. The WOMAC pain scores were collected for each of these patients. The WOMAC function scores were available for only 304 hip and 296 knee participants. Data could not be obtained for 49 hip and 45 knee patients either because the pre-operative radiograph could not be found or because the quality of the film was too poor.

The tests of inter-reader reliability between the two observers for the modified Kellgren and Lawrence scores showed a moderately good level of agreement ($\kappa = 0.55$ for the hip and 0.48 for the knee).

The WOMAC pain and function scores are presented in *Table 67*. As can be seen, the modified Kellgren and Lawrence scoring resulted in four levels of osteoarthritis severity, with reasonable numbers in each category to relate to data on pain and other baseline variables. A small number of patients had little or no evidence of radiographic damage at the time of surgery (14 hip patients and five knee patients). This is both surprising and unexplained, but has been noted in other cohorts.[477,479]

No between-group differences in mean scores of self-reported pain and function were observed for the hip participants. These findings suggest the absence of relationship between the degree of radiographic damage and the severity of either pain or function in patients about to undergo a hip replacement for their advanced osteoarthritis.

However, at the knee joint we do see some interesting in different relationships. Participants in the modified Kellgren and Lawrence 3a group (those with the least severe radiographic evidence of osteoarthritis) had the worst pain and function scores. Their mean pain scores differed significantly ($p < 0.05$) from participants in the 4a, 4b and not-gradable groups, while their mean function score differed from each of the other groups. Participants in the other three groups (3b, 4a and 4b), who have the more severe damage on radiography, had comparable pain and function score levels – suggesting a possible threshold effect – but self-reported pain and function were significantly worse in those with the least severe radiographic evidence of osteoarthritis.

TABLE 67 Pre-operative WOMAC pain and function by grade of modified Kellgren and Lawrence for patients undergoing primary hip or knee surgery

		Hip				Knee			
Outcome WOMAC[a]		*n*	mean	SD	*F*-test; *p*-value[b]	*n*	mean	SD	*F*-test; *p*-value[b]
Pain	mK&L < 3	14	37.1	8.9	$F(5,316) = 1.78$; $p = 0.116$	5	38.0	23.1	$F(5,310) = 2.42$; $p = 0.036$
	mK&L-3a	35	42.1	21.4		14	30.0	12.9	
	mK&L-3b	71	46.5	18.3		109	40.8	17.0	
	mK&L-4a	64	43.8	16.5		96	44.3	17.0	
	mK&L-4b	89	42.0	19.6		47	44.8	14.9	
	Not gradable	49	37.4	18.1		45	44.3	16.2	
Function	mK&L < 3	12	32.6	16.7	$F(5,298) = 2.06$; $p = 0.070$	4	52.6	12.1	$F(5,290) = 2.52$; $p = 0.030$
	mK&L-3a	34	45.2	16.8		10	27.9	11.8	
	mK&L-3b	68	46.8	17.6		104	45.4	16.7	
	mK&L-4a	59	43.3	19.2		92	47.2	18.6	
	mK&L-4b	86	40.5	18.8		45	48.5	19.1	
	Not gradable	45	39.1	20.5		41	46.2	16.7	

mK&L, modified Kellgren and Lawrence.
a WOMAC scores range from 0 to 100 (worse to best).
b One-way ANOVA.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Discussion

Overall, the radiographic evidence of osteoarthritis changes that we observed are consistent with other cohort studies of people with severe hip or knee osteoarthritis.[477,479] The finding of no relationship between pain and radiographic severity at the hip is also consistent with previous data.[479] The striking and new finding from this study is the quite large differences between the severity of both self-reported pain and function in those with modest radiographic evidence of osteoarthritis changes at the knee compared with those with severe radiographic changes.

This key finding is at odds with the data from a similar cohort studied in a very similar way in Australia.[477] In that cohort, no relationship was found between pre-operative radiographic severity and baseline pain and function. However, the Australian health-care system is quite different from the NHS and there are long waiting lists for joint replacement;[480] therefore, patients tend to come to surgery at a very late stage so one explanation for these differences could be the relative paucity of patients in the 3a modified Kellgren and Lawrence grade in the Australian cohort.

In our view, this finding makes sense in relation to decision-making regarding joint replacement. If a patient has significant pain and/or functional problems, and radiographic evidence of severe osteoarthritis changes, then surgery is likely to be recommended. However, if the radiographic changes are less severe, then the doctors will be more cautious, questioning whether or not the joint damage is the main cause of the pain. But if the patient is complaining of terrible pain and or functional problems, then the decision to operate is more likely to go ahead, even if the radiographic changes are mild.[481] However, it is interesting to note that we found no such relationship at the hip joint, emphasising the important difference between end-stage hip and knee osteoarthritis.

Pain

Background

Pain is the primary reason for patients electing to undergo joint replacement surgery and the expectations are that the surgery will provide pain relief. However, our work has shown that 7–23% of THR patients and 10–34% TKR patients experience chronic pain after surgery.[18] The difference in the prevalence of pain after THR and TKR is important and adds to the growing body of evidence that hip and knee osteoarthritis are different diseases. Within the APEX cohort, there are longitudinal pain data on both THR and TKR patients, which allows us to compare and contrast pain pathways with the aim of informing the clinical treatment of these diseases.

Within the surgical literature, there is a growing recognition of the importance of distinguishing between pain at rest and pain on movement due to differing mechanistic pathways and clinical implications, such as differential effectiveness of pharmacological therapies and impact on functional recovery.[482] The aim of this analysis was to compare and contrast the associations between pre-operative pain, acute post-surgical pain and chronic post-surgical pain after THR and TKR, focusing on the differences between pain at rest pain and pain on movement.

Methods

Exposures/mediators

The primary exposures of interest were:

1. pre-operative pain, measured using the WOMAC pain scale
2. acute postoperative pain measured on postoperative day 1, 2 and 3 using a VAS; the severity of pain on rest and pain on movement were rated
3. chronic post-surgical pain, measured using the WOMAC pain scale at 12 months after surgery.

Confounding variables

This analysis involved analysing data from the APEX trials as cohort data and, therefore, additional adjustment was required to control for confounding factors (as per any cohort study) and trial randomisation. Analyses were adjusted for sex and socioeconomic status, which consisted of employment status, cohabitation and educational attainment.

Statistical methods

Descriptive statistics

Population characteristics and outcome measures are reported as means, SDs and interquartile cut-off points for continuous measures, and as frequencies for categorical variables.

Traditional approach

Using linear (OLS) regression, the association between pre-operative pain, acute postoperative pain on movement and at rest, and chronic pain were investigated. Results are reported in natural units (per unit increase in the exposure) and the association with the outcome, 95% CIs, standard errors and *p*-values are also reported.

Pre- and postoperative WOMAC pain scores were transformed to a 0–100 scale and VAS scores were converted into a 10-point ordered response scale. Acute pain on movement and acute pain at rest scores were averaged across the nine measurement occasions.

Structural equation modelling approach

A structural equation modelling (SEM) framework was adopted for three reasons: (1) it provides a framework to conduct mediation analyses, that is, investigate the direct effect of pre-operative pain on chronic pain and indirectly via acute pain on movement or acute pain at rest, (2) it allows multi-item pain assessments to be investigated without simple aggregation of scores and (3) it can be estimated in the presence of missing data under the missing at random assumption using maximum likelihood with missing values.[483]

Importantly, results from SEM are interpreted with respect to the latent constructs of pre-operative pain, acute pain on movement, acute pain at rest and chronic pain. The results are interpreted on the same scale as the scores were originally measured, that is the WOMAC pain scale (a 5-point scale), and the acute pain on movement or acute pain at rest are 10-point scales. Although using a SEM approach does not affect the interpretation of the association between pre-operative and chronic pain compared with the more traditional approach (as the scales are changed equally), the association between pre- and postoperative pains scores and VAS scores will be approximately 1/20th of the size, as the WOMAC is scored from 0 to 100 in the traditional approach.

Further analyses were conducted by grouping items in the pre-operative/postoperative WOMAC assessment more strongly associated with acute pain on movement and acute pain at rest. This subdivision enables the two main constructs of the WOMAC pain scale to be investigated simultaneously.

All analyses were investigated in THR and TKR patients separately. All analyses were conducted in Stata 13.1. Traditional analyses were conducted using the `regress` command and SEM models were estimated using the `sem` command using maximum likelihood with missing values.[483]

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Results

Descriptive data

Baseline characteristics of participants are provided in *Table 68*. Patients undergoing THR had a mean age of 66.2 years (SD 10.9 years), which was slightly younger than the mean of 69.1 years (SD 18.6 years) for TKR patients. A total of 321 THR and 316 TKR patients completed a pre-operative WOMAC pain scale and were included in the analyses. Pre-operative WOMAC pain scales contained very little missing information and pain levels were very similar between THR and TKR patients (*Table 69*).

During the acute post-surgical phase, VAS scales were well completed (90% and 87% for THR and TKR patients, respectively); however, lower completion rates were observed on postoperative day 3 (see *Table 69*). At 12 months postoperatively, 15% of patients with THR and 33% of patients with TKR reported severe/extreme pain, defined as WOMAC pain score of ≤ 50.

Traditional approach

Using simple linear regression, the association between pre-operative WOMAC (0/100) pain and chronic WOMAC (0/100) pain, adjusted for confounding factors, was investigated in THR and TKR patients (see *Table 69*). Pre-operative pain was significantly positively associated in both instances; however, the association in TKR patients was four times as large as in THR patients.

Acute pain on movement and acute pain at rest were also significantly positively associated with chronic pain in both THR and TKR patients. Owing to the traditional inverse coding of the WOMAC pain score (0 extreme pain, 100 no pain), this was an inverse association. The association between acute pain at rest and chronic pain was stronger than the association between acute pain on movement and chronic pain (*Table 70*).

Adjusting the association between pre-operative and chronic pain for acute pain on movement and/or acute pain at rest resulted in minor attenuation of the association in THR patients, and a slightly stronger attenuation in TKR patients.

Structural equation modelling approach

Using the SEM approach resulted in a stronger association between pre-operative and 12-month WOMAC pain in both THR and TKR patients. The majority of the increase in the strength of association can be attributed to the more efficient use of data via the latent constructs as opposed to excluding those individuals with missing data (results not shown). Similarly, the associations between acute pain on movement, acute pain at rest and chronic pain have changed. In THR patients, the association between acute pain on movement and chronic pain has been attenuated ($0.074 \times 20 = |1.48|$ vs. $|-1.86|$), and the association between acute pain at rest and chronic pain has been enhanced ($0.176 \times 20 = |3.52|$ vs. $|-2.2|$). The pattern of change in TKR patients is different with the strength of association between acute pain at rest or acute pain on movement being greater than the traditional approach (see *Table 70*).

Furthermore, when the association between pre-operative pain and chronic pain is adjusted for acute pain, either on movement or at rest, there is stronger attenuation in the SEM approach, suggesting a stronger mediating effect of acute pain (see *Table 70*).

TABLE 68 Demographic characteristics of APEX hip and knee patients

Location	Variable	*n*	Missing
Hip	Randomisation		
	Standard care	159	
	Intervention	163	0
	Sex		
	Male	134	
	Female	188	0
	Employment		
	Unemployed	195	
	Employed	103	24
	Retired		
	Not retired	133	
	Retired	189	0
	Cohabitation		
	Alone	74	
	Not alone	232	16
	Education		
	≤ 16 years	208	
	> 16 years	99	15
Knee	Randomisation		
	Standard care	159	
	Intervention	157	0
	Sex		
	Male	150	
	Female	166	0
	Employment		
	Unemployed	220	
	Employed	66	30
	Retired		
	Not retired	98	
	Retired	218	0
	Cohabitation		
	Alone	84	
	Not alone	213	19
	Education		
	≤ 16 years	224	
	> 16 years	69	23

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 69 Pre- and postoperative WOMAC pain scores, and acute postoperative VAS pain on movement and at rest

Location	Time	Measure	*n*	*n* (complete)	% item response in missing	Mean	SD	25th percentile	Median	75th percentile
Hip	Pre operation	WOMAC	321	320	80	44.04	20.41	30.0	45.0	55.0
	Acute									
	Move (VAS)	Day 1	301	271	58	5.76	2.33	4.0	5.7	7.7
		Day 2	295	260	57	4.58	2.53	2.3	4.5	6.7
		Day 3	272	227	56	3.89	2.39	2.0	3.3	6.0
	Rest (VAS)	Day 1	301	283	54	3.14	1.99	1.7	2.7	4.3
		Day 2	296	264	57	2.40	1.85	1.0	1.8	3.4
		Day 3	272	229	56	2.06	1.71	1.0	1.3	2.7
	Post operation	WOMAC	283	279	80	89.04	16.85	85.0	95.0	100.0
Knee	Pre operation	WOMAC	316	316	0	43.15	17.74	30.0	45.0	55.0
	Acute									
	Move (VAS)	Day 1	279	228	58	6.17	2.41	4.7	6.3	8.0
		Day 2	284	259	56	5.87	2.39	4.2	6.0	7.7
		Day 3	260	217	59	4.70	2.48	2.7	5.0	6.3
	Rest (VAS)	Day 1	280	239	54	4.34	2.29	2.7	4.2	6.0
		Day 2	284	264	55	3.97	2.36	2.0	4.0	5.7
		Day 3	260	223	57	3.04	2.12	1.0	2.7	4.3
	Post operation	WOMAC	277	268	78	79.75	21.23	65.0	85.0	100.0

TABLE 70 Regression (OLS and SEM) analysis of pre-operative and acute pain assessments and postoperative pain in hip and knee patients

Region	Outcome	Model	Exposure	Adjusted	Beta	SE	95% CI	*p*-value
OLS regression								
Hip	Postoperative WOMAC	1	Pre-operative WOMAC	Confounders	0.105	0.05	0.006 to 0.204	0.0385
		2	Acute move	Confounders	–1.866	0.57	–2.986 to –0.746	0.0012
		3	Acute rest	Confounders	–2.200	0.62	–3.414 to –0.986	0.0004
		4	Pre-operative WOMAC	Confounders + acute move	0.095	0.05	–0.003 to 0.192	0.0575
		5	Pre-operative WOMAC	Confounders + acute rest	0.092	0.05	–0.005 to 0.190	0.0631
		6	Pre-operative WOMAC	Confounders + acute move + acute rest	0.092	0.05	–0.005 to 0.190	0.0636
Knee	Postoperative WOMAC	1	Pre-operative WOMAC	Confounders	0.434	0.07	0.295 to 0.574	0.0000
		2	Acute move	Confounders	–1.996	0.65	–3.283 to –0.708	0.0025
		3	Acute rest	Confounders	–2.234	0.62	–3.452 to –1.016	0.0004
		4	Pre-operative WOMAC	Confounders + acute move	0.402	0.07	0.258 to 0.546	0.0000
		5	Pre-operative WOMAC	Confounders + acute rest	0.389	0.07	0.245 to 0.534	0.0000
		6	Pre-operative WOMAC	Confounders + acute move + acute rest	0.389	0.07	0.244 to 0.533	0.0000
SEM (MLMV)								
Hip	1LV postoperative WOMAC	1	Pre-operative WOMAC	Confounders	0.169	0.07	0.038 to 0.300	0.0112
		2	Acute move	Confounders	0.074	0.03	0.008 to 0.140	0.0289
		3	Acute rest	Confounders	0.176	0.05	0.087 to 0.266	0.0001
		4	Pre-operative WOMAC	Confounders + acute move	0.158	0.07	0.028 to 0.289	0.0174
		5	Pre-operative WOMAC	Confounders + acute rest	0.141	0.07	0.013 to 0.268	0.0311
		6	Pre-operative WOMAC	Confounders + acute move + acute rest	0.147	0.07	0.019 to 0.275	0.0247

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 70 Regression (OLS and SEM) analysis of pre-operative and acute pain assessments and postoperative pain in hip and knee patients (*continued*)

Region	Outcome	Model	Exposure	Adjusted	Beta	SE	95% CI	*p*-value
Knee	1LV postoperative WOMAC	1	Pre-operative WOMAC	Confounders	0.669	0.11	0.452 to 0.886	0.0000
		2	Acute move	Confounders	0.138	0.04	0.052 to 0.224	0.0016
		3	Acute rest	Confounders	0.218	0.06	0.104 to 0.331	0.0002
		4	Pre-operative WOMAC	Confounders + acute move	0.622	0.11	0.403 to 0.841	0.0000
		5	Pre-operative WOMAC	Confounders + acute rest	0.583	0.12	0.353 to 0.812	0.0000
		6	Pre-operative WOMAC	Confounders + acute move + acute rest	0.567	0.13	0.305 to 0.830	0.0000

1LV, one latent variable; MLMV, maximum likelihood with missing values; SE, standard error.

Notes

Confounding variables include trial randomisation, education, cohabitation, employment and sex. WOMAC pain scale in OLS regression-based analyses range from 0 to 100 (extreme pain/no pain). SEM analyses are based on a 1LV analyses of WOMAC pain items which range from 1 to 5 (extreme pain/no pain); SEM models are estimated using MLMV which assumes missing data are missing at random given other covariates.

In OLS analyses, acute pain on movement and acute pain at rest are based on a.m., noon and p.m. averages across the 3 days, and acute pain assessments range from 0 to 10.

In SEM analyses, acute pain on movement and pain on rest are modelled using a latent variable approach for which the three daily assessments (a.m., noon and p.m.) on days 1, 2 and 3 are used to model the acute pain on movement/rest latent variables. *p*-values in OLS regression models are based on student *t*-distribution and SEM *p*-values are based on *z*-distributions.

Mediation analysis

Single latent variable WOMAC

Using the WOMAC score as a single latent variable, the association between pre-operative pain, acute pain on movement/rest and chronic pain was investigated. *Figure 34a* and *b* illustrates the path models between latent variables for the THR and TKR patients, respectively. Arrows indicate the direction of effects. Coefficients are in the natural units of the measurement scales and *p*-values are based on *z*-distribution. Models are estimated using maximum likelihood allowing for missing values.

The WOMAC single latent variable models differ to those presented in *Table 70*, by allowing for pre-operative pain to influence acute pain on movement and acute pain at rest. In THR patients, the direct effect of pre-operative pain on chronic pain is nearly identical and only a minor increase in the standard error is observed. This model also highlights that the attenuation observed in model 6 compared with model 1 (see *Table 70*) is primarily as a result of the acute pain at rest pathway and not acute pain on movement.

The pattern of results in TKR patients is somewhat less clear. There is a strong association between pre-operative pain and both acute pain on movement and acute pain at rest. However, there is only a relatively weak effect of acute pain on movement and acute pain at rest on chronic pain.

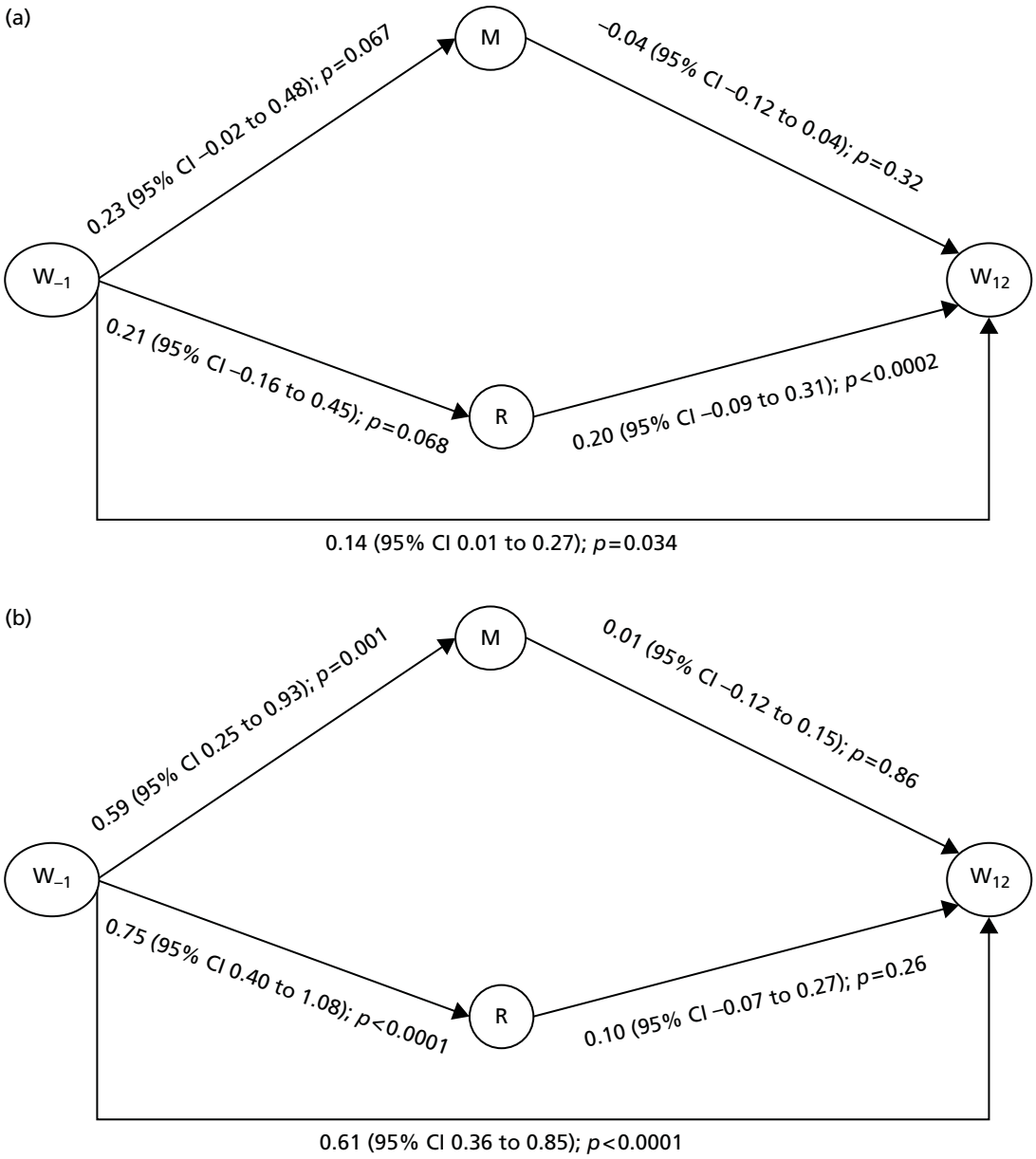


FIGURE 34 Structural equation model of the association between latent variables pre-operative WOMAC (W_{-1}), acute postoperative pain on movement (M), acute pain at rest (R) and postoperative WOMAC (W_{12}). (a) Hip patients ($n = 322$); and (b) knee patients ($n = 316$).

Two latent variable WOMAC

Using the WOMAC score as a two latent variable (rest/movement) pain model pre- and postoperatively, the direct and indirect effects of pre-operative pain (rest/movement) were investigated with acute pain on movement/acute pain at rest and chronic pain (rest/movement). *Figures 35* and *36* illustrate the path models between latent variables for the THR and TKR patients, respectively. Single-headed arrows indicate direction of effects, coefficients are in the natural units of the measurement scales, and *p*-values are based on z-distribution. Double-headed arrows indicate correlation coefficients. Models are estimated using maximum likelihood allowing for missing values.

In THR patients, the SEM approach clearly shows that the majority of the association previously seen in the single latent variable model between pre-operative and chronic pain is mediated directly via pre-operative pain at rest, with little or no effect of indirect pathways or directly via pre-operative pain on movement. However, an independent association of acute pain at rest is positively associated with chronic pain both on movement and at rest.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

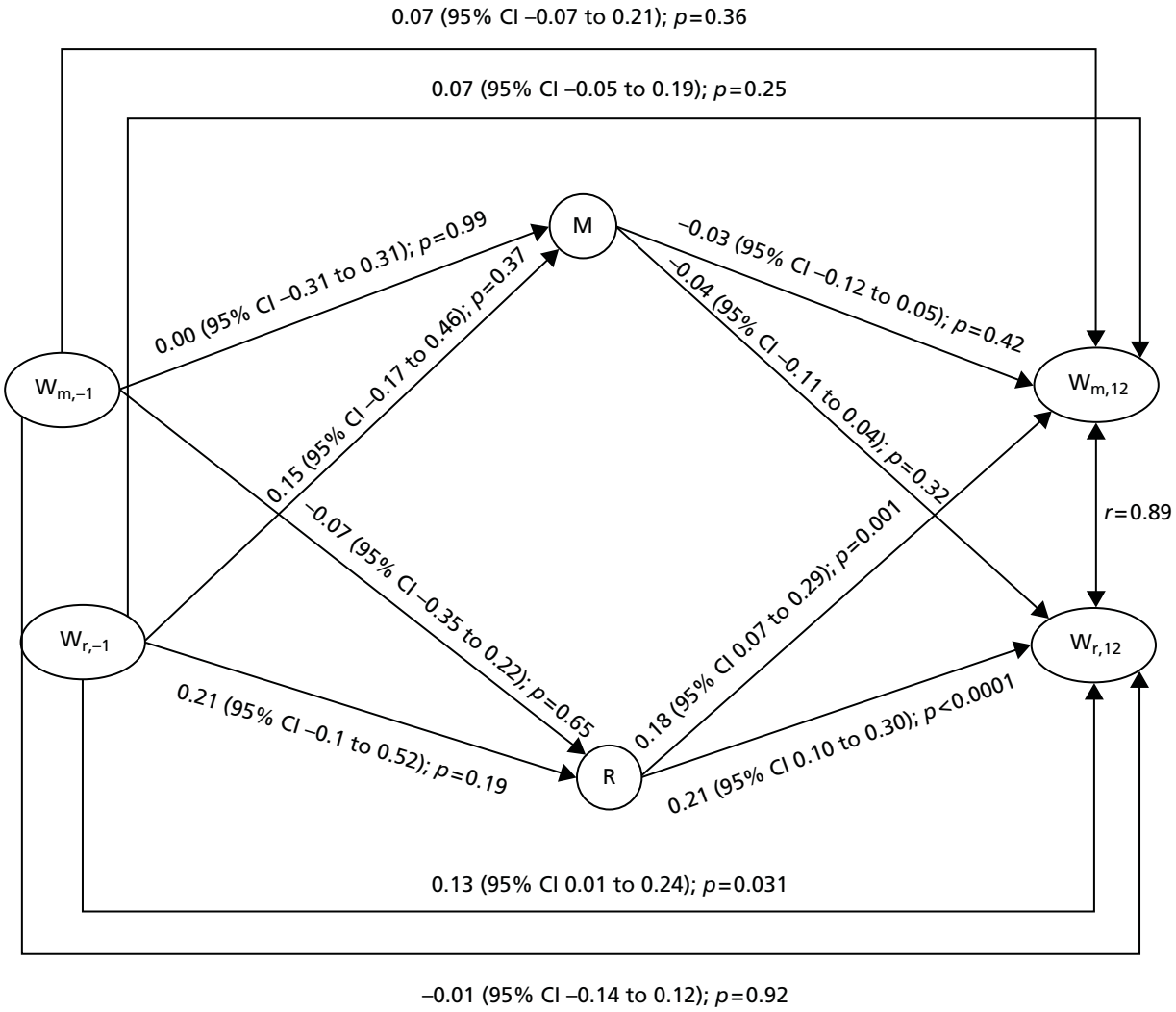


FIGURE 35 Structural equation model of the association between latent variables pre-operation WOMAC movement ($W_{m,-1}$), pre-operation WOMAC rest ($W_{r,-1}$), acute post-operation pain on movement (M), acute pain at rest (R), post-operation WOMAC movement ($W_{m,12}$) and post-operation WOMAC rest ($W_{r,12}$) in hip patients ($n = 322$).

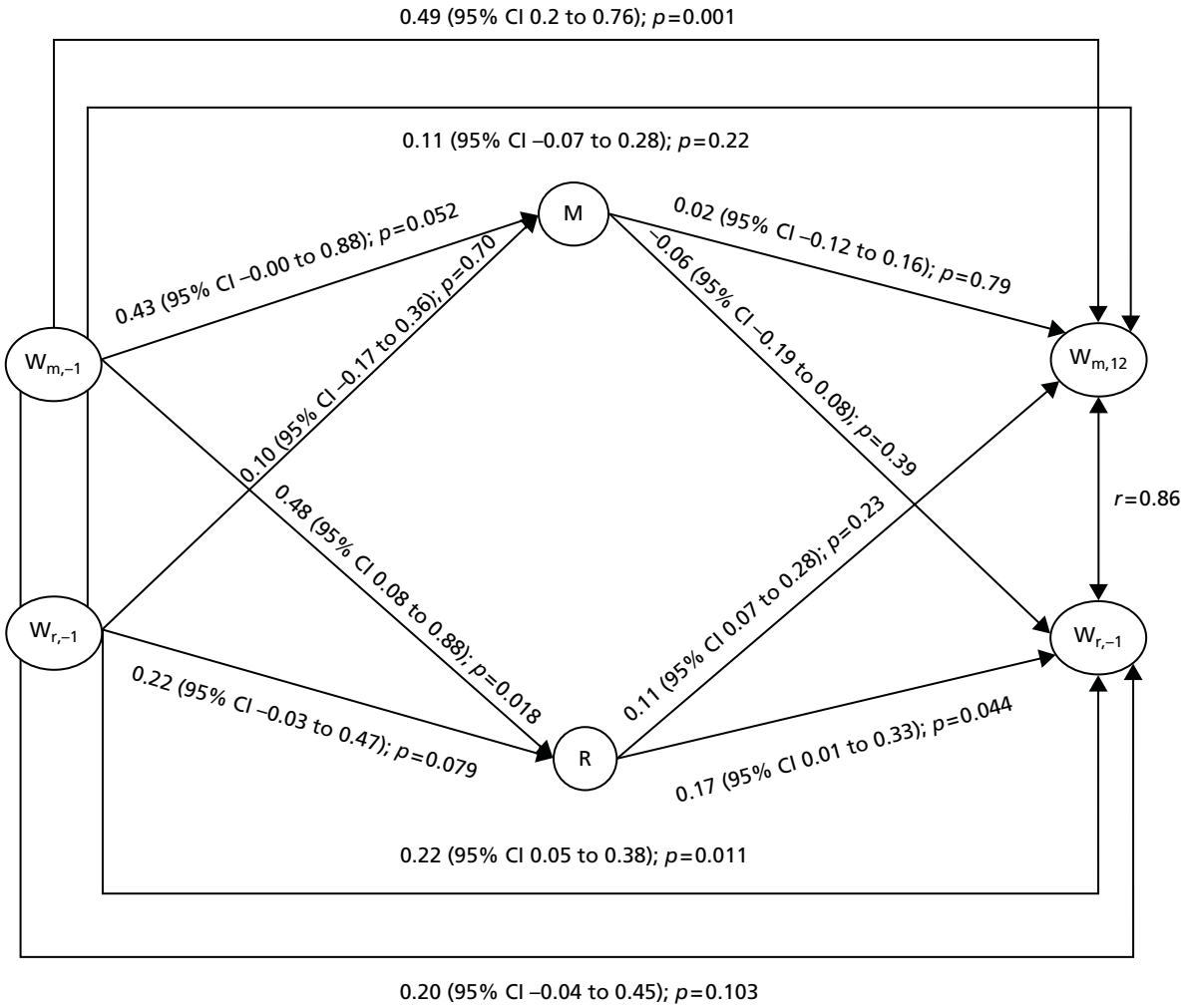


FIGURE 36 Structural equation model of the association between latent variables pre-operation WOMAC movement ($W_{m,-1}$), pre-operation WOMAC rest ($W_{r,-1}$), acute post-operation pain on movement (M), acute pain at rest (R), post-operation WOMAC movement ($W_{m,12}$) and post-operation WOMAC rest ($W_{r,12}$) in knee patients ($n = 316$).

In TKR patients, the results are quite different and the two latent variable model highlights that the strongest association is between pre-operative pain on movement and chronic pain on movement. Similar to the THR patients, pre-operative pain at rest is also associated with chronic pain at rest, and acute pain at rest is also associated with chronic pain at rest, but not chronic pain on movement.

In *Figure 35*, the strong association between pre-operative pain and acute pain on movement/rest is clarified, demonstrating that pre-operative pain on movement is the strongest predictor of chronic pain at rest or on movement.

There was no evidence of significant indirect effects in either THR or TKR patients despite significant intermediate paths.

Discussion

Using a traditional OLS regression approach and a SEM approach, we have demonstrated that the associations between pain over time are different in THR and TKR patients, which has clinical implications for the treatment of painful hip and knee osteoarthritis. Furthermore, we have explored the unique constructs of pain on movement and pain at rest to gain further insights and further understand pain within the context of orthopaedic surgery.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Our study has highlighted the complex and unique relationships between pre-operative, acute postoperative and chronic post-surgical pain in patients undergoing THR and TKR. The different contributions of pain at rest and pain on movement were stark; chronic pain after THR was driven predominantly by pain on rest and chronic pain after TKR was driven predominantly by pain on movement. These findings allude to different patterns of pain mechanisms within hip and knee osteoarthritis and highlight the importance of future work to identify the sources and potential treatment options for these different pain mechanisms.

Pain sensitivity

Background

Understanding pain within the context of joint replacement surgery is one of the core themes of the RESTORE programme. In the previous analyses, we explored the associations between pre-operative, acute postoperative and chronic post-surgical pain after THR and TKR. In the analyses presented in this section, we are interested in further understanding why people develop chronic pain after joint replacement by exploring whether or not pre-operative pain sensitivity was a risk factor for developing this condition.

Previous research has been undertaken to identify risk factors for the development of chronic pain after joint replacement. However, this work has highlighted that very little of the variation in pain severity after joint replacement can be explained by pre-operative risk factors such age, sex, depression, joint pain and BMI.[52] This highlights the need to explore other pre-operative factors that could be used to identify patients at a high risk of chronic post-surgical pain. There is some preliminary research which suggests that pre-operative central pain sensitisation is associated with chronic pain after joint replacement.[107,484] Central pain sensitisation involves amplification in neuronal activity that occurs at a generalised level, leading to increased sensitivity to nociceptive input and reduced pain thresholds at sites distant to the painful area. It is now well established in the research literature that some patients with painful osteoarthritis have evidence of central pain sensitisation.[485] It is possible that patients with central pain sensitisation may be at a higher risk of experiencing chronic post-surgical pain after joint replacement because removal of the peripheral pain source may not reverse augmented central pain processing changes. Further research is needed to explore whether or not pre-operative central pain sensitisation, assessed using QST, contributes to the development of chronic pain after joint replacement.

The aim of these analyses was to determine if pre-operative PPTs measured at a pain-free body site are predictive of chronic post-surgical pain at 12 months after primary THR and TKR, independent of pre-operative pain.

Methods

Exposure

Quantitative sensory testing is a non-invasive method that measures participants' responses to external stimuli of controlled intensity. Pre-operative PPTs were assessed at the volar forearm using a digital algometer (Somedic, Hörby, Sweden) with a 1-cm probe. The probe was held perpendicular to the skin and force applied at a constant rate of 10 kPa per second. The patient was instructed by the research nurse to say 'stop' when the sensation of pressure became the very first sensation of pain. Pressure algometry was repeated three times and between each reading the position of the algometer on the skin was altered very slightly to avoid sensitisation of the test area. The primary exposure is a standardised average of the three PPT measurements.

Outcome

The primary outcome for this analysis was the WOMAC pain score at 12 months after surgery. Total WOMAC pain scores were calculated as an average of all five items. As our previous analyses demonstrated the importance of distinguishing between movement pain and rest pain, we conducted further analysis with these subcomponents of the WOMAC pain score. Movement pain was calculated as an average of items 1, 2 and 4 and rest pain was calculated as an average of items 3 and 5.

Confounding variables

This analysis was adjusted for trial randomisation, age at recruitment, sex, cohabitation (living alone), employment status, educational attainment (after 16 years of age), height and weight.

Statistical methods

Descriptive statistics

Population characteristics and outcome measures are reported as means, SDs, interquartile cut-off points for continuous measures and as frequencies for categorical variables. In addition, the SD of the individual three PPTs was also calculated and summarised to indicate the variability of the QST measurements.

Cross-sectional/prospective analysis

Simple linear regression was used to investigate the association between average pre-operative pain (cross-sectional analysis) and postoperative pain (prospective analysis) and standardised PPTs. Three adjusted models were fitted: (1) minimally adjusted for sex and randomisation, (2) more fully adjusted, that is, model 1 and age, height, weight, cohabitation, employment and education, and (3) baseline adjusted, that is, model 2 and pre-operative pain score. The analyses were repeated using the average of all five WOMAC pain items, WOMAC items associated with movement pain and WOMAC items associated with rest pain. Results are interpreted per SD increase in PPT and its association with 1-unit change in pain response on the WOMAC pain scale either pre-operatively or postoperatively while holding all other factors constant.

Longitudinal analysis

Using a multilevel model, a longitudinal analysis of pain was assessed pre-operatively and at 12 months postoperatively. A multilevel approach allows simultaneous investigation of the effect of PPT on pre-operative pain and change in pain following surgery. This is subtly different from model 3 described in the prospective analysis, as the effect of PPT on pre-operative pain is not modelled. The effect of PPT on pre-operative pain is investigated by the inclusion of an interaction between the pre-operative measurement occasion and standardised PPT. Results are interpreted as per SD increase in PPT and its association with pre-operative pain. In addition, the effect of PPT on the change in pain response is also modelled by the inclusion of an interaction between standardised PPT and time. Results are interpreted as per SD increase in PPT and its association with change in reported pain from pre- to postoperative pain assessments while taking into account any effect of PPT on pre-operative pain.

To investigate the linearity of the PPT pain response on pre-operative pain and change in pain, two additional models were fitted. Using quintiles of pre-operative PPT, a longitudinal model was refitted with separate intercepts and a common slope. In addition, a fully stratified model of pain was fitted using five different intercepts and five different slopes. Models were compared using likelihood ratio tests.

All models are fitted using iterative generalised least squares in MLwiN (MLwiN, Centre for Multilevel Modelling, Bristol, UK) using the **runmlwin** command[486] in Stata.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Results

Descriptive data

A total of 254 patients undergoing THR and 239 patients undergoing TKR had complete covariate information and were included in these analyses. Baseline characteristics of participants are provided in *Table 71*. Patients undergoing THR had a mean age of 66.5 years (SD 10 years), which was slightly younger than the mean of 69.1 years for the TKR patients.

Pre-operative WOMAC pain scores were similar between patients undergoing THR and TKR, for both total pain scores and movement pain scores (*Table 72*). However, patients undergoing TKR had more severe pre-operative rest pain than those undergoing THR. WOMAC pain scores at 12 months after surgery were generally worse in patients undergoing TKR than in those undergoing THR, whether considering overall pain severity, movement pain or rest pain. The mean pre-operative PPT (kilopascals, kPa) for THR patients was 212 kPa (SD 98 kPa), which was similar to the mean PPT of 206 kPa (SD 103 kPa) for TKR patients.

TABLE 71 Demographic characteristics of APEX hip and knee patients with QST measures

Patient characteristic	Hips	Knees
Randomised group		
Standard care	130	124
Intervention	124	115
Sex		
Male	105	114
Female	149	125
Employment		
Unemployed	163	183
Employed	91	56
Retired		
Not retired	96	58
Retired	158	181
Cohabitation		
Alone	53	70
Not alone	201	169
Education		
≤ 16 years	169	179
> 16 years	85	60

TABLE 72 Descriptive statistics for average pre-operative and postoperative total WOMAC pain scores, movement pain scores (WOMAC pain items 1, 2 and 5) and rest pain scores (WOMAC pain items 3 and 4), and mean PPTs and the average SD across the three replicates

Joint replacement	Time	Measure	Mean	SD	25th percentile	Median	75th percentile
Hip	Pre operation	PPT mean	212.17	97.68	137.7	193.3	266.0
		PPT SD	38.42	31.86	16.7	29.2	53.4
		WOMAC	3.28	0.74	2.8	3.2	3.8
		WOMAC move	3.41	0.77	3.0	3.3	4.0
		WOMAC rest	3.08	0.90	2.5	3.0	3.5
	Post operation	WOMAC	1.43	0.67	1.0	1.2	1.6
		WOMAC move	1.45	0.71	1.0	1.0	1.7
		WOMAC rest	1.40	0.70	1.0	1.0	1.5
Knee	Pre operation	PPT mean	205.65	102.62	132.0	185.7	253.0
		PPT SD	33.90	27.47	16.2	27.4	41.5
		WOMAC	3.27	0.65	2.8	3.2	3.6
		WOMAC move	3.57	0.63	3.0	3.7	4.0
		WOMAC rest	2.83	0.92	2.5	3.0	3.5
	Post operation	WOMAC	1.74	0.83	1.0	1.4	2.2
		WOMAC move	1.85	0.90	1.0	1.7	2.3
		WOMAC rest	1.59	0.83	1.0	1.0	2.0

Pain sensitivity and pre-operative pain severity

Total hip replacement

In both the minimally and fully adjusted linear regression models, pre-operative PPT was strongly associated with pre-operative pain severity ($p = 0.002$ and $p = 0.001$, respectively; *Table 73*). The same pattern of association was found using a linear mixed model ($p = 0.001$; *Table 74*). When the pre-operative WOMAC pain score was broken down in the subconstructs of movement pain and rest pain, PPT was significantly associated with movement pain but rest pain was not (see *Tables 73* and *74*).

Total knee replacement

The patterns of associations were much weaker in TKR patients than in THR patients (see *Table 73*). In minimally adjusted models, there was no evidence of an association of PPT with total, movement or rest pain before surgery ($p > 0.1$). However, following more complete adjustment, the strength of the association increased to borderline significant for total pain severity ($p = 0.047$). Similarly, a weak association between PPT and pre-operative total pain severity ($p = 0.045$), but not with movement pain or rest pain, was found in the linear mixed model (see *Table 74*).

Pain sensitivity and 12-month postoperative pain severity

Total hip replacement

In the minimally and fully adjusted linear regression models, there was strong evidence of an association between pre-operative PPT and pain severity at 12 months following surgery ($p = 0.01$ and $p = 0.015$, respectively; see *Table 73*). These models showed that lower PPTs (higher pain sensitivity) were associated with more severe pain at 12 months following surgery. When the analyses were repeated with movement pain and rest pain, PPT was associated with movement pain but not rest pain at 12 months after surgery (see *Table 73*).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 73 Associations between average PPT and total WOMAC pain scores, movement pain scores and rest pain scores, adjusted for confounding variables including sex, living alone, working status, education, height, weight and age at recruitment in hip and knee patients

Model	Outcome	Model adjustments	Beta	SE	95% CI	*p*-value
Hip						
Cross-Sectional	Pre-operative WOMAC	1. Minimal	–0.144	0.05	–0.235 to –0.054	0.002
	Pre-operative WOMAC Move		–0.183	0.05	–0.278 to –0.088	0.000
	Pre-operative WOMAC Rest		–0.086	0.06	–0.198 to 0.026	0.131
Prospective	WOMAC 12		–0.110	0.04	–0.193 to –0.027	0.010
	WOMAC 12 move		–0.131	0.04	–0.219 to –0.043	0.004
	WOMAC 12 rest		–0.078	0.04	–0.165 to 0.009	0.079
Cross-Sectional	Pre-operative WOMAC	2. Adjusted	–0.148	0.05	–0.238 to –0.058	0.001
	Pre-operative WOMAC move		–0.187	0.05	–0.281 to –0.092	0.000
	Pre-operative WOMAC rest		–0.091	0.06	–0.203 to 0.021	0.111
Prospective	WOMAC 12		–0.104	0.04	–0.187 to –0.020	0.015
	WOMAC 12 move		–0.127	0.05	–0.216 to –0.038	0.005
	WOMAC 12 rest		–0.068	0.04	–0.155 to 0.019	0.126
	WOMAC 12	3. Adjusted + pre-operative pain	–0.091	0.04	–0.176 to –0.006	0.036
	WOMAC 12 move		–0.114	0.05	–0.205 to –0.022	0.015
	WOMAC 12 rest		–0.059	0.04	–0.147 to 0.028	0.181
Knee						
Cross-Sectional	Pre-operative WOMAC	1. Minimal	–0.068	0.04	–0.156 to 0.019	0.126
	Pre-operative WOMAC Move		–0.067	0.04	–0.152 to 0.019	0.125
	Pre-operative WOMAC Rest		–0.071	0.06	–0.193 to 0.052	0.258
Prospective	WOMAC 12		–0.063	0.06	–0.174 to 0.047	0.259
	WOMAC 12 move		–0.064	0.06	–0.184 to 0.056	0.292
	WOMAC 12 rest		–0.062	0.06	–0.173 to 0.049	0.271
Cross-Sectional	Pre-operative WOMAC	2. Adjusted	–0.088	0.04	–0.175 to –0.001	0.047
	Pre-operative WOMAC move		–0.080	0.04	–0.165 to 0.005	0.066
	Pre-operative WOMAC rest		–0.100	0.06	–0.222 to 0.022	0.106

TABLE 73 Associations between average PPT and total WOMAC pain scores, movement pain scores and rest pain scores, adjusted for confounding variables including sex, living alone, working status, education, height, weight and age at recruitment in hip and knee patients (*continued*)

Model	Outcome	Model adjustments	Beta	SE	95% CI	*p*-value
Prospective	WOMAC 12	–0.093	0.06		–0.204 to 0.017	0.097
	WOMAC 12 move	–0.097	0.06		–0.217 to 0.023	0.114
	WOMAC 12 rest	–0.088	0.06		–0.199 to 0.023	0.118
	WOMAC 12	3. Adjusted + pre-operative pain	–0.053	0.05	–0.157 to 0.051	0.313
	WOMAC 12 move		–0.062	0.06	–0.177 to 0.054	0.293
	WOMAC 12 rest		–0.059	0.05	–0.165 to 0.047	0.273

SE, standard error; WOMAC 12, WOMAC at 12 months.

Notes

The overall average WOMAC score is calculated using items 1 to 5, whereas average WOMAC movement pain is calculated using items 1, 2 and 4 and WOMAC rest pain is calculated using items 3 and 5.

PPT measurements are averaged across three replicates and standardised using a *z*-transformation. *p*-values and CIs are based on *t*-distributions.

Three different models adjustments are used: model 1 = sex, randomisation; model 2 = model 1 + age, height, weight, education, cohabitation, employment; and model 3 = model 2 + pre-operative pain score.

TABLE 74 Linear mixed model of WOMAC pain scores adjusted for confounding variables including sex, living alone, working status, education, height, weight, and age at recruitment in hip ($N = 254$) and knee ($N = 239$) patients

Outcome	Beta	SE	95% CI	*p*-value	Likelihood
Hip					
Pre-operative WOMAC pain	–0.157	0.05	–0.250 to –0.065	0.001	–507.2
Change WOMAC pain	0.047	0.06	–0.071 to 0.164	0.44	
Pre-operative WOMAC movement pain	–0.196	0.05	–0.293 to –0.099	0.000	–536.9
Change WOMAC movement pain	0.057	0.06	–0.069 to 0.183	0.37	
Pre-operative WOMAC rest pain	–0.101	0.06	–0.215 to 0.013	0.083	–572.9
Change WOMAC rest pain	0.031	0.07	–0.103 to 0.164	0.65	
Knee					
Pre-operative WOMAC pain	–0.087	0.04	–0.173 to –0.002	0.045	–491.8
Change WOMAC pain	–0.013	0.05	–0.119 to 0.093	0.81	
Pre-operative WOMAC movement pain	–0.076	0.04	–0.160 to 0.008	0.075	–514.3
Change WOMAC movement pain	–0.036	0.06	–0.153 to 0.080	0.54	
Pre-operative WOMAC rest pain	–0.108	0.06	–0.226 to 0.010	0.074	–577.2
Change WOMAC rest pain	0.022	0.06	–0.104 to 0.148	0.74	

Notes

Parameter estimates show the association between standardised pre-operative PPT and pre-operative pain score and the interaction between change in WOMAC pain score and its interaction with standardised pre-operative PPT. *p*-values and CIs are based on *z*-distributions. All models were adjusted for sex, age, height, weight, randomisation, cohabitation, employment and education.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Total knee replacement

There was no evidence of an association between pre-operative PPT and pain severity at 12 months after surgery in any of the linear regression models (see *Table 73*). Similarly, further analysis found that PPT was not associated with rest pain or movement pain at 12 months post operation (see *Table 73*).

Pain sensitivity and change in pain severity

Total hip replacement

After adjusting for pre-operative pain severity, the associations in the linear regression models between PPT and 12-month pain severity were mildly attenuated; however, the association persisted ($p = 0.036$). Analysis was then undertaken to explore the association between pre-operative PPT and change in WOMAC pain scores from before surgery to 12 months after surgery (see *Table 74*). There was no evidence of an association between PPT and change in pain scores ($p = 0.44$). Similarly, no association was found between PPT and change in movement pain ($p = 0.37$) or rest pain ($p = 0.65$). Further analyses using PPT quintiles to explore the relationship between pre-operative PPT and change in pain scores showed similar results (data not shown).

Total knee replacement

There was no evidence of any association between PPT and change in pain score from pre-operative to 12 months after TKR surgery ($p = 0.81$; see *Table 74*). This finding was the same when pain severity was analysed as change in movement pain ($p = 0.54$) and rest pain ($p = 0.74$). Further analyses using PPT quintiles to explore the relationship between pre-operative PPT and change in pain scores showed similar results (data not shown).

Discussion

Using data from the APEX cohort study, we found a relationship between measures of before surgery central pain sensitisation and pre-operative pain severity in a large sample of patients with advanced hip and knee osteoarthritis. Our longitudinal study design also allowed us to demonstrate that there is a strong association between pre-operative PPTs and pain severity at 12 months after THR, but not after TKR. Uniquely, we have shown there is no evidence of effect modification of PPT on the efficacy of surgery in patients undergoing THR or TKR. This suggests that pre-operative pain sensitivity, assessed through measurement of forearm PPTs, does not influence the amount of pain relief that patients gain from joint replacement.

Chapter 8 Systematic review and meta-analysis of exercise and education interventions before total hip and knee replacement

Abstract

Background

We aimed to evaluate the clinical effectiveness of exercise and education in patients waiting for total hip or knee replacement.

Methods

We searched MEDLINE, EMBASE, CINAHL, PsycINFO, Cochrane and Web of Science databases from inception to March 2014. Searches covered hip and knee replacement, randomised trials and pre-surgery. Interventions targeted optimisation of pre-surgical health, preparation for in-hospital recovery and long-term health. Outcomes extracted in duplicate were combined in meta-analyses with additional data provided by authors. Study quality was assessed.

Results

Interventions targeting optimisation of pre-surgical health ($n = 36$) showed benefit compared with controls in physical function (SMD 0.28, 95% CI 0.16 to 0.40); pain (SMD 0.21, 95% CI 0.10 to 0.33); and anxiety (SMD 0.38, 95% CI 0.11 to 0.65). Benefit was mainly limited to THR and effect sizes were largely unaffected by study quality or exercise/education content.

In studies targeting in-hospital recovery ($n = 27$), post-surgical anxiety was lower in intervention patients (SMD 0.38, 95% CI 0.13 to 0.63) who also mobilised earlier.

Interventions targeting long-term outcomes ($n = 18$) showed no benefit.

Conclusions

Exercise and education before total hip and knee replacement can improve patients' pre-surgical health and early recovery. Further research is required for knee replacement, intervention content and in relation to long-term outcomes.

Background

Previous systematic reviews of interventions before surgery have focused on the effectiveness of education[83] and physiotherapy.[82] In this section we update these with a series of more recent reviews of RCTs using systematic review methods. Acknowledging the overarching aims of exercise and education before hip and knee replacement, we classified studies according to their primary objectives. Thus, interventions are targeting making improvements to one or more of pre-surgical physical and psychological health, preparedness for recovery in hospital, and long-term post-surgical outcomes.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Methods

General methods	As described in *Chapter 2*, *Systematic review methods*
Databases and dates	MEDLINE, EMBASE, CINAHL, PsycINFO and The Cochrane Library from inception to 17 October 2013. Citations of key articles in ISI Web of Science and reference lists. Previous systematic reviews and meta-analyses were checked
Search strategy	Hip or knee replacement/RCT/pre-surgery. MEDLINE search strategy based on terms in *Appendix 3*
Study design	RCTs with individual or cluster randomisation. Quasi-randomised designs (e.g. alternate allocation)
Patients	Adults waiting for total hip or knee replacement
Intervention	Non-pharmacological pre-surgical intervention with the aim of improving outcomes before or after joint replacement. Interventions between being placed on the waiting list and surgery: • optimising pre-surgical health • preparation for recovery in hospital • improving long-term outcomes • not electrical stimulation, acupuncture, or smoking cessation
Controls	Usual care or minimal intervention
Follow-up	≥ 3 months
Data extraction	Country, baseline dates, participants (indication, age, sex), inclusion and exclusion criteria, intervention and control group content, setting, timing, duration and intensity, follow-up time, losses to follow-up and reasons
Outcomes	Patient-reported physical function, pain and anxiety measured before surgery Patient-reported anxiety and pain, mobilisation measured in hospital or < 1 month after surgery, and length of hospital stay Patient-reported physical function and pain from 3 months after surgery (longest follow-up reported unless large loss to follow-up)
Quality assessment	Good, reasonable (e.g. non-blind follow-up with self-complete questionnaires), or possible bias (unequal or major loss to follow-up, or important baseline differences)

Studies were classified into groups A, B and C independently by two reviewers with final decisions on classifications decided by consensus with input from other programme contributors.

Results

Review progress is summarised as a flow diagram in *Figure 37*. Searches identified 5073 articles. After screening and detailed evaluation, 48 articles describing 52 interventions met the inclusion criteria and study characteristics are summarised in *Table 75*. Studies reported interventions in patients before hip ($n = 22$),[487–508] knee ($n = 21$),[500,503,509–525] or either hip or knee replacement ($n = 9$).[526–534] Interventions focused on optimising pre-surgical health ($n = 36$), preparation for recovery in hospital ($n = 27$) and improving long-term outcomes ($n = 18$). Potential sources of bias are summarised in *Appendix 8*. Results of meta-analyses are summarised in *Table 76*.

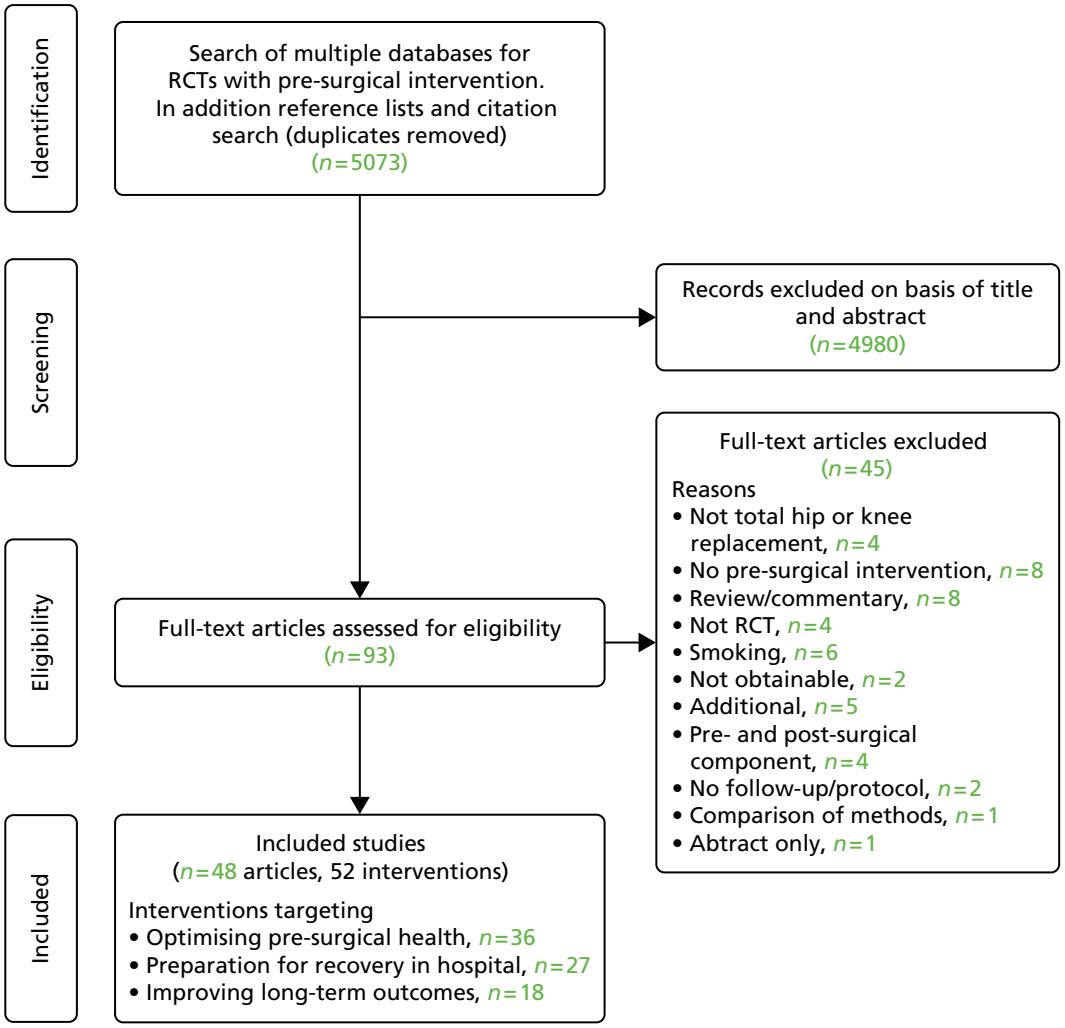


FIGURE 37 Systematic review and meta-analysis of exercise and education interventions before total hip and knee replacement: flow diagram.

Optimising pre-surgical health

Of the 36 interventions (32 articles) targeting optimisation of pre-surgical health, 14 interventions were in patients waiting for THR,[487–489,493–497,500–504,507] 17 in patients waiting for TKR,[500,503,509–515,517,519–521,523–525] and five in total hip and knee patients together.[526–529,534]

Eighteen interventions were specifically exercise based,[488,494,497,502,503,509,511–515,519,520,523–525] nine were education based,[52,489,495,500,501,526,527,529] while nine were multifactorial with exercise and education components and, in some cases, an occupational therapy base.[487,493,496,504,507,510,517,521,528]

Effect on pre-surgical physical function

Physical function before surgery was measured after 21 interventions using WOMAC (physical function or total), SF-36 physical function, HHS, HOOS, HSS, Arthritis Impact Measure Score 2 (AIMS2), AKSS or locally devised scores.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 75 Systematic review and meta-analysis of exercise and education interventions before total hip and knee replacement: included studies

Publication; location; date of study; focus of intervention (A = optimising health, B = hospital preparation, C = long term)	Hip or knee; indication; number randomised (intervention : control); mean age (years) (% female)	Primary focus of intervention; study setting; timing, duration and intensity; control group care	Follow-up interval; outcomes; losses to follow-up (intervention : control)
Aoki and colleagues 2009;[509] Japan; 2004–5; A	Knee; severe knee osteoarthritis; $n = 36$ (17 : 19); 73.4 years (100%)	Exercise (stretching); home; from registration for surgery until admission; control: no intervention	After admission to hospital; VAS pain; no losses to follow-up
Beaupre and colleagues 2004;[510] Canada; date not specified; A, B and C	Knee; non-inflammatory arthritis; $n = 131$ (65 : 66) – 16 patients (10 intervention, 6 control) did not have joint replacement: still eligible for review A. It is possible that the intervention was 'highly effective' in improving function and pain; 67 years (55%)	Multifactorial: exercise (gait re-education, functional, ROM, strengthening) and education; community physical therapy clinic group; three times per week for 4 weeks, 6 weeks before surgery; control: no intervention	Pre-operation, 3, 6 and 12 months after surgery; WOMAC, SF-36, LOS; 16 (10 : 6) patients cancelled surgery, six (4 : 2) patients lost to 12-month follow-up
Berge and colleagues 2004;[487] UK; date not specified; A and C	Hip; osteoarthritis; $n = 40$ (19 : 21) – 4 intervention patients dropped out before programme; 71.3 years (67.5%)	Multifactorial: exercise (strengthening and stretching) and education with relaxation pain management programme; outpatient group; once or twice a week for 6 weeks, ≥ 6 months pre-surgery; control: no intervention	Follow-up 3 months after programme and minimum 1 year; NRS pain, AIMS; 3 (0 : 3) patients lost to first follow-up (surgery early). Overall 7 (1 : 6) lost to 1-year follow-up
Bitterli and colleagues 2009;[488] Switzerland 2004–7; A and C	Hip; unilateral osteoarthritis or avascular necrosis; $n = 80$ (41 : 39); 66.8 years (38.8%)	Exercise (strengthening and balance); home; two times per day, 10 repetitions for 2–6 weeks; control: no intervention	Follow-up at 10 days, 4 months and 12 months after surgery; SF-36, WOMAC; (5 : 2) lost to pre-surgical follow-up; 18 (9 : 9) lost to 12-month follow-up
Bondy and colleagues 1999;[526] USA; date not specified; A and B	Hip and knee; not specified; $n = (65 : 69)$ – 200 patients randomised but baseline and pre-surgery questionnaires completed by 134 patients; 65.2 years (59.5%)	Education; home; < 3 weeks before surgery; control: pre-operative anaesthetist visit	No follow-up after surgery; STAI anxiety; of 200 randomised, 148 returned questionnaires of which 134 (67%) were completed sufficiently
Börjesson and colleagues 1996;[511] Sweden; date not specified; A	Knee; unilateral medial osteoarthrosis I-III; $n = 68$ (34 : 34); 64 (50%)	Exercise (strengthening, ROM); hospital outpatient group; three times per week lasting 40 minutes for 5 weeks; control: no intervention	After 3 months (as close to end of intervention as possible), no follow-up after surgery; pain on walking using Borg scale; 0 losses to follow-up
Brown and colleagues 2012;[512] USA; date not specified; A and C	Knee; osteoarthritis; $n = 32$ (17 : 15); age and sex not described	Exercise; home and physical therapy clinic; partially supervised resistance and flexibility exercises and step training, training booklet; twice a week at home and once a week at physical therapy clinic for 50 minutes from 8 weeks before surgery; usual pre-operative care	3 months; SF-36 (physical functioning and bodily pain); 14 (6 : 8) lost to follow-up

TABLE 75 Systematic review and meta-analysis of exercise and education interventions before total hip and knee replacement: included studies (*continued*)

Publication; location; date of study; focus of intervention (A = optimising health, B = hospital preparation, C = long term)	Hip or knee; indication; number randomised (intervention : control); mean age (years) (% female)	Primary focus of intervention; study setting; timing, duration and intensity; control group care	Follow-up interval; outcomes; losses to follow-up (intervention : control)
Butler and colleagues 1996;[489] Canada; 1993–4; A and B	Hip; not specified; $n = 80$ (32 : 48); 62.6 years (51.3%)	Education; home; 4–6 weeks before surgery; control: mailed preadmission package only	To discharge; anxiety STAI, LOS; one patient died and no follow-up data from eight patients
[a]Clode-Baker and colleagues 1997;[490] UK; date not specified; B	Hip (76% primary); not specified; $n = 78$ (41 : 37) – 91 randomised, 13 operations cancelled or postponed; mean age not specified (66.7%)	Education; home; approximately 4 weeks before surgery; control patients seen routinely by nursing staff on admission	Day before surgery, days 1–7 after surgery and 8 days after discharge; NHP, Hamilton Anxiety and Depression, days to mobilisation, LOS, pain (descriptive ordinal scale); four (1 : 3) lost to postoperative anxiety follow-up
Cooil and Bithell 1997;[491] UK; date not specified; B	Hip; not specified; $n = 42$ (21 : 21); 69 years (71.4%)	Education; hospital during admission, individual; day before surgery; control: information sheet but no further contact	Days 1 and 2 after operation; no outcomes relevant to review; no losses to follow-up reported
Crotty and colleagues 2009;[527] Australia; 2005–6; A	Hip or knee; osteoarthritis; $n = 152$ (77 : 75); 67.5 years (60.5%)	Education; home, outpatient and community; individual and group; 5 weeks' duration; control: no intervention	6 months after intervention (11 patients in each group followed up mean 106 days after surgery); WOMAC; no losses to follow-up reported
[a]Crowe and Henderson 2003;[528] Canada; date not specified; A and B	Hip or knee; osteoarthritis, rheumatoid arthritis; $n = 133$ (65 : 68); 70 years (80%)	Multifactorial: exercise (strengthening and endurance), education and occupational therapy; hospital outpatient, individual and group; one session soon after randomisation with additional physiotherapy and attendance at day care hospital; control: single standard pre-operative clinic visit	To hospital discharge; LOS, anxiety STAI, days to mobilisation; one patient did not receive surgery
[a]Cuñádo Barrio and colleagues 1999;[529] Spain; 1996–7; A and B	Hip or knee; not specified; $n = 84$ (42 : 42); 65 years (66.7%)	Education; hospital, individual; 2 days before the operation lasting 20 minutes; control: standard pre-operative programme	Pre-operative and 4 to 5 days post operation (as appropriate); anxiety STAI, mobilisation, LOS; eight (1 : 7) lost to follow-up
Daltroy and colleagues 1998;[530] USA; 1985–7; B	Hip or knee; rheumatoid or osteoarthritis; $n = 222$, 2×2 factorial (58 : 58 : 52 : 54); 64 years (66%)	Education; hospital, individual; day before surgery; control: usual pre-operative preparation	Day 4 post operation; anxiety STAI, pain (Likert scale), LOS, no data were suitable for meta-analysis; data not available for six patients

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 75 Systematic review and meta-analysis of exercise and education interventions before total hip and knee replacement: included studies (*continued*)

Publication; location; date of study; focus of intervention (A = optimising health, B = hospital preparation, C = long term)	Hip or knee; indication; number randomised (intervention : control); mean age (years) (% female)	Primary focus of intervention; study setting; timing, duration and intensity; control group care	Follow-up interval; outcomes; losses to follow-up (intervention : control)
D'Lima and colleagues 1996 (cardiovascular);[513] USA; date not specified; A and C	Knee; rheumatoid or osteoarthritis; $n = 20$ (10 : 10); 70.6 years (35%)	Exercise (stretching, strengthening, cardiovascular conditioning); hospital, individualised; 45-minute sessions, three times a week for 18 weeks commencing 6 weeks before surgery; control: one meeting with physical therapist	Follow-up at 6 weeks and 1 week preoperation, and 3, 12, 24 and 48 weeks postoperatively; HSS; no losses to follow-up reported
D'Lima and colleagues 1996 (physical therapy);[513] USA; date not specified; A and C	Knee; rheumatoid or osteoarthritis; $n = 20$ (10 : 10); 69.0 years (60%)	Exercise (strengthening, ROM); hospital, one-on-one programme; 45-minute sessions, three times a week for 18 weeks commencing 6 weeks before surgery; controls: one meeting with physical therapist	Follow-up at 6 weeks and 1 week preoperation, and 3, 12, 24 and 48 weeks postoperatively; HSS; no losses to follow-up reported
[a]Doering and colleagues 2000;[492] Austria; date not specified; B	Hip; osteoarthritis; $n = 100$ (46 : 54); 59.6 years (38%)	Education; hospital, individual; day before surgery; control: no intervention	1, 2 and 3 days post operation; STAI anxiety, VAS pain, LOS
Evgeniadis and colleagues 2008;[514] Greece; 2006; A and C	Knee; idiopathic osteoarthritis; $n = 48$ (24 : 24); 68.3 years (76.3%)	Exercise (strengthening); home; 1 month before surgery for 3 weeks, three alternative days a week; controls: standard pre- and postoperative care	Day before surgery and 2, 6, 10 and 14 weeks after surgery; SF-36, ILAS; five (3 : 2) lost to follow-up
Ferrara and colleagues 2008;[493] Italy; 2006–7; A and C	Hip; end-stage osteoarthritis; $n = 23$ (11 : 12); 63.4 years (60.9%)	Multifactorial: exercise (strengthening, stretching, cardiovascular) and occupational therapy; hospital, individual and group; 1 month prior to surgery, 60 minutes per day for 5 days per week; controls: no intervention	Day before surgery and 15 days, 4 weeks and 3 months after surgery; SF-36, WOMAC; two (0 : 2) patients lost to 3-month follow-up
Gilbey and colleagues 2003;[494] Australia, 1997–9; A (C not included as post-surgical intervention)	Hip; osteoarthritis, post-traumatic and inflammatory arthritis, osteonecrosis, Paget's disease; $n = 68$ (37 : 31) – a further eight patients withdrew before surgery; 65.2 years (61.8%)	Exercise (strengthening, ROM, gait re-education, hydrotherapy); clinic and home, group and individual; 8 weeks before surgery, two clinic- and two home-based sessions per week, clinic sessions lasted 1 hour; control group received in-hospital physical therapy	Week before surgery and 3, 12, and 24 weeks after surgery; WOMAC; two (2 : 0) chose to delay surgery

TABLE 75 Systematic review and meta-analysis of exercise and education interventions before total hip and knee replacement: included studies (*continued*)

Publication; location; date of study; focus of intervention (A = optimising health, B = hospital preparation, C = long term)	Hip or knee; indication; number randomised (intervention : control); mean age (years) (% female)	Primary focus of intervention; study setting; timing, duration and intensity; control group care	Follow-up interval; outcomes; losses to follow-up (intervention : control)
Giraudet-Le Quintrec and colleagues 2003;[495] France; 1997–9; A and B	Hip; osteoarthritis; $n = 100$ (48 : 52); 63.5 years (56%)	Education; teaching hospital, small group (three to six patients); 2–6 weeks before surgery, one class lasting half day; controls received verbal information and leaflet	Follow-up 1–7 days post surgery; VAS pain, STAI anxiety, days to standing, LOS; one (0 : 1) patient did not complete STAI after surgery
Gocen and colleagues 2004;[496] Turkey; date not specified; A, B and C	Hip; primary or secondary osteoarthritis; $n = 59$ (29 : 30); 51.3 years (35.6%)	Multifactorial: exercise (strengthening, stretching) and education; home and hospital; 8 weeks before surgery, three times per day; control: no intervention	Immediately pre-operative, at discharge, 3 months and 2 years; HHS, VAS pain, days to walking; one (1 : 0) not operated
Gstoettner and colleagues 2011;[515] Austria; date not specified; A and C	Knee; severe unilateral osteoarthritis; $n = 38$ (18 : 20); 69.8 years (79%)	Exercise (strengthening, proprioception, balance, functional); home and hospital; 6 weeks before surgery, taught once per week for 45 minutes, then at home; control treatment received no intervention	Intervention patients followed up 6 weeks before surgery for WOMAC, 6 weeks after surgery; WOMAC; three (3 : 0) lost to follow-up
Heikkinen and colleagues 2008;[516] Finland; 2005–6; B	Knee (study also included patients with shoulder arthroscopy); $n = 59$ (27 : 32) specifically knee; age and sex of knee patients not described	Education; home; website used on an average of 14 days before surgery (SD 19.1, range 1–121 days); control group received face-to-face education with nurse	2 weeks postoperatively; no outcomes relevant to review; three (1 : 2) lost to follow-up but some of these may be shoulder arthroscopy patients
Hoogeboom and colleagues 2010;[497] The Netherlands; 2007–8; A	Hip; end-stage osteoarthritis; $n = 21$ (10 : 11); 76 years (66.6%)	Exercise (strengthening, cardiovascular, function); outpatient and home, individual and group; 3–6 weeks before surgery, twice a week for 60 minutes; control group received usual pre- and postoperative care	Pre-operative and to discharge; HOOS; one (0 : 1) lost to follow-up
Huang and colleagues 2012;[517] Taiwan; 2008–10; A and B	Knee; advanced osteoarthritis; $n = 243$ (126;117); 70.2 years (71.6%)	Exercise (strengthening) and education; clinic and home, group and individual; 2–4 weeks before surgery, 40-minute meeting in clinic followed by home-based programme; control: no intervention	To discharge and complications; LOS, VAS pain; no losses to follow-up reported

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 75 Systematic review and meta-analysis of exercise and education interventions before total hip and knee replacement: included studies (*continued*)

Publication; location; date of study; focus of intervention (A = optimising health, B = hospital preparation, C = long term)	Hip or knee; indication; number randomised (intervention : control); mean age (years) (% female)	Primary focus of intervention; study setting; timing, duration and intensity; control group care	Follow-up interval; outcomes; losses to follow-up (intervention : control)
Johansson and colleagues 2007;[498] Finland; 2003–4; B	Hip; elective; *n* = 123 (62 : 61); 62.4 years (51.2%)	Education; hospital pre-operative clinic, individual; 2 weeks before surgery, for up to 1 hour; control group received written education materials only	To discharge; LOS; 17 (7 : 10) lost to follow-up
Lewis and colleagues 2002;[531] USA; date not specified; B	Hip or knee; not specified; *n* = 58 (29 : 29); 68.5 years (58.6%)	Education (interactive); pre-admission test centre, individual; controls were shown a non-interactive video	Days 1, 2 and 3 post operation; LOS; two (1 : 1) lost to follow-up
Lilja and colleagues 1998;[499] Sweden; date not specified; B	Hip; consecutive patients waiting for THR; *n* = 50 (22 : 28) – further five patients excluded after randomisation; median 65 years (34%)	Education; hospital; day before surgery, 30 minutes; control: no intervention	Days 1, 2 and 3 post operation; VAS pain; no losses to follow-up further than one refused to participate after randomisation and four (3 : 1) withdrawn for medical reasons
Liu and Lu 2004;[532] China; 2002; B	Hip and knee surgery (also arthroscopy); not specified but included tibia and fibula wounds and leg joint fusion; *n* = 74 years (39 : 35); 53.8 years (47.3%)	Education; location of intervention not specified, individual; time scale before surgery when education given not specified; traditional education	Time after post surgery not specified; LOS; no losses to follow-up reported
Mancuso and colleagues 2008 Hip;[500] USA; 2001–3; A	Hip; 94.5% osteoarthritis; *n* = 177 (90 : 87); 70.5 years (55.9%)	Education; hospital, group; one class with additional 15-minute module; control patients received standard pre-operative class	Mean 4 days after class, no further follow-up; no relevant outcome
Mancuso and colleagues 2008 Knee;[500] USA; 2001–3; A	Knee; 94.0% osteoarthritis; *n* = 143 (70 : 73); 71.5 years (57.3%)	Education; hospital, group; one class with additional 15-minute module; control patients received standard pre-operative class	Mean 4 days after class, no further follow-up; no relevant outcome
McDonald and colleagues 2001;[533] USA; 1998–9; B	Hip and knee; osteoarthritis, primary and revision; *n* = 40 randomised, data on 31 reported (13 : 18); 74 years (74.2%)	Education; urban medical centre or home, group or individual; one session at pre-operative joint replacement class; control patients received a slide show on pain management and use of pain intensity scale	Postoperative days 1 and 2; McGill Pain Questionnaire-short form (measures sensory and effective pain and pain intensity); nine (7 : 2) lost to follow-up as some patients unable to complete questionnaires
McDonald and Molony 2004 (communication);[518] USA; 2000–1; B	Knee; osteoarthritis; *n* = 26 (17 : 9); 71.8 years (63.4%)	Education; medical centres, group; one pre-operative class; comparison group received usual pre-operative class	Postoperative days 1 and 2, and 1 and 7 days post-hospital discharge by telephone; SF-MPQ affective pain, LOS; no losses to follow-up reported

TABLE 75 Systematic review and meta-analysis of exercise and education interventions before total hip and knee replacement: included studies (*continued*)

Publication; location; date of study; focus of intervention (A = optimising health, B = hospital preparation, C = long term)	Hip or knee; indication; number randomised (intervention : control); mean age (years) (% female)	Primary focus of intervention; study setting; timing, duration and intensity; control group care	Follow-up interval; outcomes; losses to follow-up (intervention : control)
McDonald and Molony 2004 (pain management);[518] USA; 2000–1; B	Knee; osteoarthritis; $n = 24$ (15 : 9); 71.8 years (63.4%);	Education; medical centres, group; 10-minute film at pre-operative class; comparison group received usual pre-operative class	Postoperative days 1 and 2, and 1 and 7 days post-hospital discharge by telephone, no longer-term follow-up; SF-MPQ affective pain, LOS; no losses to follow-up reported
McGregor and colleagues 2004;[501] UK; 1998–9; A, B and C	Hip; osteoarthritis; $n = 39$ (19 : 20); 71.9 years (42.9%)	Education; hospital and home, group; hip class 2–4 weeks before surgery; controls received standard care	3 months postoperatively; WOMAC, LOS; four (4 : 0) patients lost to follow-up
McKay and colleagues 2012;[519] Canada; 2010; A and C	Knee; osteoarthritis, primary; $n = 22$ (10 : 12); 61.9 years (59%)	Exercise (strengthening); research facility; 3 times a week for 6 weeks; control: non-specific upper-body strength training	Follow-up immediately before surgery and at 6 and 12 weeks after surgery; WOMAC; five (3 : 2) lost to 12-week follow-up
Mitchell and colleagues 2005;[520] UK; 1999–2000; A (not C as intervention patients received additional postoperative care)	Knee; osteoarthritis; $n = 114$ (57 : 57) – 160 randomised but 45 (23 : 22) withdrew; 70.3 years (57.9%)	Exercise (gait re-education, ROM) and occupational therapy; home; 8 weeks before surgery, minimum of three pre-operative visits with up to 6 postoperative visits; control group received outpatient physiotherapy	Follow-up 12 weeks; no outcome reported before additional post-surgery physiotherapy; one (0 : 1) died postoperatively
Nuñez and colleagues 2006;[521] Spain; 2001; A	Knee; osteoarthritis; $n = 100$ (51 : 49); 71.1 years (71%)	Multifactorial: exercise (strengthening, ROM, gait re-education, general) and education; hospital and home, groups of 12 patients, maximum; 3-month programme with 30-minute individual visits lasting in first week and at 3 months, and two group sessions of approximately 90 minutes in weeks 3 and 4; control group were seen individually twice by a physician	9-month follow-up (after intervention); WOMAC, SF-36, self-reported HRQoL, number of GP visits and costs; 20 (8 : 12) lost to follow-up
Oosting and colleagues 2012;[502] The Netherlands; date not specified; A and C	Hip; osteoarthritis, age > 65 years, frail; $n = 30$ (15 : 15); 78 years (80%)	Exercise (functional); outpatient and home; twice per week for 3–6 weeks and home four times per week; one physical therapist-led group session 3 weeks before surgery	2–4 days before admission and up to 6 weeks after surgery; HOOS; 0 (0 : 2) lost to follow-up at pre-surgery assessment

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 75 Systematic review and meta-analysis of exercise and education interventions before total hip and knee replacement: included studies (*continued*)

Publication; location; date of study; focus of intervention (A = optimising health, B = hospital preparation, C = long term)	Hip or knee; indication; number randomised (intervention : control); mean age (years) (% female)	Primary focus of intervention; study setting; timing, duration and intensity; control group care	Follow-up interval; outcomes; losses to follow-up (intervention : control)
Pellino and colleagues 1998;[534] USA; 1995–6; A (surgery delayed in control group)	Hip and knee; elective orthopaedic surgery; *n* = 74 (39 : 35), 83 eligible; 53.8 years (50%) included in analysis	Education; learning centre, group and individual; one class; controls received traditional teaching at the hospital clinic	Up to 1 month follow-up after surgery; ability to complete perioperative care; seven patients did not complete questionnaires and two had surgery cancelled
Rooks and colleagues 2006 Hip;[503] USA; 2001–3; A and C	Hip; osteoarthritis; *n* = 63 (32 : 31); 62 years (57.1%)	Exercise (strengthening, flexibility, cardiovascular, pool exercises); community fitness facility; three times per week for 6 weeks, 30–60 minutes; control: two education mailings and three telephone calls	Follow-up post intervention and at 8 and 26 weeks post surgery; WOMAC; 14 (7 : 7) lost to follow-up
Rooks and colleagues 2006 Knee;[503] USA; 2001–3; A and C	Knee; osteoarthritis; *n* = 45 (22 : 23); 67.0 years (53.3%)	Exercise (strengthening, flexibility, cardiovascular, pool exercises); community fitness facility; three times per week for 6 weeks, 30–60 minutes each, increasing intensity from 4 to 6 weeks; control: two education mailings and three telephone calls	Follow-up post intervention and at 8 and 26 weeks post surgery; WOMAC; 16 (8 : 8) lost to follow-up
Sandell and colleagues 2008;[504] UK; 2003; A and B	Hip; waiting time of 6 months or more; *n* = 89 (43 : 46); 68.2 years (65.1%)	Multifactorial: exercise (strengthening and gait), occupational therapy and pain management; outpatient clinic; 3–16 months before surgery; control: no intervention	Follow-up pre-surgery; AIMS2; 26 (10 : 16) lost to follow-up
Santavirta and colleagues 1994;[505] Finland; 1989; B	Hip; *n* = 60 (27 : 33) – 73 patients randomised; 58 years (63%)	Education; during hospital admission; 10- to 60-minute session after admission; all patients received an 18-page illustrated patient guide	During admission and 2–3 months postoperatively; no relevant outcome; 13 (7 : 6) had operation postponed or dropped out for other reasons
Sjoling and colleagues 2003;[522] Sweden; date not specified; B	Knee; osteoarthritis; *n* = 60 (30 : 30); 71 years (60%)	Education; hospital; day before surgery or 4 days pre-operatively; controls received standard information	7–8 days postoperatively; state and trait anxiety, Daily Pain Index based on multiple VAS pain scores, LOS; no losses to follow-up (some data missing at time points)
Swank and colleagues 2011;[523] USA; 2003–8; A	Knee; osteoarthritis and intractable pain; *n* = 71 (35 : 36); 62.8 years (65%)	Exercise (strengthening, stretching, walking, step training); hospital clinic and home, individual; commenced 4–8 weeks before surgery; control: no intervention	Week before surgery; VAS pain after functional tests; no losses to follow-up reported

TABLE 75 Systematic review and meta-analysis of exercise and education interventions before total hip and knee replacement: included studies (*continued*)

Publication; location; date of study; focus of intervention (A = optimising health, B = hospital preparation, C = long term)	Hip or knee; indication; number randomised (intervention : control); mean age (years) (% female)	Primary focus of intervention; study setting; timing, duration and intensity; control group care	Follow-up interval; outcomes; losses to follow-up (intervention : control)
Vukomanovic and colleagues 2008;[506] Serbia; 2005–6; B and C	Hip; osteoarthritis; $n = 45$ (23 : 22); 58.2 years (66.7%)	Multifactorial: exercise (functional) and education; home; one education appointment with physiatrist, two practical classes with physiotherapist; controls received no education or physical therapy	Pre-operative period, immediate postoperative period and 15-month follow-up; VAS pain, OHS, time to walking, LOS, VAS sense of uncertainty; four (2 : 2) lost to 15-month follow-up, nine (5 : 4) total lost to follow-up
Weidenhielm and colleagues 1993;[524] Sweden; date not specified; A and C	Knee (unicompartmental); osteoarthritis; $n = 40$ (20 : 20); 63.5 years (51.3%)	Exercise (strengthening); outpatient and home, group and individual; three times per week for 5 weeks; commenced 3 months before surgery; controls received no pre-operative therapy	Immediately before and 3 months after surgery; Pain (4 grade scale); one (1 : 0) had a heart attack and did not complete study
Wijgman and colleagues 1994;[507] The Netherlands; 1991–2; A and B	Hip; primary coxarthrosis; $n = 64$ years (31 : 33); 65 years (75% female)	Multifactorial: exercise (strengthening, gait) and education; group; single 30-minute session, 2 days to 1 month before surgery; controls received standard care	Day 1 after surgery to 14 months; VAS pain, LOS, time to standing; 1 (1 : 0) lost to follow-up with surgical complication
Williamson and colleagues 2007;[525] UK; 2004–6; A and C	Knee; osteoarthritis; $n = 121$ (60 : 61); 69.8 (52.9%)	Exercise (strengthening, balance); outpatient group; 1 hour once a week for 6 weeks; controls received an exercise and advice leaflet	7 and 12 weeks after start of intervention and 3 months postoperatively; OKS, WOMAC, VAS pain, HADS; 9 (7 : 2) at 7 weeks, 42 (23 : 19) at 3 months post surgery
Wong and Wong 1985;[508] Canada; 1982–3; B	Hip; elective; $n = 98$ (51 : 47); 66.7 years (68%)	Education; hospital; day of admission; controls received traditional pre-operative instruction	Six times daily for 4 days after surgery, no relevant outcomes; no losses to follow-up reported, three withdrawals with complications

AIMS, Arthritis Impact Measure Score; AIMS2, Arthritis Impact Measure Score 2; ILAS, Iowa Level of Assistance Scale; LOS, length of stay; NRS, numerical response scale; SF-MPQ, Short-form McGill Pain Questionnaire; STAI, State–Trait Anxiety Inventory.

a Additional information in McDonald and colleagues.[83]

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 76 Systematic review and meta-analysis of exercise and education interventions before total hip and knee replacement: meta-analysis

Subgroup	Number of interventions	Number of patients	Method	Effect size (95% CI)[a]	*p*-value	Heterogeneity I^2 (%)	Heterogeneity *p*-value
A. optimising pre-surgical health							
Physical function before surgery							
Overall	19	1026	SMD	0.28 (0.16 to 0.40)	< 0.00001	0	0.48
THR	8	343	SMD	0.40 (0.18 to 0.61)	0.0003	0	0.79
TKR	9	457	SMD	0.19 (–0.04 to 0.42)	0.10	24	0.23
Total hip or knee replacement	2	226	SMD	0.31 (0.05 to 0.58)	0.02	0	0.36
Education-based interventions	3	261	SMD	0.33 (0.09 to 0.58)	0.007	0	0.60
Exercise-based interventions	12	494	SMD	0.26 (0.08 to 0.44)	0.004	0	0.46
Multifactorial interventions	4	271	SMD	0.32 (–0.03 to 0.66)	0.07	46	0.13
Overall, higher-quality studies	10	610	SMD	0.21 (0.04 to 0.38)	0.02	8	0.37
THR, higher-quality studies	5	102	SMD	0.34 (0.06 to 0.62)	0.02	0	0.50
TKR, higher-quality studies	4	256	SMD	0.07 (–0.25 to 0.39)	0.65	35	0.20
THR: high physiotherapy frequency/duration	7	308	SMD	0.39 (0.16 to 0.62)	0.0008	0	0.69
TKR: high physiotherapy frequency/duration	9	457	SMD	0.19 (–0.04 to 0.42)	0.10	24	0.23
THR: strengthening	5	223	SMD	0.36 (0.09 to 0.62)	0.009	0	0.52
THR: cardiovascular exercise	3	93	SMD	0.48 (0.03 to 0.93)	0.04	11	0.32
TKR: strengthening	9	457	SMD	0.19 (–0.04 to 0.42)	0.10	24	0.23

Subgroup	Number of interventions	Number of patients	Method	Effect size (95% CI)[a]	*p*-value	Heterogeneity I^2 (%)	Heterogeneity *p*-value
Pain before surgery							
Overall	21	1375	SMD	0.21 (0.10 to 0.33)	0.0004	13	0.29
THR	9	420	SMD	0.47 (0.28 to 0.67)	< 0.00001	0	0.68
TKR	11	803	SMD	0.09 (–0.05 to 0.23)	0.22	0	0.74
Total hip or knee replacement	1	152		0.10 (–0.22 to 0.41)			
Overall, higher-quality studies	16	1141	SMD	0.24 (0.09 to 0.38)	0.001	25	0.17
THR, higher-quality studies	6	309	SMD	0.54 (0.31 to 0.77)	< 0.00001	0	0.77
TKR, higher-quality studies	9	680	SMD	0.10 (–0.05 to 0.25)	0.21	0	0.57
Education-based interventions	3	286	SMD	0.20 (–0.03 to 0.44)	0.09	0	0.38
Exercise-based interventions	13	597	SMD	0.23 (0.07 to 0.39)	0.006	0	0.47
Multifactorial interventions	5	492	SMD	0.27 (–0.04 to 0.58)	0.09	56	0.06
Anxiety before surgery							
Overall	8	660	SMD	0.38 (0.11 to 0.65)	0.006	65	0.005
B. preparation for recovery in hospital							
Anxiety shortly after surgery							
Overall	5	381	SMD	0.38 (0.13 to 0.63)	0.003	32	0.21
Pain shortly after surgery							
Overall	12	842	SMD	0.18 (–0.01 to 0.38)	0.06	40	0.07
THR	6	385	SMD	0.13 (–0.07 to 0.33)	0.21	0	0.56
TKR	4	352	SMD	0.14 (–0.29 to 0.57)	0.52	58	0.52
Total hip or knee replacement	2	105	SMD	0.53 (–0.11 to 1.17)	0.10	56	0.13

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 76 Systematic review and meta-analysis of exercise and education interventions before total hip and knee replacement: meta-analysis (*continued*)

Subgroup	Number of interventions	Number of patients	Method	Effect size (95% CI)[a]	*p*-value	Heterogeneity I^2 (%)	Heterogeneity *p*-value
Length of hospital stay							
Overall	10	997	MD	–0.16 (–0.78 to 0.45)	0.60	67	0.001
THR	5	372	MD	0.28 (–0.14 to 0.70)	0.19	0	0.73
TKR	2	358	MD	–0.93 (–1.29 to –0.57)	< 0.00001	0	0.41
Total hip or knee replacement	3	267	MD	–0.41 (–3.43 to 2.61)	0.79	67	0.05
Time to mobilisation							
Overall	6	471	MD	–0.17 (–0.30 to –0.04)	0.009	0	0.68
C. improving long-term outcomes *Long-term physical function*							
Overall	15	577	SMD	0.08 (–0.09 to 0.26)	0.35	9	0.35
THR	7	294	SMD	0.15 (–0.08 to 0.38)	0.20	0	0.47
TKR	8	283	SMD	0.01 (–0.28 to 0.30)	0.93	22	0.25
Long-term pain							
Overall	10	414	SMD	0.03 (–0.16 to 0.23)	0.73	0	0.80
THR	5	199	SMD	–0.07 (–0.35 to 0.21)	0.64	0	0.51
TKR	5	215	SMD	0.13 (–0.14 to 0.40)	0.35	0	0.89

a Random-effects model.

Data for meta-analysis were available for 19 interventions with 1026 participants.[488,493,494,496,497,501–503,510,513–515,519,521,525,527,534] In the random-effects meta-analysis shown in *Table 76* and *Figure 38*, the average SMD was 0.28 (95% CI 0.16 to 0.40) favouring intervention. Inspection of the funnel plot did not suggest publication bias. Benefit for interventions was limited to eight studies with 343 patients waiting for THR (average SMD 0.40, 95% CI 0.18 to 0.61) and two studies with 226 hip and knee patients reported together. There was no heterogeneity across all studies or in those in patients waiting for hip replacement. In eight studies with 457 patients waiting for knee replacement, there was a non-significant trend for benefit (average SMD 0.19, 95% CI –0.04 to 0.42). In three education-based interventions with 261 patients, physical function was better in intervention patients (average SMD 0.33, 95% CI 0.09 to 0.58). Similarly, in 12 exercise-based interventions with 494 patients, interventions showed benefit (average SMD 0.26, 95% CI 0.08 to 0.44).

No heterogeneity was apparent. In four multifactorial interventions with 271 patients there was a trend for benefit (SMD 0.32, 95% CI –0.03 to 0.66). Considering studies separately in patients waiting for hip and knee replacement there was no suggestion that particular types of interventions were more effective.

In a sensitivity analysis with 10 interventions of good or reasonable quality with 610 patients, benefit was still apparent (SMD 0.21, 95% CI 0.04 to 0.38). Numbers in groups were small but benefit was mainly in patients waiting for hip replacement.

To evaluate physiotherapy content we analysed studies by intervention intensity (frequency and duration) and specific components. Higher intensity interventions showed benefit in seven studies with 308 patients waiting for hip replacement (SMD 0.39, 95% CI 0.16 to 0.62), and a trend for benefit in nine studies with 457 knee arthroplasty patients (SMD 0.19, 95% CI –0.04 to 0.42). However, numbers of studies with medium or low intensity exercise content were small.

In patients waiting for THR, five interventions focusing on strengthening showed benefit (SMD 0.36, 95% CI 0.09 to 0.62), as did three studies with cardiovascular exercise (SMD 0.48, 95% CI 0.03 to 0.93). Numbers of studies including other components targeting stretching, gait re-education, ROM, balance, endurance, flexibility, proprioception, pool-based exercises and functional exercises were too low to draw conclusions on content. There was no evidence to suggest that any interventions had an adverse effect on physical function.

In patients waiting for knee replacement, nine physiotherapy exercise interventions had a strengthening component. As shown in *Table 76*, there was a non-significant trend for benefit in improved physical function for interventions with a strengthening component compared with controls (SMD 0.19, 95% CI –0.04 to 0.42). As with studies in hip replacement, there were too few studies to draw conclusions on other exercise content.

Pain

Pain measured before surgery was reported for 25 interventions, with data suitable for meta-analysis in 21 interventions with 1375 patients. Interventions were associated with reduced pain (SMD 0.21, 95% CI 0.10 to 0.33), but this was limited to patients waiting for hip replacement (SMD 0.47, 95% CI 0.28 to 0.67). There was only slight heterogeneity and the funnel plot did not suggest publication bias (data not shown).

In 16 studies judged to be of good or reasonable methodological quality comprising 1141 patients,[487,488,493–495,497,503,509–511,514,515,517,521,524,527] there was benefit for interventions (SMD 0.24, 95% CI 0.09 to 0.38), but this was statistically significant only in hip patients.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Study or subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	SMD IV, random, 95% CI
Hip								
Ferrara 2008[492]	–33.7	13.8	11	–43.5	9.5	12	2.1%	0.80 (–0.05 to 1.66)
Hoogeboom 2010[496]	51.1	10.5	10	52.3	21.2	11	2.1%	–0.07 (–0.92 to 0.79)
Oosting 2012[501]	–65.2	10.6	15	–68.7	14.9	13	2.8%	0.27 (–0.48 to 1.01)
McGregor 2004[500]	–35.8	12	15	–41	10	20	3.3%	0.47 (–0.21 to 1.15)
Rooks 2006 hips[502]	–26.9	11.9	25	–33.7	10.9	24	4.7%	0.59 (0.01 to 1.16)
Gilbey 2003[493]	–29.2	10.7	32	–36	12.5	25	5.4%	0.58 (0.05 to 1.12)
Gocen 2004[495]	51.48	18.32	29	45.3	12.98	30	5.8%	0.39 (–0.13 to 0.90)
Bitterli 2009[487]	43.4	18.3	34	40	20.6	37	7.1%	–0.17 (–0.29 to 0.64)
Subtotal (95% CI)			**171**			**172**	**33.2%**	**0.40 (0.18 to 0.61)**
Heterogeneity: $\tau^2=0.00$; $\chi^2=3.93$, df=7 ($p=0.79$); $I^2=0\%$								
Test for overall effect: $z=3.61$ ($p=0.0003$)								
Knee								
D'Lima 1996 cardiac[512]	73.33	11.47	10	66.84	16.83	5	1.3%	0.46 (–0.63 to 1.55)
D'Lima 1996 physical[512]	69.5	10.05	10	66.84	16.83	5	1.3%	0.20 (–0.88 to 1.28)
McKay 2012[518]	–28.5	12.57	10	–30.5	13.68	11	2.1%	0.15 (–0.71 to 1.00)
Rooks 2006 knees[502]	–27.7	11.6	14	–25	11.9	15	2.9%	–0.22 (–0.95 to 0.51)
Gstoettner 2011[514]	–2.2	1.2	18	–3.7	1.8	20	3.4%	0.95 (0.27 to 1.63)
Evgeniadis 2007[513]	–19.91	2.77	18	–19.67	3.4	20	3.8%	–0.08 (–0.71 to 0.56)
Nuñez 2006[520]	–35.26	10.48	43	–40.89	12.64	37	7.7%	0.48 (0.04 to 0.93)
Beaupre 2004[509]	50	14	51	51	17	58	10.9%	–0.06 (–0.44 to 0.31)
Williamson 2007 physio[524]	–49.4	17.1	53	–51.6	17.8	59	11.2%	0.13 (–0.25 to 0.50)
Subtotal (95% CI)			**227**			**230**	**44.5%**	**0.19 (–0.04 to 0.42)**
Heterogeneity: $\tau^2=0.03$; $\chi^2=10.50$, df=8 ($p=0.23$); $I^2=24\%$								
Test for overall effect: $z=1.66$ ($p=0.10$)								
Hip and knee								
Pellino 1998[533]	21.87	1.17	35	21.18	1.55	39	7.2%	0.49 (0.03 to 0.96)
Crotty 2009[526]	–53.9	15.02	75	–57.4	15.22	77	15.1%	0.23 (–0.09 to 0.55)
Subtotal (95% CI)			**110**			**116**	**22.3%**	**0.31 (0.05 to 0.58)**
Heterogeneity: $\tau^2=0.00$; $\chi^2=0.84$, df=1 ($p=0.36$); $I^2=0\%$								
Test for overall effect: $z=2.35$ ($p=0.02$)								
Total (95%CI)			**508**			**518**	**100.0%**	**0.28 (0.16 to 0.40)**
Heterogeneity: $\tau^2=0.00$; $\chi^2=17.63$, df=18 ($p=0.48$); $I^2=0\%$								
Test for overall effect: $z=4.43$ ($p<0.00001$)								
Test for subgroup differences: $\chi^2=1.67$, df=2 ($p=0.43$); $I^2=0\%$								

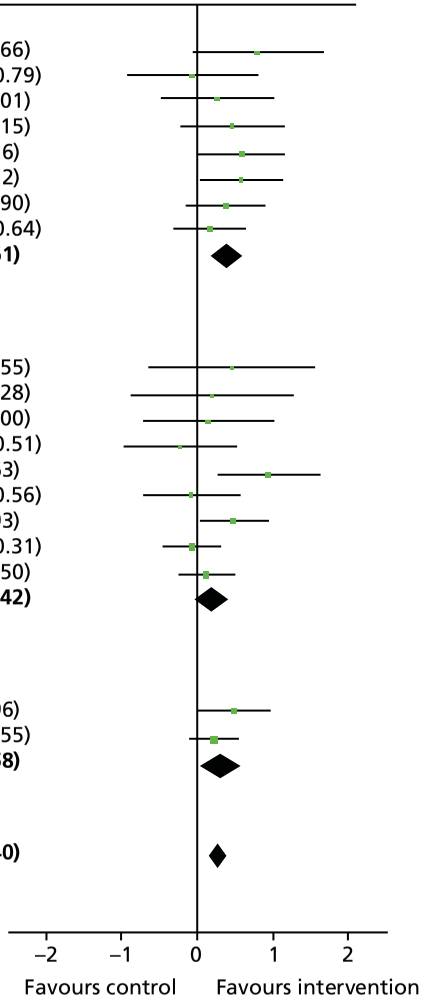


FIGURE 38 Pre-surgical physical function outcome in studies targeting optimisation of pre-surgical health. df, degrees of freedom; IV, inverse variance. SF-36 physical function: Bitterli and colleagues.[488] WOMAC function: Ferrara and colleagues,[493] Gilbey and colleagues,[494] McGregor and colleagues,[501] Rooks and colleagues,[503] Beaupre and colleagues,[510] Gstoettner and colleagues,[515] (control values were baseline), McKay and colleagues,[519] Nuñez and colleagues[521] and Crotty and colleagues.[527] WOMAC total score: Williamson and colleagues.[525] HHS: Gocen and colleagues.[496] HOOS function in daily activities: Hoogeboom and colleagues[497] and Oosting and colleagues.[502] HSS: D'Lima and colleagues.[513] SF-36 physical function: Evgeniadis and colleagues.[514] Locally devised score based on ability to perform pre- and postoperative care: Pellino and colleagues.[534]

In 13 studies with 597 patients,[488,494,497,502,503,509,511,514,515,519,524,525] exercise-based interventions showed benefit, SMD 0.23 (95% CI 0.07 to 0.39). In three education-based interventions[495,501,527] and five multifactorial interventions,[487,493,510,517,521] there were trends for benefit, with SMDs of 0.20 (95% CI –0.03 to 0.44) and 0.27 (95% CI –0.04 to 0.58). Numbers in some groups were small but all types of programme content showed benefit for patients waiting for THR.

Anxiety

Anxiety was reported pre-operatively for eight interventions, using the State–Trait Anxiety Inventory (STAI) in six studies,[489,495,526,528,529] and HADS[525] and Arthritis Impact Measure Score (AIMS) anxiety[487] in one each. In eight studies[487,489,495,525,526,528,529] with 660 patients, interventions were associated with lower anxiety with SMD 0.38 (95% CI 0.11 to 0.65). However, in quality assessment, five studies were classified as having risk of bias.[489,495,525,526,529]

Preparation for recovery in hospital

In 27 studies (26 articles), a specific focus of the intervention was preparing patients for their hospital stay, including what to expect before, during and after surgery.[489–492,495,496,498,499,501,504–508,510,516–518,522,526,528–533] We identified 14 interventions in patients waiting for hip replacement,[489–492,495,496,498,499,501,504–508] six interventions in patients waiting for knee replacement[510,516–518,522] and seven intervention in patients waiting for either hip or knee replacement.[526,528–533] Nineteen interventions[489,490,492,495,498,499,501,505,508,516,518,522,526,529–533] were primarily education based and eight were multifactorial with education and exercise content.[491,496,504,506,507,510,517,528]

Post-surgical anxiety

Eight interventions reported anxiety outcomes within a month of surgery.[489,490,492,495,506,522,529,530] Five studies with 381 patients presented data suitable for the meta-analysis in *Table 76* and *Figure 39*.[489,492,495,506,529] Four studies recorded anxiety using the STAI questionnaire during the hospital stay or the change from baseline and included either hip or hip and knee patients analysed together.[489,492,495,529] In a random-effects model, the MD was 2.97 (95% CI 0.64 to 5.30) in favour of reduced anxiety in the intervention group. One study reported sense of uncertainty on discharge using a VAS scale.[506] Inclusion of this in the meta-analysis and excluding one study with change scores gave an average SMD of 4.15 (95% CI 1.46 to 6.84).

There was no evidence of heterogeneity and exclusion of one study with differing losses to follow-up between randomised groups did not affect the outcome.[529]

Post-surgical pain

Fifteen interventions reported a pain outcome up to 1 month after surgery. For meta-analysis, we included the latest data at a fixed time point up to 1 month after surgery. If not available, we used data collected at discharge but such data may be affected by time in hospital. When possible, we used pain at movement in preference to pain at rest. Using these criteria, 12 interventions with 842 patients were included in the meta-analysis. Up to 1 month after surgery, pain was non-significantly lower in intervention groups than in controls (SMD 0.18, 95% CI –0.01 to 0.38). Similar trends were noted in hip and knee patients separately. There was no evidence of publication bias from inspection of the funnel plot but some heterogeneity was evident in trials including knee replacement patients (data not shown).

Results and heterogeneity were similar after exclusion of studies with possible bias owing to differences in patient characteristics, group follow-up rates or inclusion of data collected at discharge.

Length of hospital stay

Length of hospital stay was reported after 19 interventions with 997 patients. There was no statistically significant benefit for interventions (MD –0.16 days, 95% CI –0.78 to 0.45 days) reflecting a trend for lower length of hospital stay in intervention groups. The corresponding funnel plot did not suggest presence of publication bias. Heterogeneity ($I^2 = 67\%$) was not explained by one study with different follow-up rates in randomised groups. Although benefit for reduced length of stay was noted in knee

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Study or subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	SMD IV, fixed, 95% CI
STAI								
Butler 1996[488]	–21.57	18.44	30	–31.15	22.93	40	20.0%	0.45 (–0.03 to 0.93)
Cuñádo Barrio 1999[528]	–16	8	41	–18	10	35	22.5%	0.22 (–0.23 to 0.67)
Doering 2000[491]	–35.77	10.32	43	–39.58	9	52	27.7%	0.39 (–0.02 to 0.80)
Giraudet-Le Quintrec 2003[494]	4.16	10.74	48	2.53	11.98	52	29.8%	0.14 (–0.25 to 0.53)
Subtotal (95% CI)			**162**			**179**	**100.0%**	**0.29 (0.08 to 0.50)**
Heterogeneity: $\chi^2=1.30$, df=3 ($p=0.73$); $I^2=0\%$								
Test for overall effect: $z=2.65$ ($p=0.008$)								
VAS sense of uncertainty								
Vukomanovic 2008[505]	–0.4	1.79	20	–28.8	37.21	20	100.0%	1.06 (0.39 to 1.72)
Subtotal (95% CI)			**20**			**20**	**100.0%**	**1.06 (0.39 to 1.72)**
Heterogeneity: not applicable								
Test for overall effect: $z=3.11$ ($p=0.002$)								
Test for subgroup differences: $\chi^2=4.61$, df=1 ($p=0.03$), $I^2=78.3\%$								

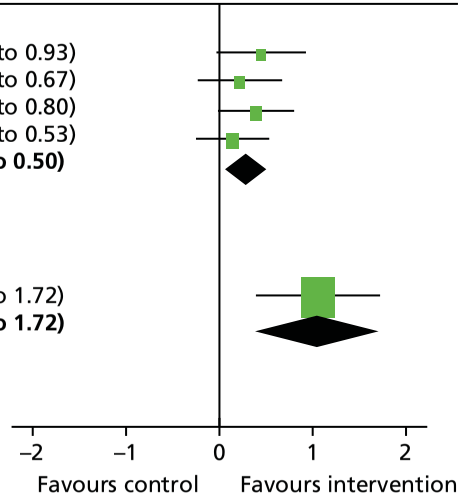


FIGURE 39 Post-surgical anxiety outcome in studies targeting preparation for recovery in hospital (MD). df, degrees of freedom; IV, inverse variance. STAI: Butler and colleagues,[489] Doering and colleagues[492] (from McDonald and colleagues[83]), Cuñádo Barrio and colleagues[529] and Giraudet-Le Quintrec and colleagues[495] (change score). VAS sense of uncertainty: Vukomanovic and colleagues;[506] used as data were suitable for inclusion in meta-analysis. Authors also recorded anxiety, intervention group 0 (SD 0), control 22.25 (SD 34.64).

replacement patients, this was based on two studies[510,517] and was not supported by studies including both hip and knee patients.[528,529,531]

Mobilisation after surgery

In six studies with 471 patients, time to mobilisation was reported.[495,496,506,507,528,529] Studies included only hip or hip and knee patients. Measures of mobilisation were time to walking in five studies[495,496,506,528,529] and time to standing in one study.[507] In meta-analysis, time to mobilisation was shorter in the intervention groups (MD –0.17 days, 95% CI –0.30 to –0.04 days) and this was little changed if only time to walking was considered. Overall, there was no heterogeneity among studies.

Improving long-term outcomes

Nine pre-surgical interventions explicitly targeted improvement in long-term outcome after hip replacement[487,488,493,496,501–503,506] and nine after knee replacement.[503,510,513–515,519,524,525] The focus of the intervention was exercise in 12 interventions, education in one intervention and multifactorial in five interventions.

Long-term physical function

All but three studies reported a functional outcome at 3 months or longer after surgery.[502,515,524] As shown in the meta-analysis in *Table 76* and *Figure 40*, including 15 studies with 577 patients, there was no overall long-term benefit in intervention compared with control groups (SMD 0.08, 95% CI –0.09 to 0.26). Only moderate heterogeneity was apparent and there was no suggestion of publication bias.

Long-term pain

As shown in *Table 76*, there was no benefit for reduced long-term pain after interventions in 10 studies with 414 patients (SMD 0.03, 95% CI –0.16 to 0.23). In addition, there was no heterogeneity among the studies.

Discussion

Before joint replacement, many interventions have been evaluated that aim to improve pre-surgical physical health, preparation for surgery and recovery, and achievement of good long-term outcomes. Studies were generally small and a minority reported long-term follow-up.

Evidence from studies considered to be of reasonable or good quality suggests that, in patients waiting for hip replacement, physical function can be enhanced and pain reduced before surgery. For patients with knee replacement, trends were apparent but were not statistically significant. There was some suggestion that interventions led to reduced anxiety before surgery but this was more convincing in patients followed up shortly after surgery in better-quality studies. Patients receiving interventions mobilised quicker after surgery but length of hospital stay did not differ significantly. For patients followed up after surgery, there was little to suggest that interventions had long-term benefit.

Interpretation of the effect size when using SMDs as the outcome can be difficult. Cohen interpreted effect sizes as ‘small’ (0.10), ‘medium’ (0.25) and ‘large’ (0.40).[535] Thus, interventions in patients waiting for hip replacement can be considered to show a medium to large effect on pre-surgical physical function and pain, depending on the study quality. The effect of interventions in hip and knee patients on reducing post-surgical anxiety was medium to large. Mobilisation was brought forward by about 4 hours in intervention groups, a potentially large effect in the context of recent studies with mean times to mobilisation of 48–72 hours.

The small number of interventions and the size of trials limited the analysis of long-term outcomes and there was little to suggest benefit. Differences in outcomes at long-term follow-up, particularly in small,

© Queen’s Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

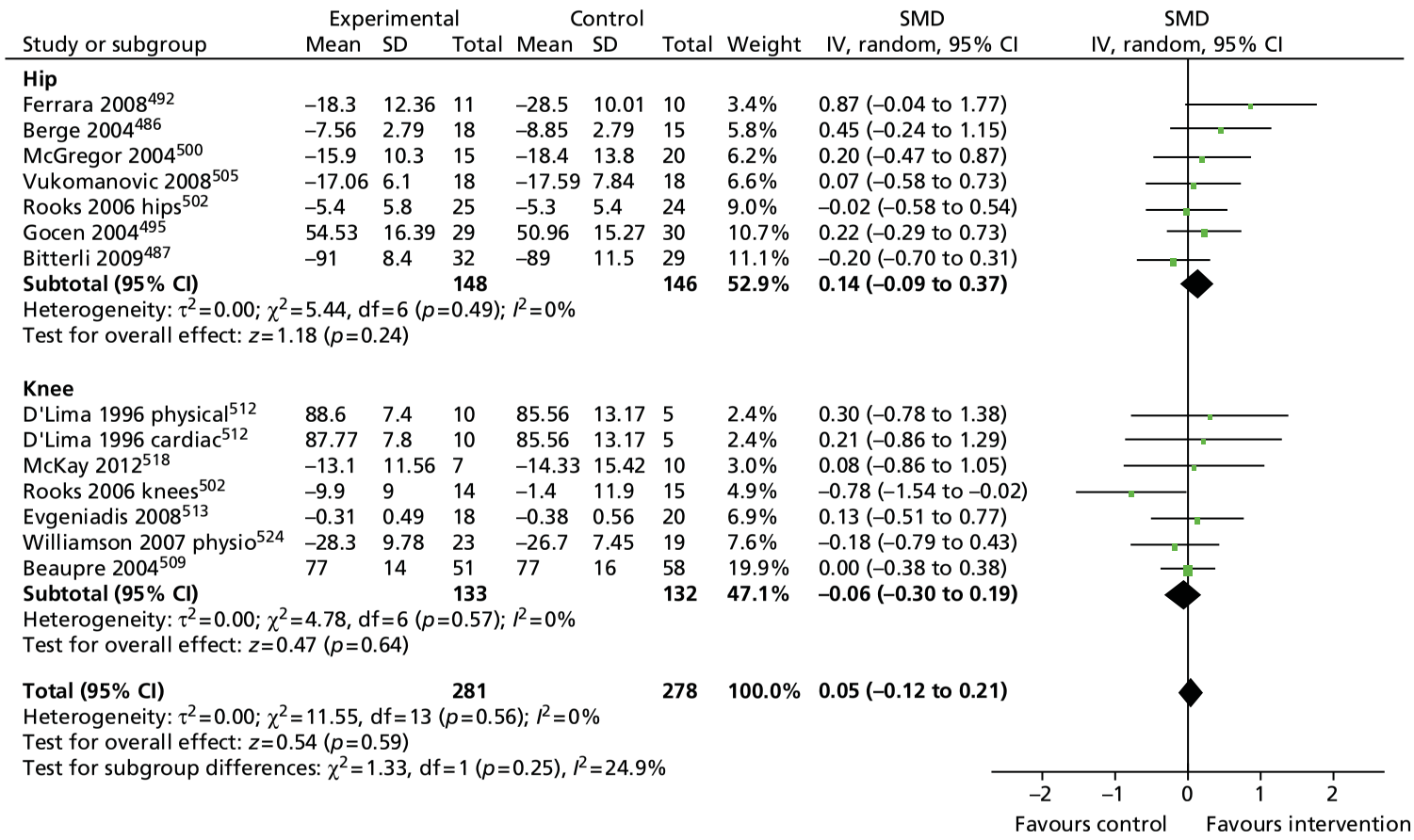


FIGURE 40 Physical function in studies targeting improvement of long-term outcomes. df, degrees of freedom; ILAS, Iowa Level of Assistance Scale; IV, inverse variance. WOMAC function: Ferrara and colleagues,[493] McGregor and colleagues[501] (supplied by author), Rooks and colleagues,[503] McKay and colleagues[519] and Beaupre and colleagues.[510] WOMAC total: Bitterli and colleagues.[488] OHS: Vukomanovic and colleagues.[506] OKS: Williamson and colleagues.[525] HHS: Gocen and colleagues.[496] AIMS: Berge and colleagues.[487] SDs based on data from Dawson and colleagues.[274] Hospital for special surgery knee rating scores: D'Lima and colleagues.[513] ILAS: Evgeniadis and colleagues.[514]

underpowered studies, are likely to be overwhelmed by changes in physical function and pain that occur after hip or knee arthroplasty in the majority of patients.[18,48]

Exercise provides the main focus of interventions aiming to improve pre-surgical physical function. However, the importance of specific exercise content was unclear. This may reflect the aims of pre-surgical physiotherapy exercise focusing on the maintenance of functional ability and prevention of decline, rather than post-surgical rehabilitation, which is substantially based on adjustment to physical changes associated with the prosthesis.

Conclusion

In randomised evaluations of pre-surgical exercise and education identified in our systematic review, there was a suggestion that physical function can be enhanced and pain reduced before surgery in patients waiting for hip replacement. Studies on patients with knee replacement did not provide strong evidence of benefit. Interventions were associated with reduced anxiety during the hospital admission and quicker mobilisation. The value of specific exercise content was unclear, which may reflect the aims of pre-surgical exercise to maintain functional ability and prevent decline whereas post-surgical rehabilitation is substantially based on adjustment to physical changes associated with the prosthesis.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Chapter 9 Clinical effectiveness and cost-effectiveness of a group-based pain self-management intervention for patients undergoing total hip replacement: feasibility study for a randomised controlled trial – SPIRAL

Parts of this chapter have been reproduced from Wylde and collegaues.[536] © 2014 Wylde *et al.*; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited.

Abstract

Background

We conducted the SPIRAL study to evaluate the feasibility of a definitive RCT to assess the clinical effectiveness and cost-effectiveness of a group-based pain self-management course for patients undergoing THR.

Methods

Participants were randomised to attend a pain self-management course plus standard care or standard care only. The course consisted of two half-day sessions before surgery and one full-day session after surgery. Participants provided outcome and resource-use data prior to surgery and 1 month, 3 months and 6 months after surgery. Telephone interviews were conducted with non-participants to explore barriers to participation.

Results

Out of the 385 eligible patients with THR, 88 (23%) consented to participate. Common reasons for non-participation were views about the course and transport difficulties. Of 43 patients randomised to the intervention, 28 attended the pre-operative sessions and 11 attended the postoperative session. Participant satisfaction was high and feedback highlighted that patients enjoyed the group format. Retention of participants in the RCT was acceptable (83%) with high questionnaire return rates, with the exception of resource-use diaries.

Conclusions

Although participation in the group-based pain self-management course was low, those who attended provided positive feedback. The SPIRAL study highlights the importance of conducting feasibility work and evaluating the acceptability of an intervention prior to undertaking a full-scale RCT to assess the clinical effectiveness and cost-effectiveness of an intervention.

Background

Evidence is needed on the clinical effectiveness and cost-effectiveness of pain self-management programmes for patients undergoing THR. Previous studies of self-management programmes for patients with arthritis have faced challenges owing to low recruitment rates, poor uptake of the intervention and high attrition rates.[537–541] Therefore, prior to undertaking a RCT with an economic evaluation component of a pain self-management programme for patients undergoing THR, it is important to evaluate the feasibility of such a trial and the acceptability of the intervention to patients.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Feasibility and pilot work to explore trial processes can include testing trial procedures and data collection methods, randomisation processes, recruitment rates and attrition rates.[542] For example, attrition rates for self-management programmes have been found to be as high as 40–50%,[540,541] and in one research study 29% of recruited patients attended none of the sessions on a 6-week self-management course.[537] Preliminary work prior to undertaking the definitive trial can often highlight unanticipated issues with trial design and conduct,[543,544] which can then be addressed to maximise the success of intervention evaluation in a full-scale RCT. The importance of feasibility work to evaluate trial processes has been highlighted in a systematic review of cluster RCTs in primary care, which concluded that a number of reported issues with recruitment, adherence to trial protocol and data collection methods could have been pre-emptively identified and addressed through feasibility work.[545]

In addition to testing trial processes, another objective of preliminary work prior to a full-scale RCT can be to test the acceptability of an intervention, particularly if the intervention is complex in nature.[546] Preliminary work to develop, refine and pilot complex interventions is recommended by the MRC.[94] Early evaluation of the acceptability of a complex intervention can highlight aspects of the intervention which can then be modified prior to a definitive trial. For example, feasibility work highlighted that booster sessions for a group-based cognitive–behavioural therapy intervention were poorly attended.[547] A feasibility study of a group-based acceptance and commitment therapy for chronic pain found that some patients found the sessions too long.[548] A pilot study of a complex intervention for diet and activity behaviour change in obese pregnant women found that increased flexibility of the timing of sessions was necessary to improve attendance and some activities, such as goal-setting, were better conducted individually rather than in a group setting to minimise perceptions of being judged.[549]

Therefore, the aims of this study were twofold: (1) to evaluate the feasibility of conducting a RCT to assess the clinical effectiveness and cost-effectiveness of a group-based pain self-management course for patients undergoing THR, and (2) to assess the acceptability of the intervention. Specific objectives were to assess the feasibility of trial design and procedures, ascertain recruitment and retention rates, identify barriers to participation, develop resource-use data collection methods, assess questionnaire completion rates, and evaluate uptake and patient satisfaction with the course.

Patients and methods

The study was approved by the South West Central Bristol Research Ethics Committee (reference 11/SW/0056) and all participants provided their informed, written consent to participate. The trial was registered on the NIHR Clinical Research Network Portfolio (UKCRN ID 11270) and ISRCTN register (ISRCTN52305381).

Participant recruitment

Between June 2011 and June 2012, potential participants were identified from the joint replacement waiting list at one elective orthopaedic centre and sent a postal study invitation. Patients interested in participating in the study were asked to return a signed consent form and reply slip to the research team. Study recruitment materials were designed with input from patient representatives through the unit's dedicated patient forum (PEP-R).[550] A researcher then contacted interested patients to ensure that they met the eligibility criteria and answer any questions they may have about the study. The inclusion criterion was being listed for a primary THR because of osteoarthritis. Exclusion criteria comprised lack of capacity or unwillingness to provide informed consent and inability to complete English-language questionnaires. In order to explore whether or not the patients enrolled in the study were representative of those undergoing joint replacement, basic demographic data on age and sex were recorded for all eligible patients who were approached about the study.

Telephone interviews with non-participants

To explore potential barriers to participating in the study, short, structured telephone interviews were conducted with patients who declined to participate in the study but returned a reply form giving permission for a researcher to telephone them to discuss why they decided not to participate. Reasons for non-participation were recorded on a standardised proforma by the researcher and entered into a Microsoft Excel spreadsheet.

Randomisation

Participants were randomised after recruitment using a computer-generated randomisation system (Minim).[551] Blinding of the research team or patients was not possible because the intervention involved attending a course. Participants were informed of the results of randomisation via a letter and those randomised to the intervention group were contacted by telephone to discuss course arrangements.

Assessment times

All participants completed postal questionnaires at baseline (after recruitment), prior to surgery and then at 1, 3 and 6 months after surgery. If no reply was received after 2 weeks then a single reminder was sent.

Questionnaires

At each assessment time, participants completed the following validated PROMs.

WOMAC[114]

This consists of 24 items and produces individual scores for hip pain, function and stiffness. Scores were transformed onto a 0–100 scale (worst to best).

Pain Self-Efficacy questionnaire[275]

This consists of 10 items regarding a person's confidence in their ability to perform general activities, despite their pain. Scores range from 0 to 60, with a higher score reflecting stronger perceived self-efficacy.

Brief COPE[276]

This consists of 28 items about coping strategies and provides 14 distinct two-item subscales of coping reactions. Each subscale is scored from 1 to 4, with higher scores representing a greater reliance on a particular coping strategy.

Beliefs about Medicines Questionnaire – Specific[277]

This consists of 10 items assessing a person's beliefs about their medication (limited to pain medication in this study). The questionnaire produces two subscales about the necessity of prescribed medication and concerns about potential adverse effects of prescribed medications, both of which are scored from 5 to 25, with a higher score indicating stronger beliefs.

European Quality of Life-5 Dimensions-5 Levels[278]

This consists of five questions with five levels each (from no problems to severe problems) which provides a standardised measure of general HRQoL across five dimensions.

Patients also completed questions about pain in other joints, fatigue and pain distress (both measured on a VAS), length of time spent on various exercises each week and current pain medication usage. In the baseline questionnaire, medical comorbidities were recorded using the Functional Co-morbidity Index[279] and information was collected about socioeconomic status.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Resource use

The 3- and 6-month postoperative questionnaire included a full resource-use questionnaire to identify and measure NHS resources used including community-based doctor and nurse visits, physiotherapy and occupational therapy visits, secondary care inpatient and outpatient visits and medication, use of social services, patient expenses, informal care and productivity losses incurred in the period. Participants were given a pre-operative resource-use diary to record any resources used from randomisation until they had their surgery. They were asked to return the completed pre-operative diary to the research team when they returned their 1-month postoperative questionnaire. At 1 and 3 months post operation, patients were given a resource-use log to prospectively record their use of resources in the following period in order to aid them in the completion of the resource-use questions in the 3-month and 6-month questionnaires.[432] The aim of these questionnaires was not to formally evaluate the differences in costs and consequences of delivering a pain self-management course to patients undergoing THR, but to refine resource-use data collection methods. Therefore, analyses of these questionnaires focused on rates of missing data, which is a common issue with patient-completed postal resource-use questionnaires.[432]

Intervention

The Challenging Pain and Keep Challenging Pain courses were delivered by Arthritis Care, a registered UK charity that has been delivering self-management courses since 1994. The courses were delivered by two lay trainers, who had experience of living with chronic pain. All the courses were held at the AOC, Southmead Hospital. Reimbursement of travel costs (mileage and parking fees) or a pre-paid taxi was offered to all participants who attended the courses.

Challenging Pain course

The pre-operative Challenging Pain course consisted of two sessions running over consecutive weeks, with each session lasting 2.5 hours. The 2-week course was developed from a longer 6-week course and has been evaluated by Arthritis Care.[552] The emphasis of the course was on pain management and introduced participants to a variety of cognitive pain management techniques, with the aim of providing coping skills to enable patients to manage their pain and its impact more effectively. Delivery involved a combination of presentations, group work, pair work, practical demonstrations and interactive sessions. The first session included introductions to conscious breathing, full-body relaxation, exercise, goal-setting and managing stress. The second session reviewed these topics and introduced pacing, medications and other therapies, guided imagery, managing negative thoughts and effective communication.

Postoperative Keep Challenging Pain course

All participants randomised to the intervention group were invited to attend an additional top-up Keep Challenging Pain course at between 6 weeks and 3 months post operation. This course was designed by Arthritis Care in conjugation with a physiotherapist specifically to be delivered to postoperative THR patients. This 5-hour session reviewed the pain management strategies that were introduced in the pre-operative course, provided advice on recovery after THR, reviewed goal-setting and problem solving, and included a practical exercise session lead by a registered physiotherapist.

Course evaluation

A short structured feedback questionnaire about the course was completed by participants at the end of the both the Challenging Pain and Keep Challenging Pain courses.

Surgery and postoperative physiotherapy

All participants received a primary THR using a posterior or anterolateral approach, at the discretion of the surgeon. Standard postoperative inpatient physiotherapy at the AOC consists of strengthening of the hip abductor muscle, flexor and extensor exercises, transfers to and from bed, and walking and stair climbing, with hydrotherapy and gym exercises if required. Outpatient physiotherapy is not routinely provided after discharge.

Sample size

No formal sample size calculation can be performed for a feasibility study. The average sample size for feasibility studies assessing trial design and the acceptability of interventions is approximately 60 patients.[553] A minimum of 80 patients (40 per arm) was deemed an appropriate sample size for this trial to allow an estimate of recruitment and retention rates and explore the acceptability of the intervention.

Analysis

In line with recommendations about good practice in the analysis and reporting of feasibility and pilot trials, analysis is descriptive and no comparisons of the outcomes between the two arms of the trial was conducted.[542] Descriptive statistics on recruitment rates, baseline patient characteristics, retention of participants and questionnaire return rates are presented as means and 95% CIs, medians and IQRs or percentages. Resource-use data collected from patient self-completed questionnaires were considered complete when the patient recorded enough data to allow costing using a national tariff. Completion rates were reported per question and aggregated per two economic perspectives – the NHS and PSS perspective – and a broader societal perspective. Data on reasons for non-participation in the trial were coded into themes by one researcher and these themes were then discussed and agreed with a second researcher.[445]

Results

Recruitment rate and participants

Postal invitations were sent to 385 eligible patients and 88 patients consented to participate, giving a recruitment rate of 23%. A CONSORT flow diagram is shown in *Figure 41*.

Baseline demographic and clinical characteristics of the participants are displayed in *Table 77*. Mean WOMAC scores indicated that patients had high levels of hip pain and functional limitations prior to surgery. Mean pain self-efficacy scores indicate the patient population were suitable for a pain management intervention.[275] Participants underwent THR surgery at a median of 12 weeks (IQR 8–15 weeks) after recruitment into the study. Non-participants had a similar median age (67 years, 95% CI 66 to 69 years) to participants but were more likely to be male (46% male).

Reasons for non-participation

Brief telephone interviews were conducted with 57 (19%) non-participants. These patients had a mean age of 71 years (95% CI 68 to 74 years) and 37 were female. Patients gave 91 reasons for non-participation, most frequently relating to perceptions and views about the pain self-management course (*Table 78*). These reasons included previously attending pain self-management courses and finding them unhelpful, a perceived lack of need because pain was adequately managed, a dislike of group formats and concerns over difficulty in attending the course because of pain, age and/or other health conditions. The second most frequently given reason for non-participation concerned issues around travelling to the hospital to attend the course.

Retention

Fifteen patients were withdrawn from the study (17% of recruited participants): seven from the intervention group and eight from the standard care group (see *Figure 41*). Of the withdrawn patients, nine were withdrawn because they did not undergo surgery during the study period, five self-withdrew and one was withdrawn because they were recruited into another trial whose protocol precluded participation in two trials.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

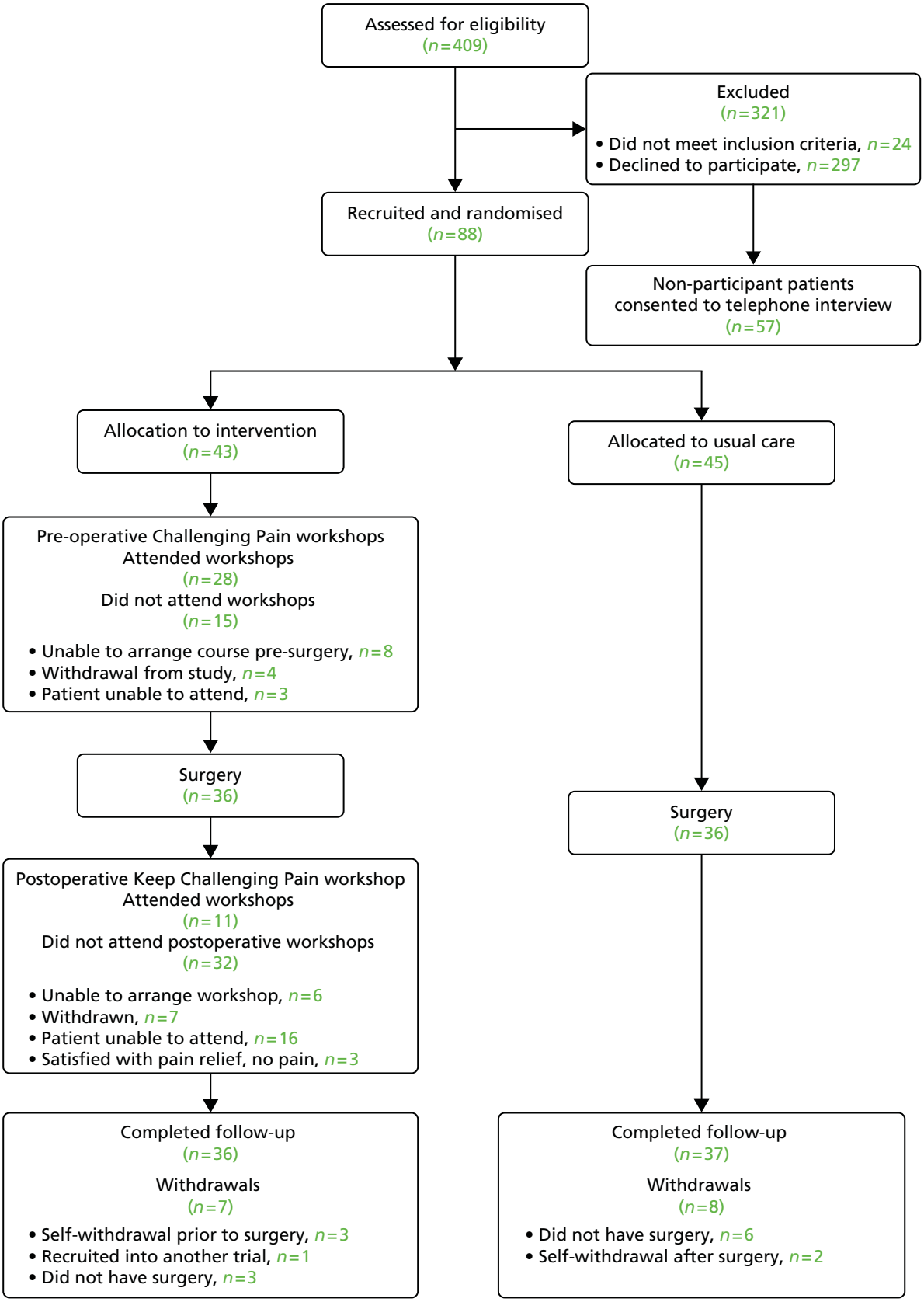


FIGURE 41 SPIRAL CONSORT flow diagram.

TABLE 77 SPIRAL baseline demographic and clinical characteristics of participants

Patient characteristics	Overall ($n = 88$)	Allocated to intervention ($n = 43$)	Allocated to standard care ($n = 45$)
Mean age (95% CI)	66 (64 to 68)	65 (61 to 69)	67 (64 to 70)
Female : male, %	65 : 35	65 : 35	64 : 36
Living alone, %	19	18	20
With college or university education, %	35	32	39
Retired, %	60	61	59
Mean WOMAC pain score (95% CI)	38 (33 to 42)	37 (31 to 43)	38 (32 to 44)
Mean WOMAC function score (95% CI)	37 (33 to 41)	39 (33 to 45)	35 (30 to 41)
Pain self-efficacy score (95% CI)	32 (29 to 35)	35 (30 to 39)	30 (26 to 34)

Notes
WOMAC pain and function scores range from 0 to 100 (worst to best).
Pain Self-Efficacy questionnaire scores range from 0 to 60 (low self-efficacy to high self-efficacy).

TABLE 78 SPIRAL reasons for non-participation

Barriers to participation (number of patients)	Examples of reasons given
Thoughts about attending the course (25)	Difficult to sit and concentrate during workshops because of pain/age/other health conditions
	Dislike of group session format
	Found previous pain management course unhelpful
	Can already manage pain
	Workshops would not be helpful as pain not too bad
	Difficult to attend because of other health conditions
	Would rather spend time doing other things
Difficulty getting to hospital (22)	Unable to drive/use public transport owing to hip problems
	Distance to hospital perceived as too far
	Would have to rely on family/friends for transport
	Limited mobility or uses wheelchair
Other commitments (13)	Carer for family member
	Employment
	Children
Questionnaires (8)	Dislike of completing questionnaires
	Difficult to complete because of other health conditions
	Lack of time because of other commitments
Other hospital appointments (6)	Lack of time for additional visits to hospital
	Inconvenient to make additional visits to hospital
Feels already has enough knowledge (6)	Previous hip replacement
	Knows people who have had hip replacement
	Has attended physiotherapy/exercise session
Health-care related (6)	Operation may not be going ahead
	Dissatisfied with co-ordination of care
Other (5)	Emigrating
	Recently widowed
	Has taken part in research before

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Intervention: attendance and acceptability

Pre-operative Challenging Pain course

Four pre-operative Challenging Pain courses were held, with between four and nine participants on each course. Out of the 43 participants randomised to the intervention group, 28 patients attended the pre-operative course (17 attended both workshops, 11 attended one workshop) at a median of 5 weeks (IQR 2–8 weeks) prior to surgery. Reasons for non-attendance are presented in *Figure 41*. Results from the course evaluation questionnaire are presented in *Table 79*. Free-text comments on the evaluation questionnaires frequently gave positive feedback on the group format of the workshop, which provided the opportunity to meet other people undergoing THR.

Postoperative Keep Challenging Pain course

Three postoperative Keep Challenging Pain course were held, with between two and five participants on each course. Out of the 43 participants randomised to the intervention group, 11 patients attended the postoperative course at a median of 9 weeks post operation (IQR 5–14 weeks). Reasons for non-attendance are presented in *Figure 41*. The results of the course evaluation questionnaire are presented in *Table 79*. Free-text comments on the evaluation questionnaires most frequently gave positive feedback on the physiotherapy session and the group format of the workshop.

Outcomes assessment and economic evaluation

The questionnaire return rates at each assessment time were high, ranging from 72% to 93% (*Table 80*). The rate of questionnaire return was similar between trial arms, with < 10% difference in return rates at each time point, except for the 3-month postoperative questionnaire, which was returned by more patients in the standard care arm than in the intervention arm (91% vs. 72%, respectively). Return rates for the pre-operative resource-use diaries were low, with only 35% of patients returning their diary.

TABLE 79 Results from the Challenging Pain and Keep Challenging Pain evaluation questionnaires

Evaluation question	Challenging Pain course ($n = 27$)	Keep Challenging Pain course ($n = 11$)
Has the course been useful? (% yes)	100	100
Recommend for other THR patients? (% yes)	100	100
Mean usefulness (95% CI)	7.3 (6.5 to 8.1)	8.9 (8.4 to 9.5)
Mean satisfaction with content (95% CI)	8.0 (7.2 to 8.7)	9.0 (8.4 to 9.6)
Men satisfaction with delivery (95% CI)	8.4 (7.7 to 9.0)	9.0 (8.2 to 9.8)

Note
Usefulness and satisfaction questions rated on 0–10 scale (worst to best).

TABLE 80 Percentage completion rate of patients returning completed questionnaires at each time point

Time point	Median (25th, 75th percentile) time of completion	Intervention group, *n/N* (%)	Usual care group, *n/N* (%)	Overall, *n/N* (%)
Baseline	10 weeks (5, 13) prior to surgery	38/43 (88)	42/45 (93)	80/88 (91)
Preoperative	1 week (0.5, 1.3) prior to surgery	25/33 (76)	29/34 (85)	54/67 (81)
Pre-operative resource-use diary	Pre-operative to 1-month after surgery	11/36 (31)	15/38 (39)	26/74 (35)
1 month post operation	4 weeks (3, 5) after surgery	32/36 (89)	35/38 (92)	67/74 (91)
3 months post operation	13 weeks (13, 14) after surgery	26/36 (72)	34/37 (92)	60/73 (82)
6 months post operation	26 weeks (26, 27) after surgery	32/36 (89)	32/37 (86)	64/73 (88)

Table 81 presents the completion rates of resource-use data in the 3- and 6-month postoperative questionnaires. For those who returned the resource-use questionnaire, completion rates for NHS resource-use questions were high for secondary-care resource use (> 90% completion on both arms) and medication use (> 80%), but less for community-based resources (65% and 66% for intervention and control arms, respectively). PSS data also had high completion rates (> 86% for all categories), particularly in the intervention group. When accounting for non-returners of follow-up questionnaires (10 in the intervention group and seven in the control group), completion rates were lower, with community-based resources being the lowest completed category. Overall, data for an economic evaluation from a NHS and PSS perspective were available for 33% of patients in the intervention group and 43% of patients in the standard care group. When considering other categories of resource use beyond health and social care, cost of travel was the least completed category. As a result, for an economic evaluation from a societal

TABLE 81 Completion rates for resource-use categories over the follow-up period

	Intervention			Standard care		
Resource-use category	Number complete	% of returners ($n = 26$)	% all ($n = 36$)	Number complete	% of returners ($n = 29$)	% all ($n = 37$)
NHS resource use						
Community-based visits	17	65%	47%	19	66%	51%
Hospital inpatient visits	24	92%	67%	28	97%	76%
Outpatient and A&E visits	25	96%	69%	28	97%	76%
Prescribed medications	22	85%	61%	24	83%	65%
PSS						
Home care worker	26	100%	72%	27	93%	73%
Food at home services	26	100%	72%	26	90%	70%
Social worker visits	26	100%	72%	25	86%	68%
Home changes	24	92%	67%	25	86%	68%
NHS + PSS perspective	**12**	**46%**	**33%**	**16**	**55%**	**43%**
Other resources: productivity losses, informal care, private expenses and other						
Time off work	23	89%	64%	24	83%	65%
Time off usual and leisure activities	26	100%	72%	21	72%	57%
Informal care time	26	100%	72%	23	79%	62%
Charities and support group visits	26	100%	72%	25	86%	68%
Privately paid therapies used	23	89%	64%	25	86%	68%
Travel costs	13	50%	36%	14	48%	38%
Over-the-counter medications	25	96%	69%	27	93%	73%
Societal perspective	**6**	**23%**	**17%**	**7**	**24%**	**19%**

A&E, accident and emergency.

Note

Number of participants completing the questions in a resource-use category at both 3- and 6- month follow-ups. Data are presented for the 73 patients in the trial at final follow-up.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

perspective, complete data were available only for 17% of patients in the intervention group and 19% of patients in the standard care group. The percentage of missing data was similar between trial arms, with the exception of four categories (social worker visits, time off usual activities, informal care time, and charities and support group visits), which had > 10% difference in completion rates between the trial arms. For these categories, patients in the intervention arm had higher completion rates than those in the standard care arm.

Discussion

This study looked at the feasibility of a RCT to evaluate the clinical effectiveness and cost-effectiveness of a group-based pain self-management intervention for patients undergoing THR and the acceptability of this intervention. Although feasibility studies are conducted to address trial design and methodology, a systematic review found that articles often include only a minimal discussion of the methodological findings and implications.[554] This feasibility study highlighted several methodological considerations that warrant further discussion.

Barriers to participation

Barriers to participation were explored using brief interviews with non-participants. These interviews identified that the most frequent reasons for non-participation were views and perceptions of the pain management course. These findings are in line with previous research, that identified that perceptions of the course and satisfaction with current self-management were reasons for non-participation in a trial of an arthritis self-management programme.[538] Difficulty in getting to the hospital was the second most frequent reason for non-participation, despite the offer of reimbursement of travel costs or a pre-paid taxi. Travel issues and the burden of additional appointments are commonly reported barriers to trial participation.[538,555] Future trials of group-based interventions may benefit from consideration of the location of the intervention. For example, interventions held in the community may have greater uptake than those delivered in a hospital, although trials of community-based group interventions also found that difficulties with travel is a common reason for non-participation.[538] Conducting these short interviews with non-participants identified a number of barriers to participation that could be addressed in further refinement work, highlighting the importance and value of conducting research with non-participants in feasibility studies.

Recruitment, retention and outcomes assessment

The recruitment rate for this trial was 23%, which is lower than the 42–79% recruitment rates reported in previous trials of pain self-management interventions for patients undergoing joint replacement.[487,527] However, other feasibility and pilot studies using a postal recruitment method have reported similarly low response rates.[547,556,557] Despite the low recruitment rate, retention of participants and questionnaire completion were high and similar between the trial arms, suggesting that randomisation and outcomes assessment were acceptable.

Recruitment into trials is known to be challenging and considerable research has been conducted into improving trial recruitment. Methods such as telephone reminders to non-responders, 'opt-out' recruitment strategies and financial incentives have been found to improve recruitment rates.[558] However, potential issues around coercion and undue influence can pose challenges to the implementation of these strategies. Financial incentives for research participation is a debated issue and ambiguities remain around what level of incentive constitutes undue influence, with little standardised guidance for Ethics Committees.[559] For example, we planned to offer participants free 1-year membership to Arthritis Care but the Ethics Committee perceived this as potentially coercive and asked for this offer to be removed from the study protocol. This demonstrates the challenges researchers can face in implementing measures to maximise recruitment into trials while remaining in-keeping with preferences of the NHS Research Ethics Committee.

Economic evaluation

The economic evaluation work highlighted the difficulty of collecting resource-use data from randomisation until surgery for this patient group. However, average waiting time for surgery in this patient group was 3 months and we would not expect the intervention to lead to behaviour change that would produce differences in cost drivers in the shorter term. In comparison with the pre-operative diaries, the postoperative resource-use questionnaires achieved good completion rates, allowing for a health and social care payer evaluation perspective to be taken. The completion rates could be further improved after imputation of community-based resource data. Although completion rates for a societal perspective were low, categories on productivity losses and informal carer time were well completed and can be of added value to a sensitivity analysis in a definite economic evaluation.

Acceptability of the intervention

In addition to assessing trial processes, this study evaluated the acceptability of the intervention. Feedback on the course was positive, suggesting that the course was acceptable and well received by those who attended. In particular, positive feedback was received on the group-based format, with patients commenting that they appreciated the opportunity to meet other people undergoing THR surgery. Studies evaluating group-based interventions in other clinical settings have also reported positive feedback on this format of intervention delivery.[549,557,560] Therefore, although the group format was a reason for non-participation for some patients, those who attended the course enjoyed the format and engagement with other patients. This highlights an issue affecting many trials: a potentially biased sample because of the self-selection of participants with a preference for the intervention. Differences in the characteristics of participants and non-participants are well known, with an underrepresentation of older people, women and ethnic minorities in clinical research.[561] Addressing willingness to participate owing to the nature of the intervention in feasibility work has the potential to lead to refinements in the intervention for a definitive trial and this knowledge has implications for the roll-out and uptake of interventions if subsequently implemented in clinical practice.

The Challenging Pain and Keep Challenging Pain courses were highly rated by participants, but attendance at the postoperative course was lower than at the pre-operative course. Reasons given for non-attendance were predominantly that people were unavailable on the dates set for the course. The logistics of scheduling group-based interventions is challenging, as many patients have limited availablity owing to other commitments.[538,549] Increasing flexibility in the scheduling of group-based interventions can be challenging, particularly within the financial constraints of a trial, but having the flexibility to run multiple courses is an important factor to consider when costing a trial.

Conclusion

Undertaking feasibility work for a RCT and evaluating the acceptability of an intervention can be a labour-intensive exercise. However, this study highlights the importance of conducting such work prior to undertaking a full-scale RCT to assess the clinical effectiveness and cost-effectiveness of an intervention. Several key messages can be taken from our experience. First, conducting brief telephone interviews with non-participants is an efficient and valuable method of collecting data on barriers to participation and we recommend including this as a core component of feasibility studies. These data can also provide insight into whether or not unwillingness to participate is due to the nature of the intervention, thereby providing early indications of potential issues in a definitive trial and with uptake of the intervention if implemented into clinical practice. Second, attempts to implement methods to improve patient recruitment need to be carefully designed in light of ethical considerations, such as the potential for inducements to be seen as coercion. Third, the logistical difficulties in scheduling groups and ensuring high attendance should not be underestimated and the potential to increase flexibility by running multiple courses should be considered when designing a budget for a trial. Finally, the ability of piloting resource-use questionnaires is a major advantage to improve the quality of the resource-use data available in the definitive economic evaluation.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Chapter 10 Occupational therapy in total hip replacement: systematic review and feasibility randomised controlled trial

Parts of this chapter have been reproduced with permission from Jepson P, Sands G, Beswick AD, Davis ET, Blom AW, Sackley CM. A feasibility randomised controlled trial of pre-operative occupational therapy to optimise recovery for patients undergoing primary total hip replacement for osteoarthritis (PROOF-THR). *Clin Rehabil* 2015;**30**:156–66.[562]

Abstract

Background
Occupational therapy is routinely provided for patients with THR as part of the rehabilitation service but little is known about its clinical effectiveness.

Methods
We conducted a systematic review of the clinical effectiveness of occupational therapy interventions in patients receiving THR.

The PROOF-THR study evaluated the feasibility of a RCT of pre-surgical occupational therapy in patients waiting for THR. Primary objectives were to assess patient identification, recruitment and retention, acceptability of allocation and health resource use, and outcome measures.

Results
In patients receiving THR, the systematic review identified seven RCTs of occupational therapy, mainly combined with physiotherapy. There was a suggestion of improved function and reduced pain before surgery but this was not sustained after surgery. In the PROOF-THR study, 44 patients were randomised to pre-operative occupational therapy or usual care. Good recruitment rates, acceptability of randomisation of participants, successful intervention delivery, and reasonable attrition rates suggest a definitive trial would be feasible.

Conclusions
The successful recruitment and randomisation of participants and delivery of the intervention, plus the reasonable attrition rate, suggest that this trial design would be feasible to take forward into a definitive trial of occupational therapy provision before THR.

Background

Occupational therapy is routinely provided for patients with THR as part of the rehabilitation service but little is known about its effectiveness. The provision of compensatory equipment is a key aspect of occupational therapy practice but evidence is needed on its clinical effectiveness and to optimise its delivery. Economic pressures have had a dramatic impact on length of hospital stay following THR, such that reduction in length of stay has been a common outcome measure used to justify many pre-operative interventions. Hospitalisation for $\geq$ 10 days post surgery was common practice prior to 2000;[563] however, now most patients are discharged after 4–5 days.[564] An important corollary of this reduced length of stay is the time available in hospital for recuperation, inpatient rehabilitation, education and discharge procedures.[565] Although some variation in practice does exist, it is usual practice in the UK for OTs to provide compensatory equipment, together with education on its use, in this short post-surgery/pre-discharge period. Pre-surgery home-based provision has been identified as desirable by patients and potentially assistive in functional rehabilitation.[566]

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

To investigate evidence on the clinical effectiveness of a broad range of occupational therapy interventions in patients receiving THR, we conducted a systematic review of RCTs. We also conducted a feasibility study for a definitive randomised evaluation of the clinical effectiveness of a pre-surgery home-based occupational therapy intervention compared with hospital-based usual care.

Systematic review and meta-analysis of the effectiveness of occupational therapy interventions in total hip replacement

Background

Our aim was to identify RCTs evaluating occupational therapy interventions in isolation or as part of multifaceted interventions in patients receiving a THR. The key outcomes in occupational therapy relate to patient physical function, activity, social participation, HRQoL and pain, and prevention of dislocation.

Methods

General methods	As described in *Chapter 2*, *Systematic review methods*
Databases and dates	MEDLINE, EMBASE, CINAHL, PsycINFO, AMED, PEDro, ERIC, CIRRIE, OTDbase and The Cochrane Library from inception to 24 June 2013. Citations of key articles in ISI Web of Science and reference lists
Search strategy	Hip replacement/RCT/occupational therapy. MEDLINE search strategy based on terms in *Appendix 3*
Study design	RCTs with randomisation either at individual or cluster level. Quasi-randomised designs (e.g. alternate allocation)
Patients	Adults waiting for THR
Intervention	Occupational therapy
Controls	No occupational therapy intervention additional to usual care
Follow-up	Any post surgery
Data extraction	Country, baseline dates, participants (indication, age, sex), content of intervention and comparison group, length of follow-up, losses to follow-up
Potential outcomes	Patient-reported physical function
	Patient-reported pain
	Limitations in self-care ADL
	Restrictions in extended or instrumental ADL
	Societal reintegration or discretionary activities
	Hip dislocation
	Adverse events including deep infection or joint revision surgery
Quality assessment	Cochrane risk-of-bias table

Results

Review progress is summarised as a flow diagram in *Figure 42*. Searches identified 4865 articles. Twenty-nine articles were reviewed in full. After screening and detailed evaluation, seven interventions met the inclusion criteria.[489,493,496,501,504,567,568] Study characteristics are summarised in *Table 82*. As our review focused on THR and the specific occupational therapy content provided to this patient group, we excluded two studies with both total hip and TKR patients with no separate outcome reporting.[528,569] Two studies were conducted in the UK and one each in Iceland, Turkey, the USA, Canada and Italy.

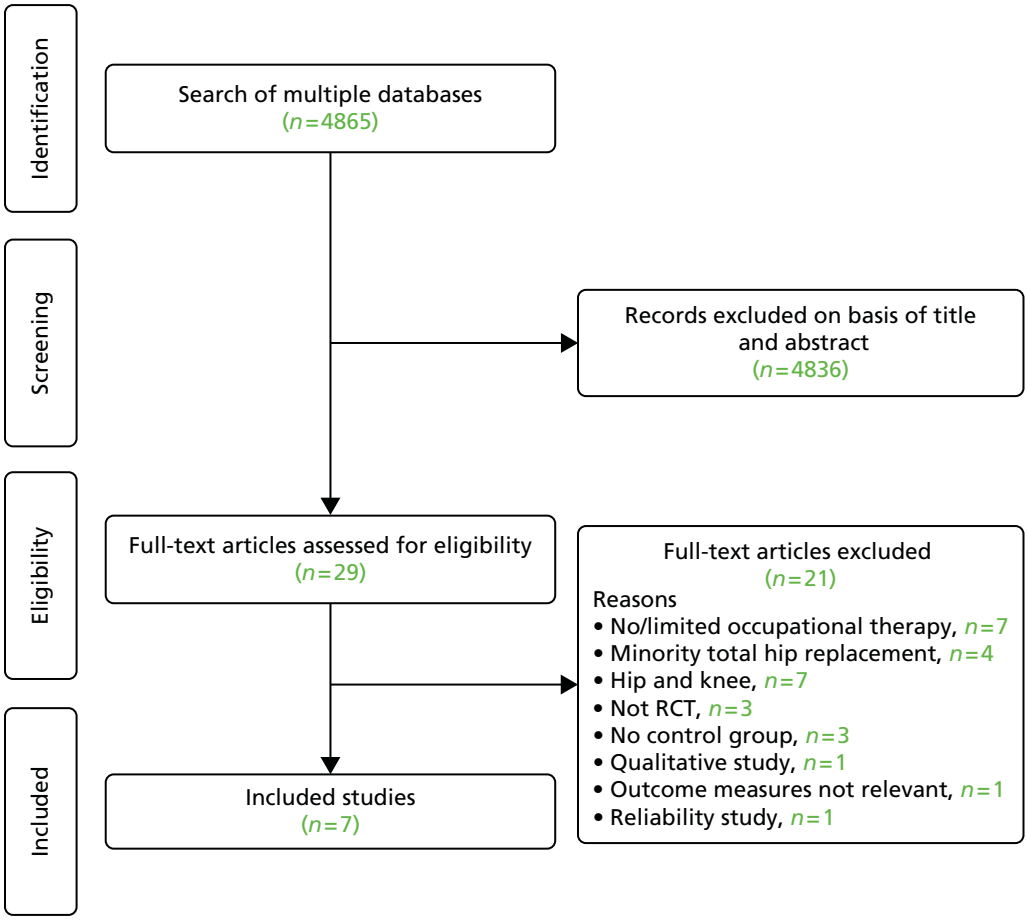


FIGURE 42 Systematic review and meta-analysis of the effectiveness of occupational therapy interventions in THR: flow diagram

TABLE 82 Systematic review and meta-analysis of the effectiveness of occupational therapy interventions in THR: study characteristics

Study; location; dates	Indication; number randomised (intervention : control); mean age (years) (% female)	Intervention; control	Outcomes; follow-up; losses to follow-up (intervention : control)
Butler and colleagues 1996;[489] Canada; 1993–4	Not specified; $n = 80$ (32 : 48); 62.6 (51.3)	Pre-admission education booklet; usual care – same information as in pre-admission booklet given following admission	State-Trait Anxiety Inventory, patient satisfaction questionnaire, exercise log and details of home adaptations, length of hospital stay; to discharge; one patient died and no follow-up data from eight patients
Ferrara and colleagues 2008;[493] Italy; 2006–7	End-stage osteoarthritis; $n = 23$ (11 : 12); 63.4 (60.9)	5-day pre-admission intervention package 1 month before admission consisting of exercise, postural advice, advice on movement restrictions and prevention of prosthesis dislocation, use of devices (crutches, elevated toilet sets, bed raises, dressing/undressing adaptive devices), washing and bathing; no pre-admission intervention	WOMAC, SF-36, VAS (pain), Barthel, hip strength and range of movement; day before surgery, 15 days, 4 weeks, 3 months; two (0 : 2) patients lost to 3-month follow-up

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 82 Systematic review and meta-analysis of the effectiveness of occupational therapy interventions in THR: study characteristics (*continued*)

Study; location; dates	Indication; number randomised (intervention : control); mean age (years) (% female)	Intervention; control	Outcomes; follow-up; losses to follow-up (intervention : control)
Gocen and colleagues 2004;[496] Turkey; not specified	Primary or secondary osteoarthritis; $n = 59$ (29 : 30) also one patient in intervention group who did not receive replacement; 51.3 (35.6)	Pre-operative exercises plus occupational therapy-based education class (movement restriction, use of adaptive devices, lifting and carrying, washing and dressing; no pre-operative intervention	HHS, VAS (pain), days to achieve functional milestones (walking, stairs, bed transfer, toilet transfer, chair transfer); day of discharge, 3 months, 2 years; no losses to follow-up
McGregor and colleagues 2004;[501] UK; 1998–9	Osteoarthritis; $n = 39$ (19 : 20); 71.9 (42.9)	Pre-admission hip class plus education booklet with information on surgery, rehabilitation, walking aids and home adaptations; usual care – no pre-operative advice	WOMAC, HHS, Barthel ADL, Positive-affect Negative-affect scale, Helplessness subscale of Rheumatology attitudes index, Cantril life satisfaction ladder, VAS (pain, fatigue and function), EQ-5D; day of admission, discharge, 3 months; four (4 : 0) patients lost to follow-up
Munin and colleagues 1998;[567] USA; 1994–6	High risk for requiring inpatient rehabilitation; $n = 35$ (19 : 16); 75 (85)	Phased postoperative rehabilitation starting day 3 post surgery; usual care – rehabilitation starting day 7 post surgery	Functional Status Index, SF-36, length of hospital stay, complications; 4 months; ITT analysis; nine (5 : 4) patients lost to follow-up
Sandell 2008;[504] UK; 2003	Waiting time of ≥ 6 months; $n = 89$ (43 : 46); 68.2 (65.1)	Preadmission multidisciplinary intervention by physiotherapist (exercises and gait improvement), nurse (additional advice). Pre-operative occupational therapy home assessment of functional constraints and provision of adaptive devices; no additional pre-operative treatment by OT or physiotherapist and standard advice from nurse	AIMS2, NHP; day of admission; 26 (10 : 16) lost to follow-up
Siggeirsdottir and colleagues 2005;[568] Iceland; 1997–2000	90% osteoarthritis; $n = 50$ (27 : 23); 68 (52)	Pre-admission training and education programme. Post-discharge home physiotherapist, OT or nurse input as required; usual care – not specified	OHS, NHP, HHS Merle d'Aubigné and Postel score; 2, 4, 6 months; 2 (0 : 2) lost to pre-operative follow-up; three lost to 6-month follow-up (0 : 3)

Participants

Studies included a total of 366 participants (range 23–89). The mean age of participants ranged from 51 to 75 years. The proportion of female patients in trials ranged from 36% to 85%.

Interventions

Five studies reported a pre-admission intervention with occupational therapy content compared with controls receiving usual care. Pre-surgical interventions were education with a booklet[489] or a booklet and class[501] or multidisciplinary with occupational therapy provided within an education and exercise programme.[493,496,504] One study evaluated a multidisciplinary intervention that provided occupational therapy as part of pre- and post-surgery education and home-based rehabilitation.[568] One study compared early rehabilitation including an occupational therapy session starting on post-surgical day 3 with similar post-surgery care commencing on post-surgical day 7.[567]

Risk of bias

Potential sources of bias are summarised in *Appendix 32*. The main sources of possible bias were high losses to follow-up in three studies.[501,504,567] In one study, possible bias was identified as 123 patients with any hip replacement were randomised but only data from 80 patients with a primary hip replacement were analysed.[489]

Outcomes

Results are summarised in *Table 83*. In analyses we only considered patient-reported physical function and pain.

Physical function

Five studies assessed patient-reported physical function using functional domains of the OHS,[568] SF-36,[567] NHP,[504] or WOMAC.[493,501] The results of meta-analyses are shown in *Table 83* and *Figure 43*. Two studies included in the meta-analyses reported change scores.[504,567]

TABLE 83 Systematic review and meta-analysis of the effectiveness of occupational therapy interventions in THR: meta-analysis

Outcome	Studies	Patients	Pooled effect size (95% CI)	*p*-value	I^2 (%)
Patient-reported physical function					
Pre-surgery	4	173	–0.40 (–0.70 to –0.09)	0.01	0
Discharge	1	39	–0.24 (–0.87 to 0.39)	0.45	
Long term	4	135	–0.52 (–1.17 to 0.13)	0.12	69
Patient-reported physical function: low risk of bias					
Pre-surgery	2	71	–0.63 (–1.12 to –0.15)	0.01	0
Discharge					
Long term	2	70	–1.09 (–1.60 to –0.58)	< 0.0001	0
Patient-reported pain					
Pre-surgery	3	125	–0.29 (–0.64 to 0.07)	0.11	0
Discharge	2	98	–0.20 (–0.59 to 0.20)	0.33	0
Long term	3	90	0.06 (–0.67 to 0.80)	0.87	66
Patient-reported pain: low risk of bias					
Pre-surgery	2	86	–0.41 (–0.84 to 0.02)	0.06	0
Discharge	1	59	–0.04 (–0.55 to 0.47)	0.89	
Long term	1	23	–0.23 (–1.06 to 0.59)	0.58	
Length of hospital stay					
MD	3	146	–2.25 (–4.15 to –0.34)	0.02	64
Length of hospital stay: low risk of bias					
MD	1	50	–3.60 (–5.29 to –1.91)	< 0.0001	
HRQoL					
Pre-surgery	3	125	–0.52 (–0.91 to –0.12)	0.01	14
Discharge	1	39	–0.06 (–0.68 to 0.57)	0.86	
Long term	3	90	–0.20 (–0.62 to 0.22)	0.35	1

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Study or subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	SMD IV, random, 95% CI
Pre-surgery								
Ferrara 2008[492]	33.7	13.8	11	43.5	9.5	12	12.5%	–0.80 (–1.66 to 0.05)
McGregor 2004[500]	35.8	12	19	41	10	20	22.7%	–0.46 (–1.10 to 0.17)
Siggeirsdottir 2005[568]	33	7.5	27	37	6.5	21	27.2%	–0.56 (–1.14 to 0.03)
Sandell 2008[503]	–0.47	12.47	33	1.44	23.13	30	37.6%	–0.10 (–0.60 to 0.39)
Subtotal (95% CI)			**90**			**83**	**100.0%**	**–0.40 (–0.70 to –0.09)**
Heterogeneity: τ^2=0.00; χ^2=2.55, df=3 (p=0.47); I^2=0%								
Test for overall effect: z=2.55 (p=0.01)								
Discharge								
McGregor 2004[500]	25.7	8.3	19	28.3	12.1	20	100.0%	–0.24 (–0.87 to 0.39)
Subtotal (95% CI)			**19**			**20**	**100.0%**	**–0.24 (–0.87 to 0.39)**
Heterogeneity: not applicable								
Test for overall effect: z=0.76 (p=0.45)								
Long term								
Ferrara 2008[492]	18.3	12.36	11	28.5	10.01	12	22.0%	–0.88 (–1.74 to –0.01)
Munin 1998[567]	–14.06	27.7	14	–19.58	16.3	12	23.9%	0.23 (–0.54 to 1.00)
Siggeirsdottir 2005[568]	14	4.3	27	21	7.2	20	27.0%	–1.21 (–1.84 to –0.57)
McGregor 2004[500]	15.9	10.3	19	18.4	13.8	20	27.0%	–0.20 (–0.83 to 0.43)
Subtotal (95% CI)			**71**			**64**	**100.0%**	**–0.52 (–1.12 to 0.13)**
Heterogeneity: τ^2=0.30; χ^2=9.78, df=3 (p=0.02); I^2=69%								
Test for overall effect: z=1.57 (p=0.12)								
Test for subgroup differences: χ^2=0.36, df=2 (p=0.84), I^2=0%								

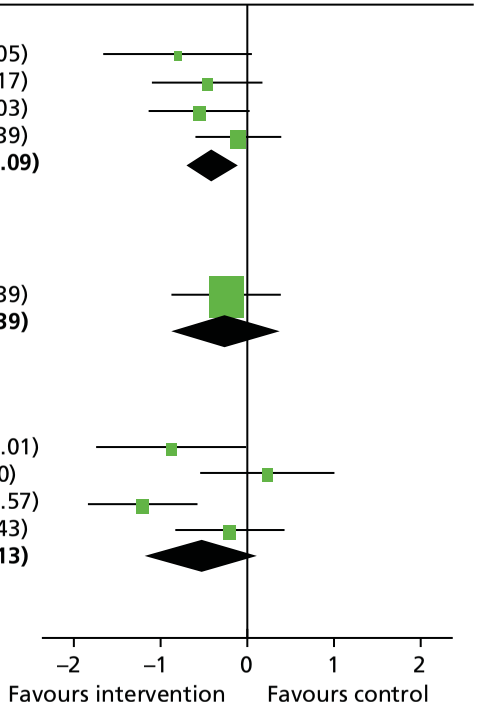


FIGURE 43 Patient-reported physical function. df, degrees of freedom; IV, inverse variance. WOMAC function: Ferrara and colleagues[493] and McGregor and colleagues.[501] OHS function: Siggeirsdottir and colleagues.[568] NHP physical: Sandell and colleagues.[504] SF-36 physical function: Munin and colleagues.[567]

In the four studies with follow-up before surgery, physical function was better in patients who received an intervention with occupational therapy content (SMD –0.40, 95% CI –0.70 to –0.09; $p = 0.01$).[493,501,504,568] Benefit was apparent in the two studies with low or no reason to assume risk of bias.[493,568] In one study with follow-up at hospital discharge there was no suggestion of benefit[501] but in four studies with longer-term follow-up there was a trend favouring occupational therapy interventions.[493,501,567,568] In two studies with low risk of bias or in which there was no reason to assume risk of bias, there was benefit for occupational therapy at long-term follow-up (SMD –1.09, 95% CI –1.60 to –0.58; $p < 0.0001$).[493,568]

Pain

Pain outcomes were reported in five studies using a VAS pain scale,[493,496,501] SF-36 bodily pain,[567] NHP pain,[504] or WOMAC pain score.[493,501] In the meta-analyses summarised in *Table 83* and *Figure 44*, we used WOMAC pain scores in preference to VAS scores when available. One study reported a change score.[567]

There was a trend in three studies for reduced pain in patients who received occupational therapy followed up before surgery,[493,501,504] but only one study had a low risk of bias.[493] Studies were small and the limited evidence available from three studies did not support a long-term benefit.[493,501,567]

Length of hospital stay

The length of stay or time to hospital discharge was reported in three studies.[489,567,568] The overall mean hospital stay was 10.1 days. As shown in *Table 83* and *Figure 45*, patients receiving occupational therapy interventions spent a mean of 2.25 days fewer in hospital (95% CI –4.1 to –0.34 days; $p = 0.02$). Only one study was at low risk of bias and in this study the hospital stay was reduced further.[568]

Health-related quality of life

Four studies reported a measure of HRQoL. These were SF-36 physical domains,[493,504,567] and EQ-5D.[501] As shown in *Table 83* and *Figure 46*, interventions with occupational therapy content before surgery showed benefit for improved HR-QoL but this was not sustained in the long term.

Other outcomes

Other key outcomes in studies of occupational therapy relate to prevention of dislocation (hip precautions) anxiety and social participation. These were infrequently reported. Dislocation was reported in one study with a total of only three events in 50 patients randomised.[568]

One study reported a measure of anxiety.[489] After adjustment for sex, anxiety before surgery and at time of hospital discharge was lower in patients who received an intervention with pre-surgical education including occupational therapy content.

Social activity domains of the AIMS2 and NHP measured after the intervention but before surgery were reported in one study.[504] There was a statistically significant difference between groups in the NHP social isolation domain favouring the intervention. For the AIMS2 social activity domain, the effect was in the opposite direction, favouring the control group, but this was marginally not statistically significant.

Discussion

Few studies have evaluated the effectiveness of occupational therapy in patients receiving THR. In the seven studies that we identified, occupational therapy was mainly evaluated in combination with physiotherapy. Only in two studies was the occupational therapy component the principal focus of the intervention. In the study of Ferrara and colleagues,[493] patients received a 5-day pre-admission occupational therapy-based intervention but only 23 patients were randomised. McGregor and colleagues[501] evaluated a pre-admission educational hip class and booklet with a major focus on occupational therapy in 39 patients.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Study or subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	SMD IV, random, 95% CI
Pre-surgery								
Ferrara 2008[492]	8	3.8	11	11	3.6	12	17.2%	–0.78 (–1.64 to 0.07)
McGregor 2004[500]	10.2	2.7	19	10.3	4.1	20	31.9%	–0.03 (–0.66 to 0.60)
Sandell 2008[503]	–1.46	22.58	33	4.93	22.77	30	50.9%	–0.28 (–0.78 to 0.22)
Subtotal (95% CI)			**63**			**62**	**100.0%**	**–0.29 (–0.64 to 0.07)**
Heterogeneity: τ^2=0.00; χ^2=1.94, df=2 (p=0.38); I^2=0%								
Test for overall effect: z=1.58 (p=0.11)								
Discharge								
Gocen 2004[495]	1.24	1.6	29	1.3	1.73	30	60.9%	–0.04 (–0.55 to 0.47)
McGregor 2004[500]	3.2	2.7	19	4.5	3	20	39.1%	–0.45 (–1.08 to 0.19)
Subtotal (95% CI)			**48**			**50**	**100.0%**	**–0.20 (–0.59 to 0.20)**
Heterogeneity: τ^2=0.00; χ^2=0.97, df=1 (p=0.32); I^2=0%								
Test for overall effect: z=0.96 (p=0.33)								
Long term								
Ferrara 2008[492]	1.7	2.35	11	2.2	1.75	12	31.0%	–0.23 (–1.06 to 0.59)
McGregor 2004[500]	2.7	2.1	19	0.1	4.4	20	36.2%	0.73 (0.08 to 1.38)
Munin 1998[567]	–39.22	22.26	16	–29.79	24.04	12	32.9%	–0.40 (–1.15 to 0.36)
Subtotal (95% CI)			**46**			**44**	**100.0%**	**0.06 (–0.67 to 0.80)**
Heterogeneity: τ^2=0.28; χ^2=5.91, df=2 (p=0.05); I^2=66%								
Test for overall effect: z=0.16 (p=0.87)								
Test for subgroup differences: χ^2=0.70, df=2 (p=0.70), I^2=0%								

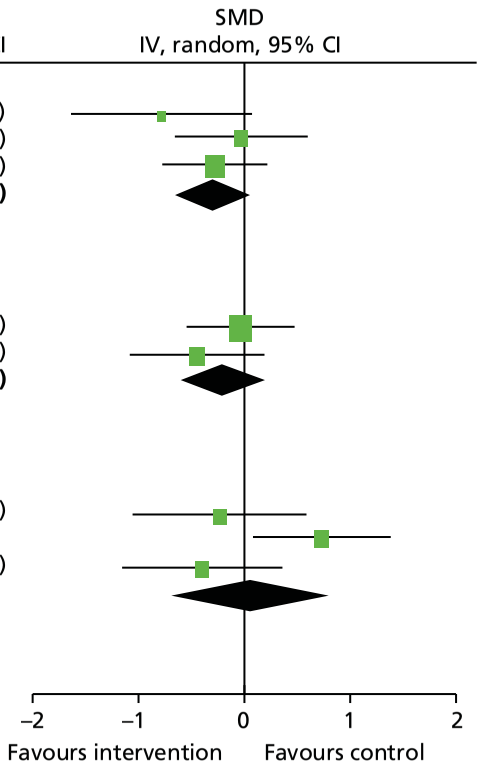


FIGURE 44 Patient-reported pain. df, degrees of freedom; IV, inverse variance. SF-36 bodily pain: Munin and colleagues.[567] NHP pain: Sandell and colleagues.[504] WOMAC pain: McGregor and colleagues,[501] Ferrara and colleagues.[493] VAS pain during activity: Gocen and colleagues.[496]

FIGURE 45 Length of hospital stay. df, degrees of freedom; IV, inverse variance.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

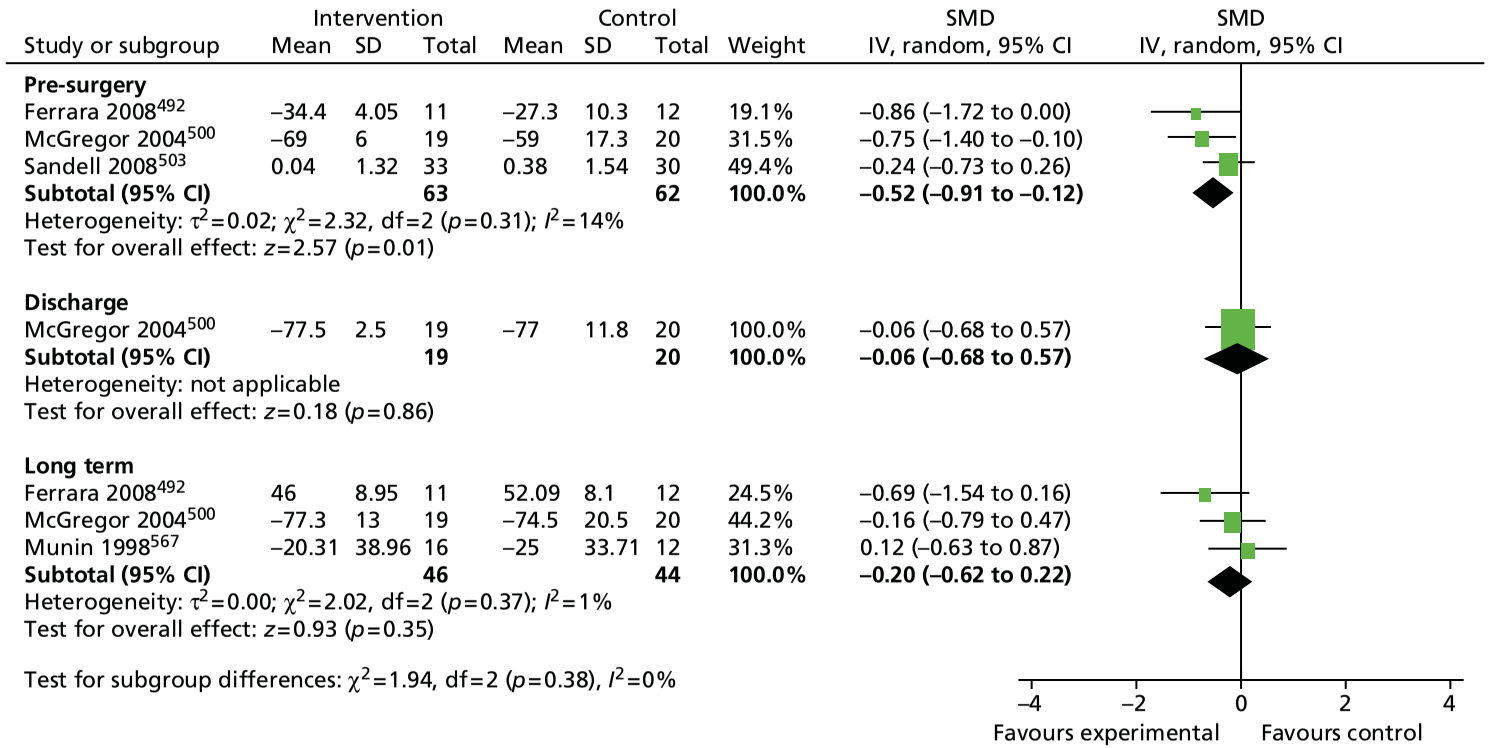


FIGURE 46 Health-related quality of life. df, degrees of freedom; IV, inverse variance. SF-36 (physical composite score): Ferrara and colleagues.[493] EQ-5D McGregor and colleagues[501] (data scaled from graph – original data not available). RAND-36 (role functioning physical): Munin and colleagues.[567] Arthritis impact measure score (satisfaction with life): Sandell and colleagues.[504]

Overall, studies suggested a possible benefit for improved function and reduced pain before surgery, but this was not sustained after surgery. However, in three studies with data, there was a reduction in length of hospital stay of over 2 days when the overall average length of stay was 10 days.

Studies were generally small with little possibility of exploring key outcomes. A primary focus of occupational therapy in THR is the prevention of dislocation. This occurs in about 1% of patients treated by a posterior approach and about 4% of people treated with a lateral approach.[570] Only one study with three events in 50 patients randomised reported this outcome. OTs teach a range of hip precautions and provide equipment designed to help avoid extreme hip flexion, adduction and rotation with the aim of reducing the risk of dislocation,[571,572] but recently their value in preventing dislocation has been questioned.[150,573,574] Recovery after hip replacement without traditional restrictions to movement may allow earlier rehabilitation.

Conclusion

The evidence base on the clinical effectiveness of occupational therapy in patients receiving THR is limited. The need for high-quality, appropriately powered randomised trials to evaluate aspects of occupational therapy in this population is indicated.

Occupational therapy: PROOF-THR

Background

We conducted a RCT to evaluate the feasibility of a randomised evaluation of a pre-surgical occupational therapy intervention in patients waiting for THR. The content of the intervention was based on evidence from literature review and discussions with the RESTORE steering group, experts in occupational therapy research and the PEP-R group. Control patients received usual care including occupational therapy after surgery as provided by the hospital.

The primary objectives were to assess rates of patient identification, recruitment and retention; acceptability of the intervention and control allocation; health resource use; and outcome measures. Secondary outcomes related to pain, functional activity and societal participation.

Methods

Study design and setting

We conducted a single-blind parallel-arm pilot RCT with randomisation at the level of the individual. Randomisation was stratified by hospital and age (< 65 years; ≥ 65 years). The feasibility study took place at the Royal Orthopaedic Hospital NHS Trust in Birmingham, which is a specialist orthopaedic hospital, and at Russells Hall Hospital, which is a general hospital and part of the Dudley Group NHS Foundation Trust. Participants were followed up for a period of 6 months after surgery and completed a series of quality-of-life questionnaires measuring function, societal participation and resource use.

Participants

Selection criteria

Inclusion criteria were:

- patients listed for primary unilateral THR following review in orthopaedic clinic
- osteoarthritis as the primary indication for surgery
- no previous lower limb joint replacement surgery
- no planned additional lower limb joint replacement surgery within 12 months
- sufficient understanding of English to complete questionnaires (or proxy completion by representative who understood English).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Exclusion criteria were:

- patients with inflammatory arthritis
- primary indication for surgery was for pain relief only and no functional improvement is anticipated
- patients who were unable to provide informed consent.

Recruitment

Research nurses screened the records of patients listed for a primary THR following assessment in participating orthopaedic assessment clinics. When eligibility was confirmed against the inclusion and exclusion criteria, the research nurse sent the potential participants an information study pack. The study pack contained the patient information leaflet, copy of the consent form and a letter of invitation to join the study. One week after posting of this information, potential participants were contacted by a member of the research team to ask if they would consider taking part in the study. Patients who expressed an interest in joining the study were approached by a member of the research team when they attended their pre-assessment clinic. The research nurses gave the potential participants time to discuss any issues or concerns they may have had prior to obtaining informed consent. Participants who did not use English as their first language were given a covering letter in their own language to invite them to take part. However, the assessments needed to be carried out using the English versions with the help of a relative or friend. Participants who were unable to do this were excluded as many of the outcome questionnaires were not validated in other languages. The patient's GP was informed of the patient's participation in the trial in writing, with the patient's consent.

Randomisation

Participants were randomised between the two groups (1 : 1) using a random assignment computer algorithm. A block allocation sequence was used with stratification by hospital site and age (< 65 years; ≥ 65 years). The randomisation and sequence generation was performed by a statistician within the Primary Care – Clinical Research Trials Unit, based at the University of Birmingham.

Allocation concealment and blinding

Following randomisation and group allocation, a study OT was contacted by the randomisation team when a participant was allocated to receive the intervention and given the study ID of the participant. The OT then obtained participant contact details from the password-protected database and arranged a convenient time to deliver the intervention. Within the research team, group allocation was revealed to the treating therapist only. As is usual in non-pharmacological trials, the participants could not be blinded to their group assignment. All other investigators, and the trial statistician, were blind to the randomisation outcome and to all information indicating assignment.

Treatment as usual

Patients randomised to the control 'treatment as usual' arm of the study received the usual NHS care provided to all patients undergoing elective THR in the NHS trust where they received surgery. At both NHS trusts in this feasibility study, OTs provided compensatory equipment in hospital post surgery, which is usual UK practice. Both NHS trusts also provided a pre-surgery multidisciplinary education package.

Intervention

Patients randomised to the intervention arm of the study were visited prior to surgery by an OT, who assessed the individual needs of each participant and their home circumstances. The OT delivered an intervention package that included providing the compensatory devices required by the participant and educating them in how they should be used. In addition, the OT discussed with the participants any expectations and anxieties they (or their carer) may have had, gave explanations about the surgery, hospital stay and postoperative inpatient rehabilitation, and discussed in depth with the participant how they planned to manage when they returned home. This included liaising with other professionals as appropriate. In addition, the OT explained how the layout of the participant's home may need temporary adaptation to reduce the risk of accidental dislocation. A structured home safety assessment was also

performed by the OT, based on the Westmead Home Safety Assessment form.[575] In order to standardise the intervention effect, the OT delivered the intervention to all participants at 4 weeks prior to their individual planned admittance date for surgery.

Once the home-based intervention had been delivered, the participant received the usual care pathway of the trust providing their THR surgery. This included access to the pre-surgery multidisciplinary education session.

Outcomes

The primary outcomes address the feasibility issues with respect to a full-scale RCT:

- Recruitment procedures and rates: recruitment procedures, identification of eligible patients, willingness of participants to be randomised, rates of recruitment and retention of participants in the trial.
- Suitability of outcome measures: to refine the choice of outcome measures to be taken forward to the main trial.
- Fidelity of the intervention: to investigate practicalities of OT compliance to the intervention delivery as designed in the protocol, the quality of the delivery and patient adherence with the intervention. An intervention study log will be completed which has been used successfully in previous studies.
- Effect size and sample size: to provide data on the effect size to allow for an accurate estimate of the sample size required for the main trial.
- Economic evaluation: to refine data collection required in order that an economic evaluation can be performed in the main trial.

Secondary outcomes

- Pain.
- Functional activity.
- Societal participation.

Outcome measurement timing

Baseline assessments were completed before randomisation immediately after patients consented to participate. For follow-up assessments, a questionnaire pack with pre-paid return envelope was posted to all participants for completion at 4, 12 and 26 weeks post surgery. This questionnaire pack contained the following validated self-completed questionnaires:

- OHS[274,576]
- WOMAC[114]
- Ab-IAP[285]
- HADS – anxiety subscale (HADS-A) and depression subscale (HADS-D)[281]
- Nottingham Extended Activities of Daily Living scale (NEADL)[298]
- EQ-5D-3L[278]
- ICEpop CAPability measure for Older people (ICECAP-O).[299]

At the final 26-week time point, the Client Service Receipt Inventory (CSRI)[577] was used to record the frequency and duration with which participants used education, health and social care services and support over the duration of the assessment period. Records included accommodation and personal care/staff arrangements, and relevant informal care inputs. The CSRI allows systematic recording of service use in a manner commensurate with estimating the costs of support packages. Once the data were collected, all services and supports were listed, and a unit cost (per day, per hour, per contact, etc.) estimated for each one. When available, service costs were taken from publicly available sources for health such as the Department of Health NHS Reference Costs[435] and social care costs from the PSS Research Unit health and social care unit costs.[441] In other cases, when services were unusual or likely to absorb a significant proportion of the total costs of support packages, service-specific unit costs were estimated using an equivalent methodology.[578] Each unit cost was multiplied by the frequency with which each participant

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

uses each service to arrive a total care package cost for each person. This total can be disaggregated in various ways, for example, by perspective or by different groups of participants. This information was then be used in conjunction with the EQ-5D and the ICECAP-O results to establish the feasibility of conducting a cost per QALY analysis from the data collected.

Statistical analysis

The primary aims of this feasibility study were to identify effective recruitment procedures, suitability of outcome measures and the fidelity of the intervention. This was evaluated by assessment of recruitment rates and response rates to all the outcome measures at 4, 12 and 26 weeks following surgery in the intervention and control arms of the study.

Secondary outcome analyses of the data collected were by ITT with no interim analysis.

Results

The recruitment of participants for this study ($n = 44$) fell short of the initial target of 60. The CONSORT flow diagram in *Figure 47* details the participant pathway through the study from the number of participants screened for inclusion in the study through to the number analysed.

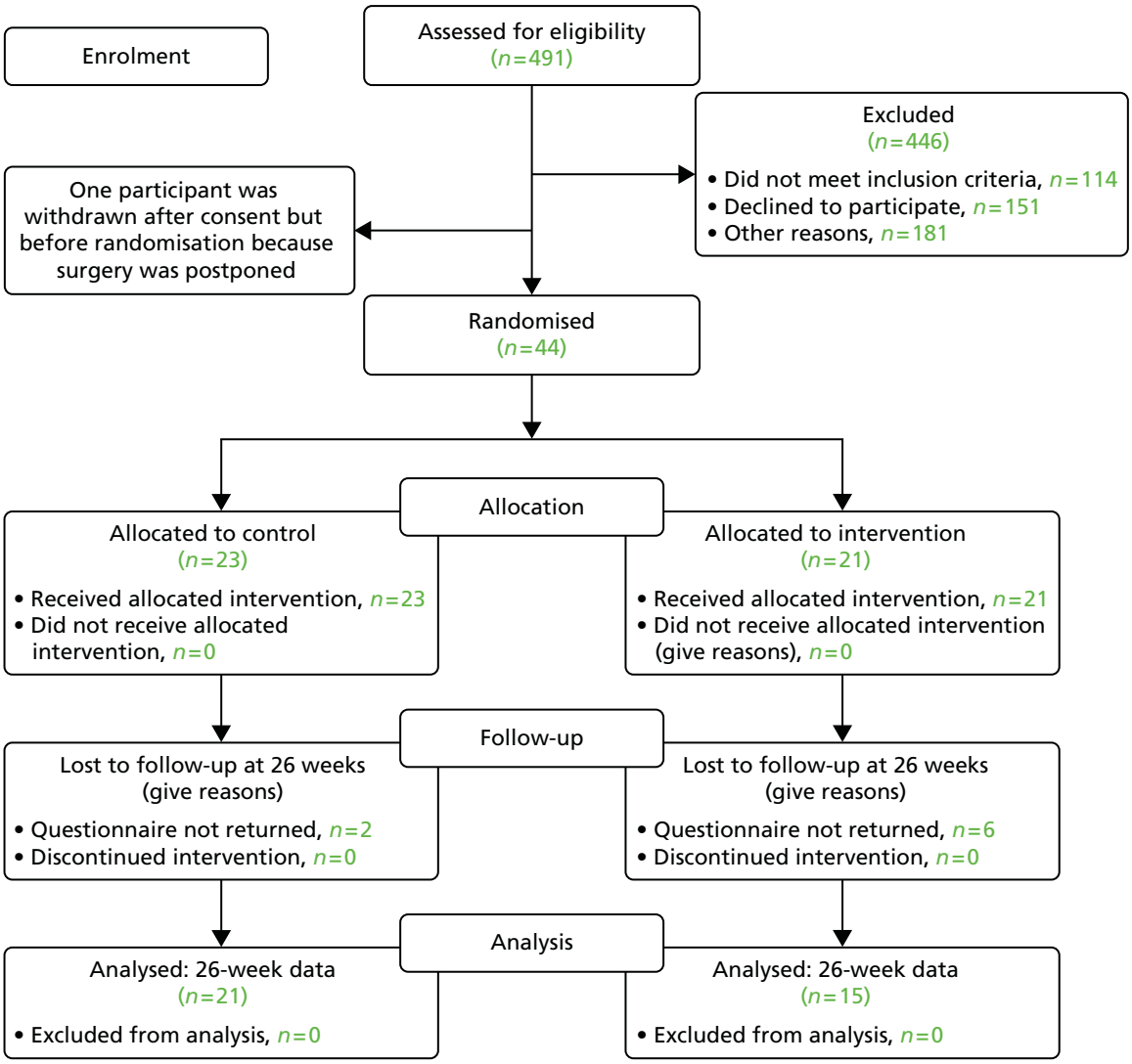


FIGURE 47 PROOF-THR CONSORT flow diagram.

PROOF-THR descriptive statistics

Retention and missing data

Baseline demographic and clinical characteristics of the participants are shown in *Table 84*. The mean age at the time of surgery was 66 years (SD 10.8 years), with similar means observed in the intervention group, 67 years (SD 11.2 years), and standard care group, 65 years (SD 10.7 years). Overall, there were more male patients (54%), although the distribution of sex differed between the intervention (67% male, 33% female) and standard care (44% male, 56% female) groups. In total, 14% of the study participants lived alone, with 5% of these randomised to the intervention group and 22% allocated to standard care.

Forty-four participants completed the baseline questionnaire. The retention rates for each of the follow-up periods are presented in *Table 85*. The retention rate remained consistent throughout the study period, with 82% of the participants retained after 26 weeks for the follow-up questionnaire, although the CSRI return rate was slightly lower (70%) despite being sent alongside the 26-week questionnaire.

Questionnaire completion rates are presented in *Table 86*. Although the number of fully complete returned questionnaires was reasonable at baseline and at 26 weeks, completion rates were low in weeks 4 and 12, and for the CSRI questionnaire (< 50% complete).

TABLE 84 Baseline demographic and clinical characteristics of participants

Characteristic	Overall ($n = 44$)	Allocated to intervention ($n = 21$)	Allocated to standard care ($n = 23$)
Mean age at surgery (years) (SD)	66 (10.8)	67 (11.2)	65 (10.7)
% female : male	46:54	33:67	56:44
% lives alone	14	5	22

TABLE 85 PROOF-THR retention and follow-up data

Time point	Participants recruited, *n*	Data collected, *n* (%)	Lost to follow-up, %
Baseline	44	44 (100)	0
4 week	44	37 (84)	16
12 week	44	37 (84)	16
26 week	44	36 (82)	18
CSRI	44	31 (70)	30

TABLE 86 PROOF-THR questionnaire completion rates

Time point/questionnaire	Number of completers	% of returners (*n*/*N*)	% all (*n*/*N*)
Baseline	33	75 (33/44)	75 (33/44)
4 weeks	13	35 (13/37)	30 (13/44)
12 weeks	18	49 (18/37)	41 (18/44)
26 weeks	23	64 (23/36)	52 (23/44)
CSRI (26 weeks)	15	48 (15/31)	34 (15/44)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Table 87 presents the distribution of missing (non-answered) questions for each scale used in the study and each time point. Missing data are most prevalent in the WOMAC (122 total missing) and NEADL (105 total missing), while a number of scales exhibit little in the way of missing data (e.g. HADS-A, HADS-D, Ab-P). Of the total missing data, the 4-week returned questionnaires are the greatest contributor, accounting for more than half of the missing WOMAC and NEADL data. Questionnaires with the least missing data were observed in the baseline (54 total missing) and 26-week (35 total missing) follow-ups.

Descriptive statistics of scales

Tables 87–89 show the descriptive statistics for each of the outcome measures. Data for participants that had two or fewer missing questions per scale were filled using the mean of the data from the rest of the questions in that scale. Participants missing three or more questions per scale did not have a score calculated for that scale and were classed as missing ($n = 6$).

Table 88 presents the descriptive statistics for the functional section of the questionnaire comprising the WOMAC, OHS, Ab-IAP, NEADL, and HADS (-A and -D). The means for each scale grouped by allocation are also presented in *Table 89*. Data for each scale showed improvement at 4 weeks, apart from the NEADL scale, which showed improvement at 12 weeks. Improvement then continued to 26 weeks.

TABLE 87 PROOF-THR summary of missing data

Questionnaire (number of questions)	Baseline missing	4-week missing	12-week missing	26-week missing	Total missing
WOMAC (24)	14	66	30	12	122
OHS (12)	3	8	2	1	14
Ab-I (9)	4	5	1	1	11
Ab-A (17)	9	26	21	3	59
Ab-P (9)	0	3	0	1	4
NEADL (20)	21	59	13	12	105
HADS-A (7)	2	2	0	0	4
HADS-D (7)	1	2	0	0	3
EQ-5D (6)	0	8	0	4	12
ICECAP (5)	0	6	0	1	7
Total	54	185	67	35	341

ICECAP, ICEpop CAPability measure.

TABLE 88 PROOF-THR descriptive statistics (functional scales)

Scale	Scale range	Baseline mean (SD)	4-week mean (SD)	12-week mean (SD)	26-week mean (SD)
WOMAC	0[a]–100	59.13 (17.47)	31.38 (18.79)	23.93 (19.09)	13.31 (14.32)
OHS	0–48[a]	17.85 (7.32)	27.80 (9.99)	35.57 (9.69)	40.43 (7.43)
Ab-I	9[a]–45	31.62 (7.42)	18.79 (7.60)	16.21 (6.44)	14.71 (5.51)
Ab-A	17[a]–85	50.78 (14.15)	33.61 (14.15)	28.92 (12.57)	25.24 (8.43)
Ab-P	9[a]–45	21.57 (7.31)	17.21 (6.65)	13.43 (6.78)	11.47 (3.63)
NEADL	0–66[a]	48.32 (12.46)	44.20 (13.51)	52.09 (17.34)	59.63 (13.04)
HADS-A	0[a]–21	6.63 (4.89)	4.57 (4.32)	3.27 (4.07)	3.25 (3.61)
HADS-D	0[a]–21	6.04 (3.59)	4.46 (3.82)	2.81 (3.44)	2.28 (2.77)

a Best outcome.

TABLE 89 PROOF-THR descriptive statistics by allocation (functional scales)

Scale (scale range)	Baseline mean			26-week mean		
	Overall (SD)	Control (SD)	Intervention (SD)	Overall (SD)	Control (SD)	Intervention (SD)
WOMAC (0[a]–100)	59.13 (17.47)	61.41 (18.32)	56.50 (16.51)	13.31 (14.32)	15.67 (16.60)	9.95 (9.86)
OHS (0–48[a])	17.85 (7.32)	17.00 (6.28)	18.79 (8.38)	40.43 (7.43)	39.03 (8.33)	42.40 (5.63)
Ab-I (9[a]–45)	31.62 (7.42)	32.04 (6.15)	31.13 (8.79)	14.71 (5.51)	15.46 (6.41)	13.67 (3.89)
Ab-A (17[a]–85)	50.78 (14.15)	52.98 (13.82)	48.48 (14.46)	25.24 (8.43)	27.00 (9.53)	22.79 (6.09)
Ab-P (9[a]–45)	21.57 (7.31)	22.83 (6.36)	20.19 (8.17)	11.47 (3.63)	11.57 (3.08)	11.33 (4.41)
NEADL (0–66[a])	48.32 (12.46)	49.26 (10.32)	47.28 (14.67)	59.63 (13.04)	57.34 (16.18)	62.53 (6.95)
HADS-A (0[a]–21)	6.63 (4.89)	6.56 (4.58)	6.71 (5.33)	3.25 (3.61)	3.52 (3.66)	2.87 (3.62)
HADS-D (0[a]–21)	6.04 (3.59)	5.64 (2.50)	6.48 (4.51)	2.28 (2.77)	2.00 (2.00)	2.67 (3.64)

a Best outcome.

Tables 90 and *91* present the categorised HADS scores for anxiety and depression, respectively. The categories are as follows: low (0–7), borderline (8–10) and clinically significant (11–21). Percentages at both baseline and at 26 weeks are relatively consistent with those observed in the intervention and standard care groups, especially in the 'low' category. This is most apparent in the HADS-A data (see *Table 90*) where, at 26 weeks, the overall mean, mean intervention or mean standard care percentages are identical. Both the HADS-A and HADS-D mean data exhibit an increase in 'low' categorised responses from baseline to 26 weeks, in conjunction with a decrease in 'borderline' and 'clinically significant' responses.

Tables 92 and *93* present summaries of the EQ-5D and ICECAP-O scales from the health economics section of the questionnaire. All three of the scales used exhibit a mean increase in HRQoL, with high values observed at 26 weeks. A detailed breakdown of the answers to the EQ-5D and ICE-CAP-O questions is given in *Appendices 33* and *34*.

TABLE 90 PROOF-THR HADS-A scores

HADS-A score	Baseline mean ($n = 44$)			26-week mean ($n = 37$)		
	Overall (%)	Control (%)	Intervention (%)	Overall (%)	Control (%)	Intervention (%)
Low (0–7)	61	61	62	86	86	86
Borderline (8–10)	18	22	14	8	9	7
Clinically significant (11–21)	21	17	24	6	5	7

TABLE 91 PROOF-THR HADS-D scores

HADS-D score	Baseline mean ($n = 44$)			26-week mean ($n = 37$)		
	Overall (%)	Control (%)	Intervention (%)	Overall (%)	Control (%)	Intervention (%)
Low (0–7)	75	82	67	97	100	93
Borderline (8–10)	14	9	19	0	0	0
Clinically significant (11–21)	11	9	14	3	0	7

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 92 PROOF-THR summary of EQ-5D and ICECAP-O data

Scale	Scale range	Baseline mean	4-week mean	12-week mean	26-week mean
EQ-5D-3L	–0.594–1[a]	0.36	0.62	0.76	0.86
EQ-5D health state	0–100[a]	66.27	72.97	79.24	83.63
ICECAP-O	0–1[a]	0.80	0.83	0.87	0.91

a Best outcome.

TABLE 93 PROOF-THR summary of EQ-5D and ICECAP-O data

	Baseline mean ($n = 44$)			26-week mean ($n = 37$)		
Scale (scale range)	Overall	Control	Intervention	Overall	Control	Intervention
EQ-5D-3L (–0.594–1[a])	0.36	0.40	0.33	0.86	0.86	0.86
EQ-5D health state (0–100[a])	66.27	65.17	67.48	83.63	81.50	86.47
ICE-CAP-O (0–1[a])	0.80	0.82	0.79	0.91	0.90	0.92

a Best outcome.

Resource-use data

Table 94 presents a summary of the number of items missing from the returned CSRI questionnaires. Missing data are most prevalent in the 'medication' and 'friends/relatives help at home' sections, while both the 'friends/relatives time off work' and 'current work situation' sections were mostly returned complete. Comparing the randomisation arms of the study, the greatest number of missing data was observed in the control group, in particular in the 'medication' and 'friends/relatives help at home' sections, which have a considerably higher number of missing values than the same sections in the intervention group.

TABLE 94 Summary of resource-use questionnaire missing responses

	Total missing responses	
Question (number of possible responses per resource use)	Control	Intervention
Hospital resource use (A&E, outpatient appointments, overnight stays) (3)	12	13
Service use (e.g. GP, physiotherapy) (16)	16	11
Medication (type and payment) (7)	51	26
Personal costs incurred for NHS/social services (e.g. transport, cleaning, child care) (5)	23	16
Time off work (5)	4	1
Friends/relatives help at home (how many hours of help needed for household tasks) (11)	106	29
Friends/relatives time off work (how many hours taken off work to provide help) (1)	1	1
Current work situation (7)	3	0
Total	216	97

A&E, accident and emergency.

Discussion

This study looked at the feasibility of a pre-surgical occupational therapy intervention in patients waiting for THR. The primary objectives were to assess rates of patient identification, recruitment and retention; acceptability of the intervention and control allocation; health resource use; and outcome measures. Secondary outcomes related to pain, functional activity and societal participation.

Rates of patient identification

Participants were identified by research nurses screening patient notes in participating orthopaedic assessment clinics. Of the 491 patients screened, 332 patients (68%) were identified as eligible for inclusion in the trial. This represents a good rate of participant identification, with only 114 ineligible, mainly owing to previous or planned lower limb replacement (75%), which was an exclusion criterion.

Recruitment and retention

The recruitment rate for this trial was 22% of eligible patients, which is lower than the 48–85% recruitment rates reported in similar trials of rehabilitation regimes prior to or following THR surgery.[503,579,580] However, the recruitment rate may have been disproportionately influenced by the exclusion of patients enrolled in another conflicting trial (24% of the total excluded, $n = 109$). This is quite substantial as it is almost as many as the number of patients excluded because they did not meet the inclusion criteria ($n = 114$, 26%). In addition, of the 151 patients classified as 'declined to participate', there were 43 patients who expressed interest in the trial but were not randomised either because clinic appointments were brought forward, making it impractical to deliver the intervention, or because there was insufficient OT capacity to deliver the intervention. Therefore, the research nurses scheduled only 154 recruitment appointments, of which 20 were missed. In effect, this resulted in only 88 out of the 134 patients actually contacted refusing to participate. This makes the recruitment rate of patients contacted by the research nurses 34%.

Retention of participants in the study was high, with a follow-up questionnaire return rate of 82% at 26 weeks. This compares favourably with the 44–99% retention rates in clinical trials conducted between 1990 and 1999 reported by Davis and colleagues.[581]

Of the returned follow-up questionnaires, 64% were fully complete with no missing answers. This is a slightly lower rate of completion than the 75% noted in other trials;[582] however, it is not unusual for this type of trial to have some missing outcome data.[583] Through researcher contact with the participants involved with PROOF, it became apparent that some participants felt that the questionnaire pack was too long and repetitive. This was mainly due to this study comparing a number of outcome measures to determine which were most appropriate and useful for inclusion in a future definitive trial. Therefore, in a future trial, the questionnaire pack would probably be shorter, which may result in higher rates of response[584] and fewer missing data.

Acceptability of the Intervention

There were no participant withdrawals after allocation and there was no crossover from the intervention to control arm. In addition, all participants allocated to the intervention arm received the occupational therapy intervention. This suggests that the content of the occupational therapy intervention was acceptable to the participants and easily deliverable by the therapists involved. Therefore, the content of the intervention in this feasibility study is suitable to be carried through to a definitive trial.

Health resource use

The health resource-use questionnaire (CSRI) had quite a poor rate of both return and completion, with only 34% of the 44 participants returning correctly completed forms. This would suggest that for a future definitive trial the CSRI form would need to be adapted perhaps to make it simpler to complete. Other methods that could be considered would be for participants to keep a diary of NHS appointments and other resource information or the sending of more frequent questionnaires to capture data rather than asking people to think back over 6 months.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Outcome measures

The outcome measures used in this trial varied in their level of completeness and number of missing data, which ranged from 7 to 122 over the trial period. The scales with the most missing questions across the four time points were WOMAC (122 missing items) and NEADL (105 missing items). The scales with the fewest missing data were HADS (7 missing items), ICEpop CAPability measure (ICECAP) (seven missing items), EQ-5D (12 missing items) and OHS (14 missing items).

Some of the questions in the outcome measures also conflict with the hip precautions clinicians generally offer patients after hip replacements, for example not to bend more than 90 degrees for 6 weeks after surgery. Therefore, this may suggest that the 4-week follow-up period is not suitable and can explain higher rates of missing data.

Power calculation

We used data from PROOF to conduct a power calculation for a more definitive RCT of pre-operative delivery of occupational therapy. Based on the OHS and assuming a power of 80%, $\alpha = 0.05$ (two tailed), SD of 0.46 between arms at 26 weeks and attrition rate of 20%, we would require a total of 219 participants.

Conclusion

The PROOF-THR feasibility study has generated valuable insight into the feasibility and acceptability of an occupational therapy intervention for people having THR because of osteoarthritis. The recruitment of patients was negatively influenced by another conflicting trial taking place at the same site and, to a lesser extent, the practicalities of delivering the intervention when surgery times are very close to the pre-assessment clinic appointment. Therefore, to attain a better rate of recruitment in a future trial, ways to overcome these recruitment issues will need to be considered. The rates of follow-up were good, but there were high levels of missing data at some time points (4 weeks) and for some outcome measures (WOMAC, NEADL), which would suggest that these may need to be revised for future work. The CSRI form was not completed well by participants, so it may be necessary to use other methods of collecting health economic data in a definitive trial to accurately measure the cost-effectiveness of the intervention. However, with further strategies in place to facilitate recruitment and intervention delivery, it would be feasible to evaluate this intervention in a phase III definitive trial.

Chapter 11 Physiotherapy exercise after total knee replacement: systematic review, survey of provision and feasibility randomised controlled trial

Parts of this chapter have been reproduced with permission from Artz N, Dixon S, Wylde V, Beswick A, Blom A, Gooberman-Hill R. Physiotherapy provision following discharge after total hip and total knee replacement: a survey of current practice at high-volume NHS hospitals in England and Wales. *Musculoskeletal Care* 2012;**11**:31–8.[78] © 2012 John Wiley & Sons, Ltd. Some parts have also been reproduced from Artz and colleagues[585] © 2015 Artz *et al.*; licensee BioMed Central. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated. Some parts of this chapter have also been reproduced from Artz and colleagues.[586] This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 3.0 License (www.creativecommons.org/licenses/by-nc/3.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access page (https://us.sagepub.com/en-us/nam/open-access-at-sage).

Abstract

Background

Evidence on the clinical effectiveness of different aspects of post-discharge physiotherapy after hip and knee replacement is limited. We aimed to review existing research, survey current provision and assess the feasibility of a physiotherapy intervention.

Methods

In the light of other ongoing studies in THR we focused on TKR except in the survey of physiotherapy provision.

We conducted a systematic review of the clinical effectiveness of physiotherapy exercise in patients receiving TKR.

Physiotherapy services were surveyed at 24 high-volume orthopaedic centres in England and Wales.

In the ARENA study, the feasibility of a RCT evaluating a 6-week activity-orientated rehabilitation programme for patients with TKR was assessed.

Results

Systematic review and meta-analysis identified a few small studies suggesting that physiotherapy exercise can have short-term benefits for patients with TKR.

In the UK, physiotherapy is usually provided for patients with THR depending on clinical need. After TKR, group exercises focus on knee-specific strengthening, stretching and functional exercises.

In the ARENA study, we evaluated a 6-week group-based activity-orientated rehabilitation programme for patients with TKR. Of 124 eligible patients, 46 were randomised (37%). The main reasons for non-participation were travel related and the inability to commit to the intervention. The intervention was generally well received, and attendance was good (73%), with 84% of participants reporting that they were satisfied.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Conclusions

Our systematic review and survey suggest that research is required into effective provision of physiotherapy after TKR. The ARENA study suggests that a fully powered RCT of individualised and task-orientated exercise would be feasible.

Background

After TKR, current guidance recommends that in the immediate postoperative period patients have access to routine inpatient physiotherapy to improve mobility and functional independence prior to discharge.[587] However, following discharge from hospital after total joint replacement, physiotherapy service provision is perceived to vary widely between centres and there is little guidance on best practice.

In the light of other ongoing studies on THR, we focused on TKR except in the survey of physiotherapy provision, for which we also considered patients with THR.

We aimed to:

- review evidence on the effectiveness of physiotherapy exercise interventions provided for patients with TKR after hospital discharge
- survey current UK physiotherapy practice after total hip and knee replacement
- carry out a small RCT to explore the feasibility of conducting a definitive trial of a group-based physiotherapy programme with individualised exercises targeted to individual patient aims.

Systematic review and meta-analysis of the effectiveness of physiotherapy exercise after total knee replacement

Background

As with all health technologies, evidence is required on the effectiveness of physiotherapy exercise after TKR. Our aim was to update a previous review[84] and further explore the possible benefit of specific physiotherapy exercise modalities after TKR.

Methods

General methods	As described in *Chapter 2*, *Systematic review methods*
Databases and dates	MEDLINE, EMBASE, CINAHL, PsycINFO and The Cochrane Library databases from inception to 4 October 2013. Previous systematic reviews. Citations in Web of Science and reference lists
Search strategy	Knee replacement/RCT/exercise, rehabilitation or physiotherapy. MEDLINE search strategy based on terms in *Appendix 3*
Study design	RCTs with individual or cluster randomisation. Quasi-randomised designs
Patients	Adults with recent primary TKR
Intervention	Exercise-based or physiotherapy intervention after hospital discharge. Outpatient, community or home setting. Not electrical stimulation or acupuncture
Controls	Usual care or minimal intervention. Alternative formats of care
Follow-up	At least 3 months after surgery
Data extraction	Country, baseline dates, participants (indication, age, sex), inclusion and exclusion criteria, intervention and control group content, setting, timing, duration and intensity, follow-up time, losses to follow-up and reasons
Outcomes	Patient-reported disease-specific pain and function (e.g. WOMAC, KOOS, OKS, ILAS, VAS pain), the physiological outcome ROM and functional performance tests relating to walking
Quality assessment	Cochrane risk-of-bias table

ILAS, Iowa Level of Assistance Scale.

Results

Included studies

Review progress is summarised as a flow diagram in *Figure 48*. Searches for studies in knees and hips identified 1127 articles. After screening and detailed evaluation, 17 randomised trials met the inclusion criteria and the characteristics of the studies are presented in *Table 95*.

Studies ranged in size from 43 to 160 patients (median 102 patients) and included a total of 1682 patients. When reported, the main diagnosis was osteoarthritis and the mean age in studies ranged from 66 to 73.5 years. The duration of follow-up ranged from 3 weeks to 24 months, but we describe data in our meta-analysis from 3 months onwards.

Intervention focus

The focus of the intervention was movement and exercise,[591,596,601] exercises aimed at managing kinesiophobia,[598] functional[588,597] or strengthening exercise[514] compared with minimal physiotherapy exercise as discussed in seven studies; home compared with outpatient provision as discussed in six studies;[520,592,594,595,602] physiotherapy with additional balance[589,600] or cycling components[593] compared with standard physiotherapy as discussed in three studies; and pool-based compared with gym-based provision as discussed in one study.[590]

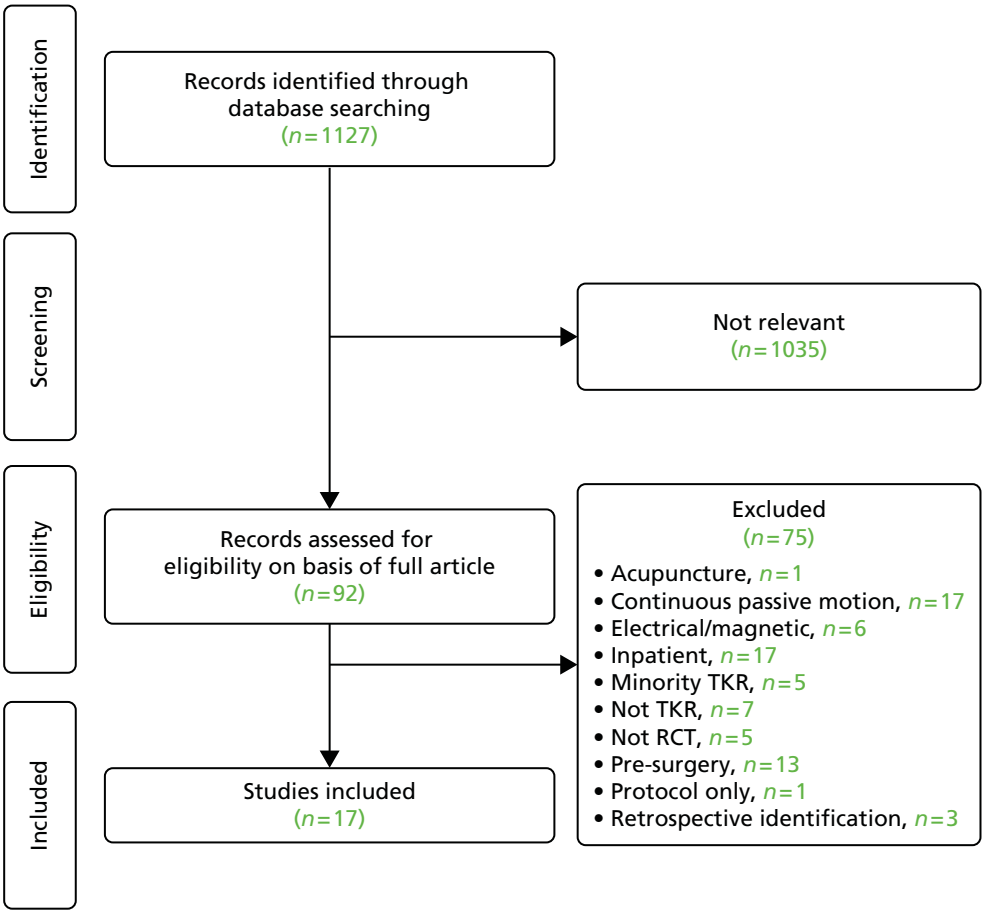


FIGURE 48 Systematic review and meta-analysis of the clinical effectiveness of physiotherapy exercise after TKR: flow diagram.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 95 Systematic review and meta-analysis of the effectiveness of physiotherapy exercise after TKR: study characteristics

Publication; location; date of study	Indication; number randomised (intervention : control); mean age (years) (% female)	Primary focus of intervention; study setting; intervention, health professional; timing, duration and intensity; control group care	Follow-up interval; outcomes; losses to follow-up (intervention : control)
Evgeniadis and colleagues 2008;[514] Greece; 2006	Osteoarthritis; $n = 48$ (24 : 24); 69 (56.3)	Strengthening; home; supervised exercise programme with emphasis on strengthening lower extremities; 8 weeks; controls received standard pre-operative and postoperative care	6, 10 and 14 weeks after surgery; SF-36, ILAS, active ROM; 13 (9 : 4) not followed up
Frost and colleagues 2002;[588] UK; 1995–6	Osteoarthritis; $n = 47$ (23 : 24); 71.3 (48.9)	Functional exercise; home; warm-up exercise, chair rise, walking and leg lifts; number of visits and duration not specified; controls given instructions to continue exercises taught in hospital	3, 6 and 12 months; VAS pain, ROM, leg extensor power, walking speed, gait speed; 20 (7 : 13) not followed up
Fung and colleagues 2012;[589] Canada; 2009–10	Not specified; $n = 50$ (27 : 23); 68.1 (66);	Balance and posture control additional to outpatient physiotherapy; outpatient department in rehabilitation hospital; Wii Fit™ (Nintendo Wii™; Nintendo of America, Redmond, WA, USA) gaming activities focused on multidirectional balance, and static and dynamic postural control; twice weekly for mean of about 8 weeks; all patients received twice-weekly outpatient physiotherapy; control patients also received 15 minutes of lower extremity strengthening and balance training exercises	Discharge from physiotherapy, estimate about 3 months; ROM, 2-minute walk test, NRS pain, LEFS, Activity-specific Balance Confidence Scale, length of rehabilitation, satisfaction; 0 lost to follow-up
Harmer and colleagues 2009;[590] Australia; 2005–6	Not specified; $n = 102$ (53 : 49); 68.3 (57)	Hydrotherapy compared with gym-based therapy; community pool; supervised classes in pool with walking forward and backward, stepping sideways, step-ups, jogging, jumping, kicking, knee ROM exercises, lunges and combined squats and upper extremity exercises; twice a week, 60-minute duration for 6 weeks; control patients received gym-based rehabilitation with ergometer cycling; walking on a treadmill; stair climbing; standing isometric, balance and knee ROM exercises at a bar; and sit-to-stand exercises	8 and 26 weeks; WOMAC, VAS, 6-minute walk test, stair ascent, ROM, knee flexor and extensor, knee oedema; three (2 : 1) lost to 26-week follow-up

TABLE 95 Systematic review and meta-analysis of the effectiveness of physiotherapy exercise after TKR: study characteristics (*continued*)

Publication; location; date of study	Indication; number randomised (intervention : control); mean age (years) (% female)	Primary focus of intervention; study setting; intervention, health professional; timing, duration and intensity; control group care	Follow-up interval; outcomes; losses to follow-up (intervention : control)
Kauppila and colleagues 2010;[591] Finland; 2002–5	Osteoarthritis; $n = 86$ (44 : 42); 70.6 (75.6); included 60–80 years	Multidisciplinary rehabilitation programme; university hospital outpatient department; week 1: physiotherapist assessment; three group sessions (45 minutes) with lower limb strengthening exercises, two pool gymnastic sessions (30 minutes) with lower limb stretching and mobility, and functional exercises focused on walking; lectures by social worker (60 minutes) and nutritionist (90 minutes); week 2: two lower limb strengthening exercise group sessions (45 minutes), three pool gymnastic sessions (45 minutes); orthopaedic surgeon lecture (45 minutes) and clinical assessment (15 minutes); daily supervised group stretching exercises (30 minutes); twice weekly supervised group Nordic walking (30 minutes); four group rehearsals of relaxation strategies (30 minutes); individualised exercise recommendations (40 minutes); two group sessions on coping strategies (90 minutes) and individual visit with psychologist – total 10 days at 2–4 months after surgery; control received an exercise programme to complete at home from 2 months after surgery	2 months, 6 months, 12 months; WOMAC, 15-minute walk test, stair ascent/descent test, isometric strength, ROM; 11 (8 : 3) lost to 6- and 12-month follow-ups
Kramer and colleagues 2003;[592] Canada; date not specified	Osteoarthritis; $n = 160$ (80 : 80); 68.4 (56.9)	Basic and advanced ROM and strengthening exercises; home- and clinic-based groups; attended outpatient physical therapy; therapists able to modify or add exercises, use therapeutic modalities, joint mobilisations or other measures as appropriate; between 2 and 12 weeks after surgery, two sessions per week for 1 hour per session; home-based rehabilitation only, received a telephone call once in weeks 2–6 and once in weeks 7–12 reminding them of the importance of exercise and to give advice	12, 26 and 52 weeks; WOMAC, SF-36, AKSS, stair ascent and descent, 6-minute walk test; 26 (11 : 15) medical issues, withdrawn consent

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 95 Systematic review and meta-analysis of the effectiveness of physiotherapy exercise after TKR: study characteristics (*continued*)

Publication; location; date of study	Indication; number randomised (intervention : control); mean age (years) (% female)	Primary focus of intervention; study setting; intervention, health professional; timing, duration and intensity; control group care	Follow-up interval; outcomes; losses to follow-up (intervention : control)
Liebs and colleagues 2010;[593] Germany; 2005–6	Osteoarthritis or osteonecrosis; $n = 159$ (85 : 74); 69.8 (71.7)	Ergometer cycling (additional to standard programme); multiple hospitals; cycling with minimal resistance under guidance of a physical therapist, aim was to improve muscle coordination, proprioception and ROM; three times a week for at least 3 weeks, starting after the second postoperative week; controls received standard physiotherapy programme only	3, 6, 12 and 24 months; WOMAC, SF-36 PCS, patient satisfaction; 24 (10 : 14) lost to follow-up at 3 months
Madsen and colleagues 2013;[594] Denmark; 2010–11	Osteoarthritis; $n = 80$ (40 : 40); 66.6 (41)	Group-based programme compared with home-based programme; physiotherapist-led strength endurance training, education, patient discussion, home exercises twice weekly with strength training, endurance training on exercise bike, walking, balance, training and muscle strength training; two sessions per week for 6 weeks starting 4–8 weeks after surgery, average of 10.5 sessions (range 4–12); home exercises with one or two planned visits with a local physiotherapist	3 and 6 months; OKS, SF-36 physical function, EQ-5D, ROM, peak leg extensor power, balance test, 10-metre walk test, sit-to-stand tests, VAS pain during leg extensor power test; 10 (4 : 8) lost to follow-up
Minns Lowe and colleagues 2012;[595] UK; 2006–9	Osteoarthritis; $n = 107$; 94 (47 : 47) received surgery; 69.2 (58)	Home-based functional rehabilitation; home; two physiotherapist home visits within 2 weeks and at 6–8 weeks after discharge, assessment of function and rehabilitation progress on gait re-education, and use of walking aids; twice-daily exercise for 3 months: weight, partial knee bends/quarter squats, standing knee flexion and extension wall sits, heel and knee raises, step-overs and stretches; task training: getting in and out of a car, getting up from a chair at a table, walking outside and stairs; controls received usual physiotherapy treatment provided at the hospital without additional home visits	3, 6 and 12 months; KOOS, OKS, leg extensor press power, 30 seconds timed sit-to-stand test, 10-metre timed walk test, ROM (provided by author)

TABLE 95 Systematic review and meta-analysis of the effectiveness of physiotherapy exercise after TKR: study characteristics (*continued*)

Publication; location; date of study	Indication; number randomised (intervention : control); mean age (years) (% female)	Primary focus of intervention; study setting; intervention, health professional; timing, duration and intensity; control group care	Follow-up interval; outcomes; losses to follow-up (intervention : control)
Mitchell and colleagues 2005;[520] UK; 1999–2000	Osteoarthritis; $n = 115$ (57 : 58); 70.3 (57.9)	Home physiotherapy compared with outpatient group provision; up to six post-discharge home visits by community physiotherapist, patient assessment and individualised therapy relating to pain relief, knee flexion and extension, gait re-education, home and functional adaptations, reduction of swelling and mobilisation of soft tissues; before-surgery patients received 3 visits; controls received exercises and individual treatment 1–2 times a week	12 weeks; WOMAC, SF-36, resource use and cost; one (0 : 1) lost to ITT analysis (45 patients withdrawn mainly pre-surgery)
Mockford and colleagues 2008;[596] UK; date not specified	Osteoarthritis, rheumatoid arthritis; $n = 143$ (71 : 72); 70.2 (61.5)	Outpatient physiotherapy; outpatient department; 6 weeks starting within 3 weeks of hospital discharge; control received no outpatient physiotherapy following discharge, all patients were given a home exercise regime to follow on discharge	3 months and 1 year; OKS, SF-12, Bartlett Patella Score, ROM, walking test; seven (4 : 3) not followed up
Moffet and colleagues 2004;[597] Canada; 1997–9	Osteoarthritis; $n = 77$ (38 : 39); 67.7 (59.7)	Intensive functional rehabilitation; rehabilitation institute; 12 physiotherapist-supervised sessions from 2 months after discharge with individualised home exercises, 60–90 minutes per week for 6–8 weeks; each session included warm-up, specific strengthening exercises, functional task-oriented exercises, endurance exercises and cool-down; ROM, pain and effusion monitored to optimise intervention; control group received usual care including possibility of supervised rehabilitation at home; all patients were taught a home exercise programme before hospital discharge	4, 6, 12 months; WOMAC, SF-36, 6MWT; six (0 : 6) at 12 months
Monticone and colleagues 2013;[598] Italy; 2010	Osteoarthritis; $n = 110$ (55 : 55); 67 (64)	Home-based functional exercise programme; home; continuation of functional exercises provided in hospital, cognitive–behavioural intervention with home exercise book about the fear-avoidance model and management of kinesiophobia, monthly phone calls to strengthen adherence; twice-weekly 60-minute sessions for 6 months; no physiotherapy; advice to stay active	6 and 12 months; KOOS ADL and pain, Tampa Scale for Kinesiophobia, NRS pain, SF-36; 0 losses to follow-up

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 95 Systematic review and meta-analysis of the effectiveness of physiotherapy exercise after TKR: study characteristics (*continued*)

Publication; location; date of study	Indication; number randomised (intervention : control); mean age (years) (% female)	Primary focus of intervention; study setting; intervention, health professional; timing, duration and intensity; control group care	Follow-up interval; outcomes; losses to follow-up (intervention : control)
Piqueras and colleagues 2013;[599] Spain; 2008–10	Osteoarthritis; $n = 142$ (72 : 70), 181 randomised but 142 completed baseline measures; 73.5 (72.4)	Outpatient and home-based telerehabilitation; five sessions under therapist supervision at rehabilitation department and five sessions at home; interactive virtual telerehabilitation, patients received information needed to perform exercises and remote therapist monitoring, therapy modified as rehabilitation evolved; system used wireless movement sensors, interactive software, a touch-screen computer and a web portal; daily 1-hour sessions for 10 days; conventional out-patient physical therapy, all randomised patients received a 2-week rehabilitation programme immediately after hospital discharge	2 weeks after intervention and 3 months; ROM, muscle strength, walk speed, pain, WOMAC, timed up and go test; nine (4 : 5) lost to follow-up
Piva and colleagues 2010;[600] USA; 2007–8	Not specified; $n = 43$ (21 : 22); 68.5 (71.4)	Balance exercises (additional to supervised functional training programme); outpatient physical therapy department; additional balance exercises (agility and perturbation); control group received a supervised functional training programme without additional balance exercises; all patients received 12 sessions of functional training over 6 weeks; home exercises given to both groups at the end of the supervised programme	2 months and 6 months; WOMAC, LEFS, timed chair rise test, gait speed; eight (3 : 5) lost to follow-up
Rajan and colleagues 2004;[601] UK; 1998–9	Monoarticular arthrosis; $n = 120$ (59 : 61); 68.5 (62.9)	Outpatient physiotherapy; outpatient; average 4–6 physiotherapy sessions; control group did not receive outpatient physiotherapy; all patients given a home exercise regime on discharge	3 months, 6 months and 1 year; ROM; four (3 : 1) not followed up
Tousignant and colleagues 2011;[602] Canada; date not specified	Not specified; $n = 48$ (24 : 24); 66 (not reported)	Functional rehabilitation; home; intervention group received telerehabilitation through high-speed internet. Progressive exercises to reduce disability and improve function in ADL. Family member or friend present to ensure safety; two sessions per week for 8 weeks; approximately 1 hour in duration; control group received usual home care services and outpatient rehabilitation over a 2-month period	4 months; knee ROM, Berg balance scale, 30-second chair–stand test, WOMAC, timed get-up-and-go test, Tinetti test, functional autonomy measure (SMAF), SF-36; seven (3 : 4) not followed up

ILAS, Iowa Level of Assistance Scale; NRS, numerical response scale; SMAF, Système de Mesure de l'Autonomie Fonctionelle (Functional Autonomy Measurement System).

Outcome measures

Outcomes reported in studies were classified as patient-reported physical function or pain, physiological tests and physical performance tests. The most frequently used physiological outcome was knee ROM measured with a universal goniometer. Measures of walking were the most widely reported performance outcomes.

Study quality

We completed a risk-of-bias assessment for each study and summarise these in *Appendix 35*. The main potential source of bias was from large and unequal losses to follow-up in six studies.[514,588,591–594] Two further studies were judged to be of reasonable quality with overall losses to follow-up of between 10% and 20%.[600,602] There was no suggestion of risk of bias in nine studies.[520,589,590,595–599,601]

There was no clear evidence of publication bias from inspection of funnel plots. However, numbers of studies were small for several outcomes and in subgroup analyses.

Comparison of different physiotherapy interventions

Results for all comparisons are summarised in *Table 96*. Meta-analyses used random-effects models, an a priori decision based on the known variation in physiotherapy exercise content. Pooled effect sizes are SMDs except for ROM, for which MDs are reported.

Physiotherapy exercise compared with no intervention

In seven studies, patients randomised to physiotherapy exercise intervention were compared with a control group receiving no intervention or minimal intervention.[514,588,591,596–598,601]

Patient-reported physical function

Data were available at one or more time points for five studies that compared a physiotherapy intervention with a control that received minimal physiotherapy.[514,591,596–598] Studies reported WOMAC physical function, OKS, KOOS ADL scale or Iowa Level of Assistance Scale (ILAS) total score.

TABLE 96 Systematic review and meta-analysis of the clinical effectiveness of physiotherapy exercise after TKR: meta-analysis

Follow-up	Studies	Patients	Pooled effect size (95% CI)	*p*-value	I^2 (%)
Physiotherapy exercise compared with no intervention					
Physical function					
3- to 4-month follow-up	3	254	–0.37 (–0.62 to –0.12)	0.004	0
6-month follow-up	3	260	–0.43 (–0.95 to 0.08)	0.10	76
12-month follow-up	4	397	–0.21 (–0.70 to 0.29)	0.42	83
Physical function in studies with low risk of bias					
3- to 4-month follow-up	2	119	–0.35 (–0.62, –0.08)	0.01	0
6-month follow-up	2	185	–0.64 (–1.15 to –0.13)	0.01	65
12-month follow-up	2	253	–0.37 (–1.36 to 0.61)	0.46	93
Pain					
3- to 4-month follow-up	2	103	–0.45 (–0.85 to –0.06)	0.02	0
6-month follow-up	4	287	–0.29 (–0.68 to 0.10)	0.15	60
12-month follow-up	4	281	–0.15 (–0.64 to 0.35)	0.57	75

continued

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 96 Systematic review and meta-analysis of the clinical effectiveness of physiotherapy exercise after TKR: meta-analysis (*continued*)

Follow-up	Studies	Patients	Pooled effect size (95% CI)	*p*-value	I^2 (%)
Pain in studies with low risk of bias					
3- to 4-month follow-up	1	27	–0.27 (–1.05 to 0.50)	0.49	
6-month follow-up	2	137	–0.36 (–1.07 to 0.35)	0.32	65
12-month follow-up	1	110	–0.73 (–1.12 to –0.35)	0.0002	
ROM extension					
3- to 4-month follow-up	2	178	–4.14 (–7.10 to 1.18)	0.006	82
6-month follow-up	1	74	0.00 (–1.37 to 1.37)	1.00	
12-month follow-up	2	217	0.42 (–0.54 to 1.38)	0.39	0
ROM extension in studies with low risk of bias					
3- to 4-month follow-up	1	143	–2.60 (–4.48 to –0.72)	0.007	
6-month follow-up	0				
12-month follow-up	1	143	0.20 (–0.92 to 1.32)	0.73	
ROM flexion					
3- to 4-month follow-up	4	321	–5.23 (–11.16 to 0.70)	0.08	83
6-month follow-up	3	217	–4.06 (–6.67 to –1.46)	0.02	0
12-month follow-up	4	360	–2.21 (–4.31 to –0.10)	0.04	0
ROM flexion in studies with low risk of bias					
3- to 4-month follow-up	1	116	–2.00 (–4.78 to 0.78)	0.16	
6-month follow-up	1	116	–5.00 (–8.14 to –1.86)	0.002	
12-month follow-up	2	259	–2.38 (–4.80 to 0.05)	0.05	0
Walking					
Longest follow-up (all 12 months)	3	169	–0.17 (–0.48 to 0.13)	0.27	0
Home-based compared with outpatient delivery of physiotherapy exercise					
Physical function					
3- to 4-month follow-up	4	310	–0.03 (–0.25 to 0.19)	0.80	0
6-month follow-up	2	150	0.05 (–0.27 to 0.38)	0.74	0
12-month follow-up	2	214	0.11 (–0.16 to 0.38)	0.42	0
Physical function in studies with low risk of bias					
3- to 4-month follow-up	2	199	–0.15 (–0.43 to 0.13)	0.29	0
6-month follow-up	1	82	0.18 (–0.25 to 0.62)	0.41	
12-month follow-up	1	87	0.01 (–0.41 to 0.44)	0.95	
Pain					
3- to 4-month follow-up	3	248	–0.00 (–0.25 to 0.25)	0.98	0
6-month follow-up	1	85	–0.05 (–0.48 to 0.38)	0.82	
12-month follow-up	1	92	–0.13 (–0.53 to 0.28)	0.55	

TABLE 96 Systematic review and meta-analysis of the clinical effectiveness of physiotherapy exercise after TKR: meta-analysis (*continued*)

Follow-up	Studies	Patients	Pooled effect size (95% CI)	*p*-value	I^2 (%)
Pain in studies with low risk of bias					
3- to 4-month follow-up	2	207	–0.07 (–0.35 to 0.20)	0.59	0
6-month follow-up	1	85	–0.05 (–0.48 to 0.38)	0.82	
12-month follow-up	1	92	–0.13 (–0.53 to 0.28)	0.55	
ROM extension					
3- to 4-month follow-up	3	261	–0.21 (–0.46 to 0.05)	0.11	6
6-month follow-up	0				
12-month follow-up	1	83	–0.18 (–0.61 to 0.25)	0.41	
ROM extension in studies with low risk of bias					
3- to 4-month follow-up	3	261	–0.21 (–0.46 to 0.05)	0.11	6
6-month follow-up	0				
12-month follow-up	1	83	–0.18 (–0.61 to 0.25)	0.41	
ROM flexion					
3- to 4-month follow-up	3	329	–0.22 (–0.44 to –0.01)	0.04	0
6-month follow-up	1	68	–0.18 (–0.65 to 0.30)	0.47	
12-month follow-up	2	202	0.07 (–0.21 to 0.35)	0.61	0
ROM flexion in studies with low risk of bias					
3- to 4-month follow-up	3	329	–0.22 (–0.44 to –0.01)	0.04	0
6-month follow-up	1	68	–0.18 (–0.65 to 0.30)	0.47	
12-month follow-up	1	83	–0.05 (–0.48 to 0.38)	0.81	
Walking					
Longest follow-up (2 studies 12 months, 1 study 6 months)	3	267	–0.02 (–0.26 to 0.22)	0.87	37
Enhanced physiotherapy compared with control					
Physical function					
3–4 months	2	185	0.00 (–0.29 to 0.29)	0.98	0
6 months	2	171	–0.16 (–0.46 to 0.15)	0.31	0
12 months	2	144	0.12 (–0.13 to 0.37)	0.35	0
Pain					
3–4 months	2	185	–0.12 (–0.41 to 0.17)	0.43	0
6 months	2	171	–0.17 (–0.47 to 0.13)	0.27	0
12 months	1	126	0.16 (–0.20 to 0.51)	0.39	

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

As shown in the meta-analysis in *Table 96* and *Figure 49*, in three studies with 254 patients, physiotherapy exercise was associated with an improvement in physical function at 3–4 months (average SMD –0.37, 95% CI –0.62 to –0.12; $p = 0.004$). At 6 months there was a non-significant trend for benefit (SMD –0.43, 95%CI –0.95 to 0.08; $p = 0.10$), and little difference between groups at 12 months. Heterogeneity was high in studies reporting outcomes at six and 12 months and this was not explained by inclusion of studies with risk of bias. After exclusion of these studies with risk of bias, benefit was apparent at 3 and particularly at 6 months (SMD –0.64, –1.15 to –0.13; $p = 0.01$), but this was based on only two studies at each follow-up.

Patient-reported pain

Four studies reported a pain outcome at one or more follow-up times.[588,591,597,598] Studies reported WOMAC pain, KOOS pain or OKS pain. As shown in *Table 96* and *Figure 50*, in two studies with 103 patients a pain outcome was reported at 3–4 months with an average SMD of –0.45 (95% CI –0.85 to –0.06; $p = 0.02$) favouring physiotherapy exercise. There was a trend for benefit at 6 months in four studies with 287 patients (average SMD –0.29, 95% CI –0.68 to 0.10; $p = 0.15$). At the 12-month follow-up there was little to suggest benefit for patients receiving physiotherapy exercise compared with untreated controls in four studies with 281 patients. Heterogeneity was high at 6- and 12-month follow-ups. Only one study had low risk of bias at each of 3–4 and 12 months, precluding meta-analysis. At 6 months, two studies with low risk of bias maintained a trend for benefit but this did not approach conventional levels of statistical significance (average SMD –0.36, 95% CI –1.07 to 0.35; $p = 0.32$).

Range of motion

Range of motion extension data suitable for meta-analysis was available from three studies with 252 patients[514,591,596] and ROM flexion from five studies with 396 patients.[514,588,591,596,601] As shown in *Table 96* and *Figure 51*, there was little to suggest improved long-term ROM in patients receiving outpatient physiotherapy. Benefit was evident in only two studies with follow-up at 3 months after TKR (average MD –4.14, 95% CI –7.10 to –1.18; $p = 0.006$).[514,596]

For ROM flexion there was no suggestion of short-term benefit from physiotherapy exercise. There was evidence of long-term benefit with average MD at 6 months of –4.06 (95% CI –6.67 to –1.46; $p = 0.02$) and at 12 months of –2.21 (95% CI –4.31 to –0.10; $p = 0.04$) in three[588,591,597] and four studies,[588,591,596,597] respectively. In studies with low risk of bias, the effect was still apparent although marginal at 12 months but this was based on only one study at 6 months[601] and two studies at 12 months.[596,601]

Physical performance

Measures of walking performance (metres walked in a set time, time to walk a specified distance and walking speed) were combined with attention paid to direction of effect. An improvement in walking performance in three studies was not significant[588,591,597] (average SMD –0.17, 95% CI –0.48 to 0.13; $p = 0.27$). There was no heterogeneity across studies.

Home-based compared with outpatient delivery of physiotherapy exercise

Home-based provision was compared with outpatient physiotherapy in six studies.[520,592,594,595,599,602]

Patient-reported physical function

Physical function was measured using WOMAC, KOOS and OKS measures. Data were available at one or more time points for five studies with 437 patients.[520,592,594,595,602] As shown in *Table 96* and *Figure 52*, there was no suggestion of a difference in functional outcome between home and outpatient provision at 3–4, 6 or 12 months. For example, at 3–4 months, the average SMD was –0.03 (95% CI –0.25 to 0.19; $p = 0.80$). No heterogeneity was apparent and consideration of higher-quality studies only marginally affected the outcome at 3–4 months in two studies (average SMD –0.15, 95%CI –0.43 to 0.13; $p = 0.29$), in favour of home-based rehabilitation.

Study or subgroup	Physiotherapy exercise Mean	SD	Total	No physiotherapy exercise Mean	SD	Total	Weight	SMD IV, random, 95% CI
3–4 months								
Evgeniadis 2008[513]	0.14	0.39	15	0.38	0.56	20	13.4%	−0.47 (−1.15 to 0.21)
Mockford 2008[596]	26.3	8.3	71	29.5	9	72	56.5%	−0.37 (−0.70 to −0.04)
Moffet 2004[597]	13.6	15	38	18.9	17.7	38	30.1%	−0.32 (−0.77 to 0.13)
Subtotal (95% CI)			**124**			**130**	**100.0%**	**−0.37 (−0.62 to −0.12)**
Heterogeneity: τ^2=0.00; χ^2=0.14, df=2 (p=0.93); I^2=0%								
Test for overall effect: z=2.90 (p=0.004)								
6 months								
Monticone 2013[598]	−82.58	12.48	55	−68.11	19.23	55	34.8%	−0.89 (−1.28 to −0.49)
Moffet 2004[597]	12.4	14.4	38	18.6	18.7	37	32.5%	−0.37 (−0.83 to 0.09)
Kauppila 2010[591]	26.5	20.9	36	26.7	21.1	39	32.6%	−0.01 (−0.46 to 0.44)
Subtotal (95% CI)			**129**			**131**	**100.0%**	**−0.43 (−0.95 to 0.08)**
Heterogeneity: τ^2=0.16; χ^2=8.49, df=2 (p=0.01); I^2=76%								
Test for overall effect: z=1.64 (p=0.10)								
12 months								
Monticone 2013[598]	−87.76	8.95	55	−75.78	16.85	55	25.5%	−0.88 (−1.27 to −0.49)
Moffet 2004[597]	12	14.8	38	15.8	17.6	31	23.7%	−0.23 (−0.71 to 0.24)
Mockford 2008[596]	25.9	9.3	71	24.7	10	72	26.7%	0.12 (−0.20 to 0.45)
Kauppila 2010[591]	28.2	22.9	36	24.7	18.7	39	24.2%	0.17 (−0.29 to 0.62)
Subtotal (95% CI)			**200**			**197**	**100.0%**	**−0.21 (−0.70 to 0.29)**
Heterogeneity: τ^2=0.21; χ^2=17.86, df=3 (p=0.0005); I^2=83%								
Test for overall effect: z=0.81 (p=0.42)								
Test for subgroup differences: χ^2=0.44, df=2 (p=0.80), I^2=0%								

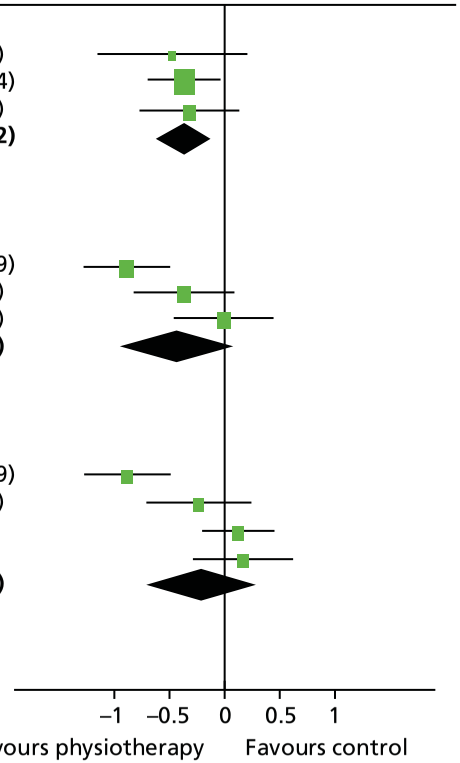


FIGURE 49 Physiotherapy exercise compared with no intervention: physical function. df, degrees of freedom; IV, inverse variance. ILAS total: Evgeniadis and colleagues.[514] WOMAC function: Kauppila and colleagues[591] and Moffet and colleagues.[597] OKS: Mockford and colleagues.[596] KOOS ADL: Monticone and colleagues.[598]

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Study or subgroup	Favours intervention Mean	SD	Total	Control Mean	SD	Total	Weight	SMD IV, random, 95% CI
3–4 months								
Frost 2002[588]	2.5	1.06	16	2.8	1.07	11	26.0%	–0.27 (–1.05 to 0.50)
Moffet 2004[597]	9.6	11.5	38	17.2	17.1	38	74.0%	–0.52 (–0.97 to –0.06)
Subtotal (95% CI)			**54**			**49**	**100.0%**	**–0.45 (–0.85 to –0.06)**
Heterogeneity: τ^2=0.00; χ^2=0.28, df=1 (p=0.60); I^2=0%								
Test for overall effect: z=2.26 (p=0.02)								
6 months								
Frost 2002[588]	2.1	1.08	16	2	1.13	11	16.1%	0.09 (–0.68 to 0.86)
Kauppila 2010[591]	23.6	22.8	36	21.7	19.1	39	27.0%	0.09 (–0.36 to 0.54)
Moffet 2004[597]	8.9	9.6	38	16	18.1	37	26.8%	–0.49 (–0.95 to –0.03)
Monticone 2013[598]	–81.8	13.26	55	–70.82	19.58	55	30.1%	–0.65 (–1.04 to –0.27)
Subtotal (95% CI)			**145**			**142**	**100.0%**	**–0.29 (–0.68 to 0.10)**
Heterogeneity: τ^2=0.09; χ^2=7.58, df=3 (p=0.06); I^2=60%								
Test for overall effect: z=1.45 (p=0.15)								
12 months								
Frost 2002[588]	1.8	0.99	16	1.5	0.93	11	18.7%	0.30 (–0.47 to 1.07)
Kauppila 2010[591]	23.5	22.3	36	19.3	17.5	39	26.7%	0.21 (–0.25 to 0.66)
Moffet 2004[602]	9.4	12.4	38	11.8	13	31	26.1%	–0.19 (–0.66 to 0.29)
Monticone 2013[598]	–87.35	11.71	55	–77.38	15.07	55	28.4%	–0.73 (–1.12 to –0.35)
Subtotal (95% CI)			**145**			**136**	**100.0%**	**–0.15 (–0.64 to 0.35)**
Heterogeneity: τ^2=0.19; χ^2=11.94, df=3 (p=0.008); I^2=75%								
Test for overall effect: z=0.58 (p=0.57)								
Test for subgroup differences: χ^2=0.94, df=2 (p=0.63), I^2=0%								

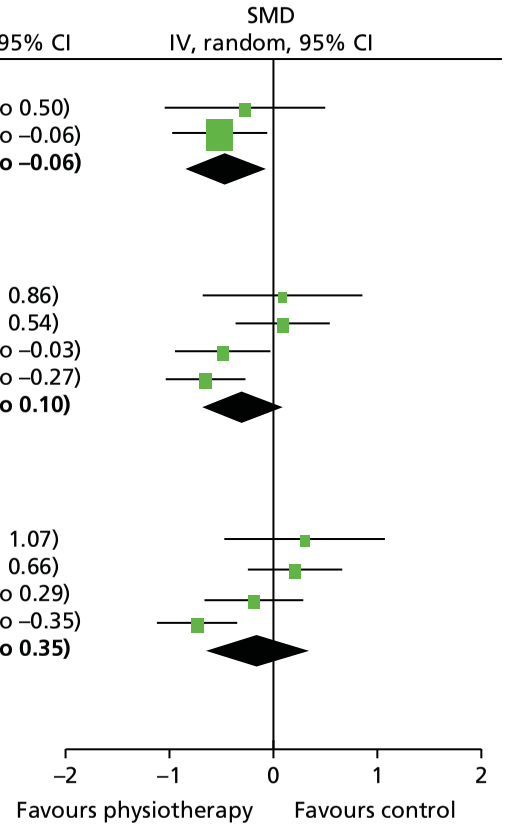


FIGURE 50 Physiotherapy exercise compared with no intervention: pain. df, degrees of freedom; IV, inverse variance. WOMAC pain: Kauppila and colleagues[591] and Moffet and colleagues.[597] KOOS pain: Monticone and colleagues.[598] OKS pain: Frost and colleagues.[588]

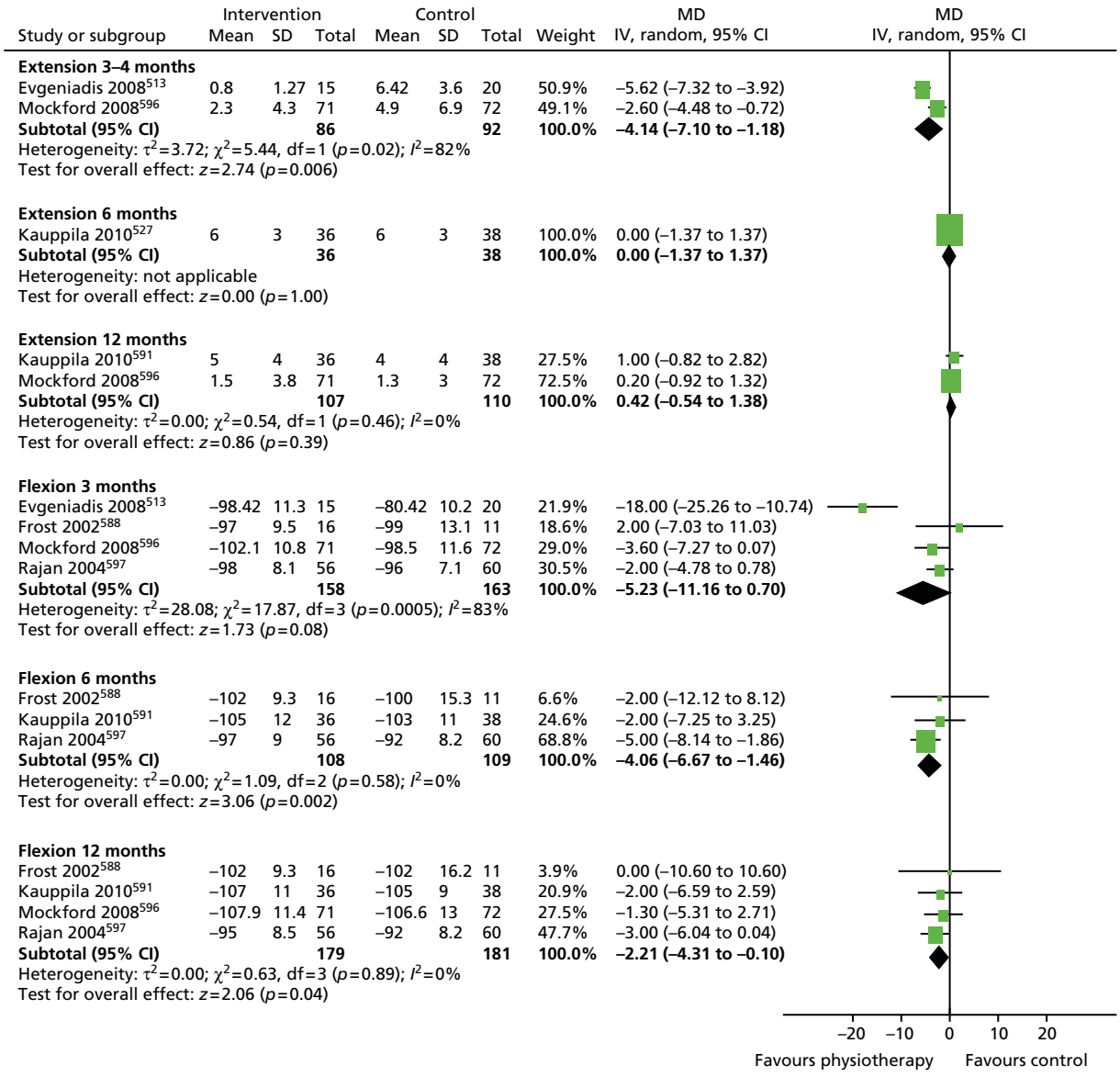


FIGURE 51 Physiotherapy exercise compared with no intervention: ROM. df, degrees of freedom; IV, inverse variance.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

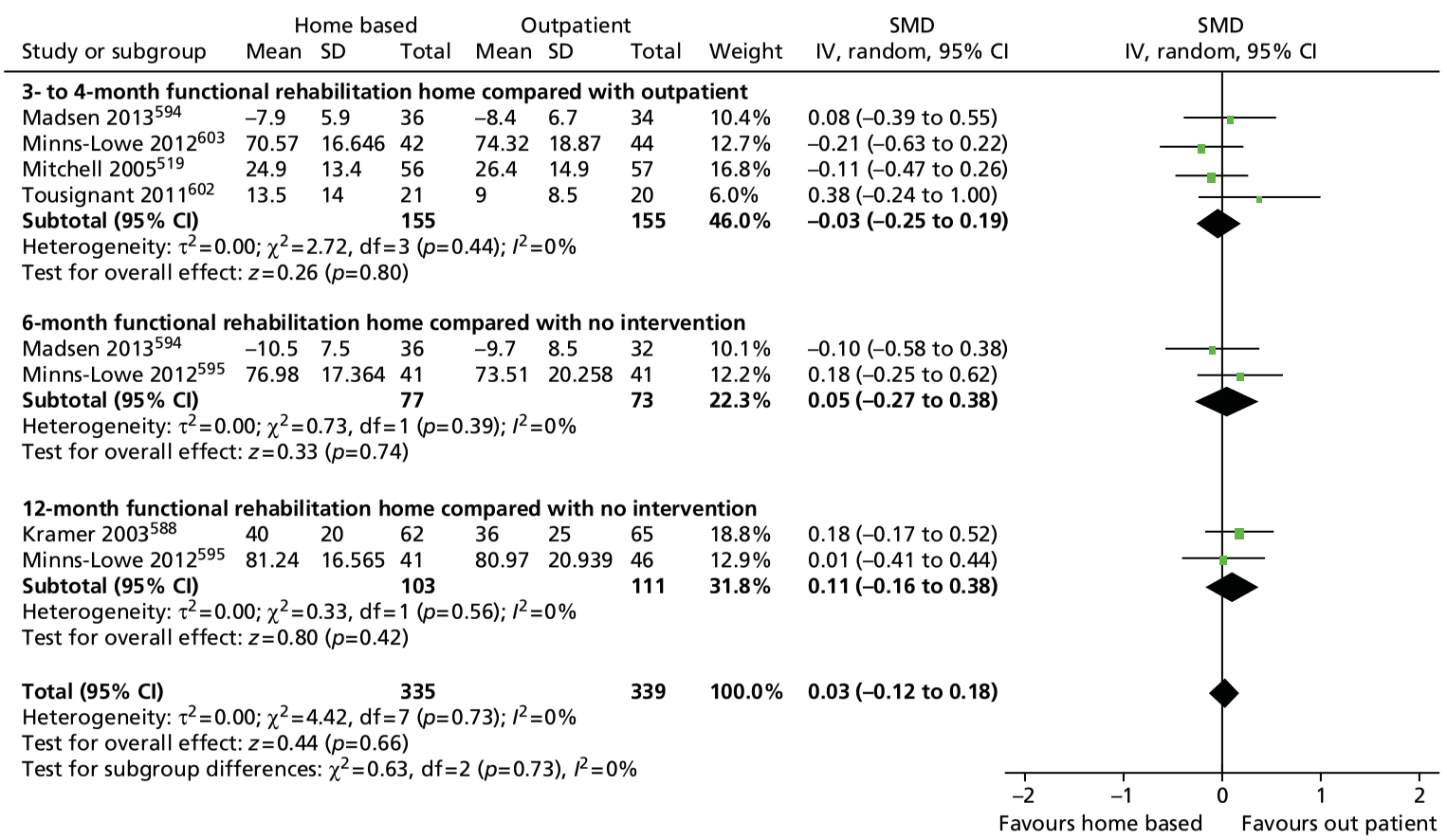


FIGURE 52 Home-based compared with outpatient physiotherapy exercise: physical function. df, degrees of freedom; IV, inverse variance. OKS: Madsen and colleagues.[594] KOOS ADL: Minns Lowe and colleagues.[603] WOMAC function: Kramer and colleagues,[588] Mitchell and colleagues[520] and Tousignant and colleagues.[602]

Patient-reported pain

Studies reported WOMAC pain, KOOS pain or VAS pain. Data were available at 3–4 months for three studies with 248 patients.[520,595,602] As shown in *Table 96* and *Figure 53*, there was no difference in pain outcome between patients randomised to home-based or outpatient physiotherapy exercise (average SMD –0.00, 95% CI –0.25 to 0.25; $p = 0.98$). One study[595] followed up 85 and 92 patients at 6 and 12 months and showed no benefit for reduced pain at either follow-up.

Range of motion

Range of motion extension was reported in three studies with 261 patients[595,599,602] and ROM flexion in five studies with 448 patients.[594,595,599,602] Outcomes are summarised in *Table 96* and *Figure 54*. There was no suggestion of a difference in ROM extension between randomised groups at any time point. For ROM flexion there was an improved ROM flexion at 3–4 months in patients who received home-based physiotherapy exercise compared with outpatient provision. This was maintained in studies with low risk of bias. There was no evidence for longer-term benefit in a small number of studies.

Physical performance

In three studies with 267 patients randomised there was no suggestion that walking performance differed between groups.[592,594,595]

Pool-based physiotherapy

One study compared pool-based physiotherapy with gym-based physiotherapy exercise.[590] There was no difference in WOMAC physical function between randomised groups. Similarly, there was no difference for WOMAC pain between groups. For ROM extension and flexion, the authors reported that there were no group differences between pool-based and gym-based provision.

Additional physiotherapy components

One study with 159 patients evaluated addition of ergometer cycling to a general physiotherapy intervention.[593] There were no differences in pain outcome between randomised groups at any of the follow-up intervals from 3–4 months to 24 months.

Two studies evaluated addition of a balancing component to a general physiotherapy intervention with a total of 93 patients randomised.[589,600] Studies reported different follow-up times but individually there was no evidence for improvement in LEFS or WOMAC physical function. Similarly, numerical response scale pain and WOMAC pain were similar at all follow-up periods. Only one study that included additional balance training reported ROM extension and flexion at short-term follow-up.[589] There were no differences in either measure between intervention and control groups.

Discussion

Randomised controlled trials of physiotherapy and exercise interventions after TKR provide some evidence for short-term effectiveness. In the key analysis comparing patients who received a programme of physiotherapy exercise with those receiving no intervention, there were short-term benefits for physical function (SMD –0.37, 95% CI –0.62 to –0.12; $p = 0.004$), and pain (SMD –0.45, 95% CI –0.8 to –0.06; $p = 0.02$). However, these small-to-medium-sized effects,[535] were based on only three studies with 254 patients[514,596,597] and two studies with 103 patients randomised, respectively.[588,597]

Facilitation of early recovery is an important objective of physiotherapy exercise-based rehabilitation.[604] However, physiotherapy should address patient expectations[603] and the key expectations of patients undergoing knee replacement relate to long-term functional and pain outcomes.[145,146,605,606] No benefit, in terms of longer-term improvements in function or reduction in pain, were found in the RCTs of physiotherapy exercise that we identified.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Study or subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	SMD IV, random, 95% CI
3–4 months								
Minns Lowe 2012[595]	67.61	17.539	46	70.21	20.505	47	37.6%	–0.14 (–0.54 to 0.27)
Mitchell 2005[519]	6.8	3.7	57	6.9	4.3	57	46.1%	–0.02 (–0.39 to 0.34)
Tousignant 2011[602]	17.6	18.1	21	12.1	9.7	20	16.3%	0.36 (–0.26 to 0.98)
Subtotal (95% CI)			**124**			**124**	**100.0%**	**–0.00 (–0.25 to 0.25)**
Heterogeneity: $\tau^2=0.00$; $\chi^2=1.76$, df=2 ($p=0.41$); $I^2=0\%$								
Test for overall effect: $z=0.02$ ($p=0.98$)								
6 months								
Minns Lowe 2012[595]	73.38	17.702	42	74.35	20.637	43	100.0%	–0.05 (–0.48 to 0.38)
Subtotal (95% CI)			**42**			**43**	**100.0%**	**–0.05 (–0.48 to 0.38)**
Heterogeneity: not applicable								
Test for overall effect: $z=0.23$ ($p=0.82$)								
12 months								
Minns Lowe 2012[595]	77.49	18.958	44	80.1	22.184	48	100.0%	–0.13 (–0.53 to 0.28)
Subtotal (95% CI)			**44**			**48**	**100.0%**	**–0.13 (–0.53 to 0.28)**
Heterogeneity: not applicable								
Test for overall effect: $z=0.60$ ($p=0.55$)								
Test for subgroup differences: $\chi^2=0.25$, df=2 ($p=0.88$), $I^2=0\%$								

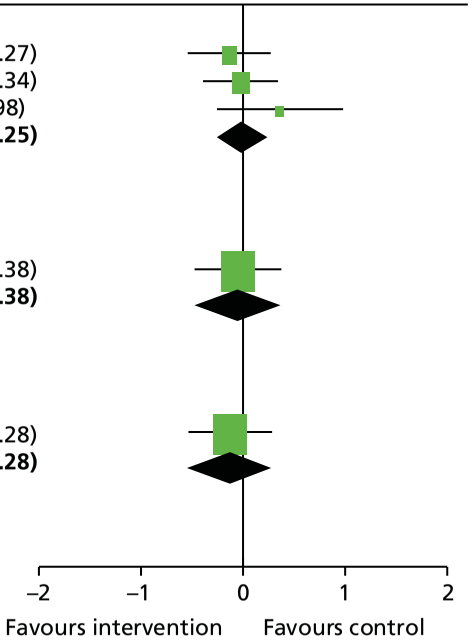


FIGURE 53 Home-based compared with outpatient physiotherapy exercise: pain. df, degrees of freedom; IV, inverse variance. KOOS pain: Minns Lowe and colleagues.[595] WOMAC pain: Tousignant and colleagues[602] and Mitchell and colleagues.[520]

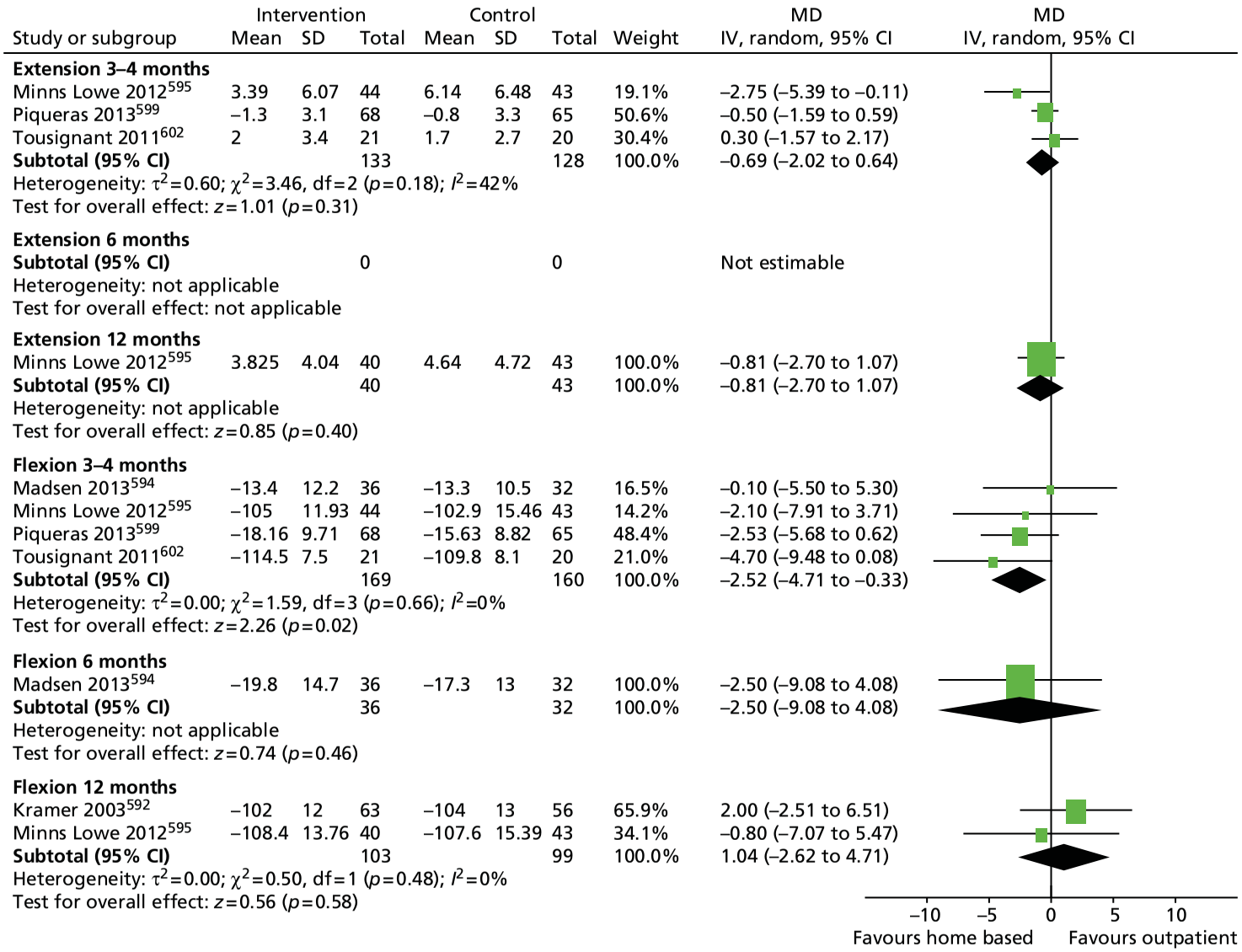


FIGURE 54 Home-based compared with outpatient physiotherapy exercise: ROM. df, degrees of freedom; IV, inverse variance.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Across the trials reporting the outcome, we observed benefit for physiotherapy exercise in studies with low risk of bias compared with controls for flexion only. ROM is a component of clinician-based outcome measures such as the Knee Society Clinical Rating System,[113] which is a useful objective measure in clinical trials; however, it is a poor marker of implant success[607,608] and does not influence patient satisfaction with their implant.[338]

A measure of walking performance was included in over half of the studies we identified, but we were unable to confirm any possible benefit from physiotherapy exercise. In three studies, there was a trend for benefit, but this was not statistically significant.[588,591,597] Parent and Moffett[609] evaluated a number of locomotor tests before and after TKR. They concluded that the 6-minute gait test is a simple and responsive measure of locomotor performance which, in conjunction with the WOMAC function difficulty subscale, provides accurate monitoring of early recovery. The need for measures of both gait and a patient-reported functional outcome was highlighted in the study of Lindemann and colleagues,[610] in which the correlation between measures was low.

The PROMs included in our meta-analyses were chosen pragmatically based on published trial outcomes and reflect the move away from surgeon-assessed scores.[95] While WOMAC and other disease- and joint-specific PROMs can be used to describe the pattern of recovery after joint replacement,[48] their sensitivity to change is affected by floor and ceiling effects. At 12 months after knee replacement, Roos and Toksvig-Larsen[306] reported ceiling effects in 11% of patients for WOMAC function and 30% for WOMAC pain.

According to the ICF, the key measures of health relate to functional limitation, activity limitations and participation restriction.[80] In a review of outcome measures commonly used in joint arthroplasty rehabilitation research, Alviar and colleagues[611] concluded that these issues are inadequately addressed. The Ab-IAP has been developed with the aim of assessing disability according to the ICF components.[285] The MyMOP2 focuses on management of symptoms but also includes assessment of a patient-specified activity restriction.[287] Use of such methods should allow assessment of an outcome pertaining to the patient's pre-operative expectations.

There were insufficient studies with adequate patient numbers to provide conclusive evidence on different methods of provision. Physiotherapy exercise provided at home is an appealing approach with the possibility of wider acceptability and uptake. However, as previously estimated, equivalence or non-inferiority trials need large numbers of patients and have yet to be undertaken. Our meta-analysis included only 310 patients for the short-term physical function outcome and fewer for the key longer-term outcomes. Similar issues of study size affect interpretation of physiotherapy exercise provided in a hydrotherapy pool or enhanced with additional cycling and balancing components. This highlights the difficulty of developing a complex physiotherapy exercise intervention.

An important problem that home-based physiotherapy exercise may address is that uptake of rehabilitation is frequently low and that patients who do not attend are more likely to be those with poorer functional health. Optimising uptake and adherence to interventions is an important issue in rehabilitation.[612,613] In their systematic review of interventions for enhancing adherence with physiotherapy, McLean and colleagues[612] found evidence of only short-term clinical effectiveness and cost-effectiveness of exercise adherence strategies. They concluded that a strategy to improve adherence to physiotherapy treatment should probably be multidimensional.

Some physiotherapy exercise will generally be provided to patients with TKR even if this comprises only advice following on from inpatient rehabilitation. Health-care professionals and policy-makers need to know what content and duration of physiotherapy exercise is necessary to improve short- and long-term outcomes and which patients are likely to benefit. Appropriate care can then be provided to each individual patient.

Despite the inclusion of 17 RCTs compared with six trials in the review of Minns Lowe and colleagues,[84] our conclusion is similar, with a possible short-term benefit for physiotherapy exercise after TKR. Future studies should include credible evaluation of methods with well-designed and appropriately powered randomised trials with a focus on completeness of follow-up.

Physiotherapy: current provision

Background

To provide information about physiotherapy provision after THR and TKR, we conducted a survey of current post-discharge physiotherapy services provided to patients at high-volume orthopaedic centres in England and Wales.

Methods

The National Joint Registry for England and Wales 2010[614] online database was screened for high-volume orthopaedic centres, defined as orthopaedic centres with > 500 hip or knee procedures,[615] for inclusion in this survey. Twenty-four centres were identified and contacted. Fourteen centres were included in the survey of physiotherapy following THR and 23 centres in the survey of physiotherapy following TKR. The physiotherapy department at each orthopaedic centre was contacted by telephone by a member of the research team and an appropriate physiotherapy clinician was identified and requested to complete a short survey either over the telephone or via e-mail. The survey was conducted as a service evaluation with agreement from North Bristol NHS Trust.

Survey questionnaire

A short questionnaire, shown in *Appendix 36*, was developed to ascertain current physiotherapy delivered to patients after discharge from hospital following either primary THR or TKR. The questionnaire covered topics including routine physiotherapy pathways and referral processes following discharge, type of physiotherapy treatment provided, relevant precautions and information provided to patients. Survey information was collected on a Microsoft Word document then stored on a Microsoft Excel database for analysis. Data on hip and knee replacements were analysed separately. Orthopaedic centres participating were assigned a unique study number for anonymity and the respondent role was also recorded. Respondents were asked to confirm responses to the survey questionnaire via e-mail or post and make adjustments as necessary.

Analysis

Routine physiotherapy services provided at each centre were categorised into no routine physiotherapy (including provision of leaflets only), outpatient physiotherapy, home-based physiotherapy, or other (physiotherapy including telephone consultation and/or drop-in services). Outpatient physiotherapy was further categorised into one to one or group based. Treatment and exercises types were also categorised.

Results

Respondents from all of the 24 orthopaedic centres selected from the National Joint Registry completed the survey. The distribution of orthopaedic centres surveyed covered a large area of England and Wales with six in northern regions, four in southern regions, four in western regions, two in eastern regions, seven in the Midlands and one in South Wales. The job title of each respondent is shown in *Appendix 37*.

Physiotherapy following discharge after total hip replacement

None of the 14 centres surveyed referred patients to outpatient physiotherapy as a routine pathway of care following THR (*Table 97*). Three centres offered additional physiotherapy support either by telephone follow-up, drop-in service or a review appointment. One centre reported that the majority of patients were referred to outpatient physiotherapy at the patient's local community hospital on the day of discharge. All centres reported that patients were referred to outpatient physiotherapy depending on clinical need. In one centre, patients were referred to outpatient physiotherapy only if they were on restricted weight bearing, progressing slowly with gait or exercise, of higher functional level and keen to return to physical exercise such as running or sport, had a leg length discrepancy, or had a foot drop following surgery.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 97 Routine physiotherapy services following discharge after THR and TKR in high-volume orthopaedic centres

	THR	TKR
Total number of units	14	23
No additional routine physiotherapy input	11	6
Outpatient (1 : 1) physiotherapy	0	5
Group physiotherapy	0	11
Telephone consultation	2[a]	0
Drop-in service	1[a]	0
Review appointment/clinic	1	1

a One hospital offered both telephone consultation and a drop-in service.

Reproduced from Artz N, Dixon S, Wylde V, Beswick A, Blom A, Gooberman-Hill R. Physiotherapy provision following discharge after total hip and total knee replacement: a survey of current practice at high-volume NHS hospitals in England and Wales. *Musculoskeletal Care* 2012;**11**:31–8.[78] Copyright © 2012 John Wiley & Sons, Ltd.

Physiotherapy following discharge after total knee replacement

Sixteen out of the 23 centres surveyed referred patients to outpatient physiotherapy (see *Table 97*). Eleven of these centres referred direct to an exercise group after discharge and five referred patients directly to one-to-one outpatient physiotherapy. No physiotherapy treatment was recorded in six centres and one centre offered a short assessment within 2 weeks of discharge. Centres not providing routine outpatient physiotherapy stated that patients could be referred to one-to-one physiotherapy if a clinical need was identified. For example, in one centre, patients were referred to physiotherapy from the orthopaedic ward if they were not achieving full knee extension or 90° knee flexion, had evidence of poor quadriceps strength, required assistance to progress exercises and mobility, or if the patient was returning to hobbies or work that required a higher level of function. Difficulty achieving 90° knee flexion and evidence of poor quadriceps function were common criteria for provision of one-to-one outpatient physiotherapy.

Group physiotherapy following total knee replacement

All 11 orthopaedic centres providing group outpatient physiotherapy referred patients within 2 weeks of discharge from hospital. Group physiotherapy sessions varied in number and duration (20–60 minutes). Staffing of group sessions ranged between two and five physiotherapist practitioners working with at least one assistant or technician. One centre reported a mixed physiotherapy and occupational therapy group with eight members of staff in attendance. Types of treatment and exercise provided within group sessions are shown in *Table 98*.

TABLE 98 Types of treatment and exercises described by the 11 high-volume centres that provided routine group physiotherapy following TKR

Strengthening	11
Stretching	11
Functional exercises	9
Task-related exercises	3
Cardiovascular exercise	5
Individualised exercise	6
One-to-one treatment	6

Reproduced from Artz N, Dixon S, Wylde V, Beswick A, Blom A, Gooberman-Hill R. Physiotherapy provision following discharge after total hip and total knee replacement: a survey of current practice at high-volume NHS hospitals in England and Wales. *Musculoskeletal Care* 2012;**11**:31–8.[78] Copyright © 2012 John Wiley & Sons, Ltd.

One-to-one physiotherapy after discharge following total knee replacement

Most (four out of five) centres providing one-to-one physiotherapy saw patients within 2 weeks of discharge. The other centre referred patients at 6 weeks post operation to a single clinic for assessment and progression of gait re-education. At this centre, further physiotherapy was provided depending on patient needs. The treatments routinely delivered during one-to-one outpatient physiotherapy included specific knee joint exercises, functional exercises and advice. Manual therapy was used as required, often for restricted range of knee motion. No centres reported use of electrotherapy or acupuncture as a routine treatment. One centre indicated that patients with chronic pain had access to a pain management team.

Discussion

This survey of high-volume orthopaedic centres describes the routine physiotherapy services provided to patients following discharge after either THR or TKR. After THR, no high-volume orthopaedic centres offered routine physiotherapy unless patients were considered in clinical need of additional physiotherapy support. It has been suggested that physiotherapy provided after discharge is not necessary to achieve excellent short-term recovery.[616] The clinical reasoning around the decision not to provide additional physiotherapy following THR was not explored but may reflect the uncertain evidence supporting long-term benefits of physiotherapy after hip replacement,[253] despite many patients continuing to have persistent muscle weakness and functional deficits compared with their age-matched peers[592] up to 2 years after surgery.

In contrast to THR, most high-volume orthopaedic centres provide physiotherapy following TKR. Greater deficits in pain and function exist after TKR than THR,[18,617] with patients reporting a greater need for physiotherapy after TKR.[618] In this survey, we found that 70% of centres routinely referred patients to outpatient services that included either one-to-one physiotherapy or an exercise group. Our findings are similar to that of previous research.[619] In addition, we found that 26% of centres did not offer routine physiotherapy after TKR – a proportion greater than that previously reported.[620] However, after TKR, centres in our survey not offering routine physiotherapy did refer on a needs basis.

Routine referral to supervised exercise groups was the most commonly reported physiotherapy treatment for patients after TKR. In patients with knee osteoarthritis, group physiotherapy can be a cost-effective way to deliver treatment without compromising effectiveness.[621,622] This approach allows patients with similar impairments to exercise within a supported environment[621] and appears to be a favoured method of delivering physiotherapy after TKR.

Knee strengthening, stretching and functional exercises were the most common exercises reported in the physiotherapy groups, similar to that seen by Naylor and colleagues.[620] This inclusion of functional exercises is important as greater functional deficits are experience by dissatisfied patients[254] and function-based exercises are of more benefit to patients after TKR.[84] Functional difficulties after TKR are observed in many patients, particularly with activities such as kneeling, squatting and gardening.[623,624] Including functional exercises in an exercise group may be a beneficial and cost-effective way to assist patients in returning to higher demanding activities and future research in this area is required.

This survey targeted high-volume orthopaedic centres and we report an excellent response rate. Although not a comprehensive survey of all orthopaedic centres in England and Wales, collecting information from these centres means the results are likely to represent the current trend in post-discharge physiotherapy provision and has allowed us to compare post-discharge physiotherapy between THR and TKR. Information was not gathered from smaller volume orthopaedic units, private or independent treatment centres limiting generalisability to all centres in England and Wales. However, future research should include such centres and gather information from other countries. Exploring the rationale behind provision of physiotherapy pathways was not investigated here; however, research is required to identify the factors that influence the physiotherapy service provision after THR and TKR.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Conclusion

The provision of physiotherapy following discharge after TKR is a more common practice than after THR for which ongoing physiotherapy is provided depending on clinical need. Group exercises are the favoured destination for patients following TKR in high-volume centres with focus on knee specific strengthening, stretching and functional exercises.

Physiotherapy: ARENA

Background

According to the WHO ICF model, rehabilitation should be patient centred and aim to maximise functional ability, facilitate activities and increase social participation.[80]

Provision of rehabilitation following TKR should address patients' individual preferences and needs,[604] with exercises orientated towards activities that they consider important. This individualised approach is the basis of an exercise class developed for this study. Group physiotherapy gives a cost-effective way of delivering treatment without compromising its effectiveness[625] and allows patients to participate in exercise within a supported environment in the company of peers with similar experiences and impairments. The inclusion of individualised exercise specific to each patient aims to increase self-efficacy and empower patients to take an active role as recommended by patient focus groups.[626] Higher levels of self-efficacy at 3 months have been associated with a greater level of functional activity at 9 months after joint replacement,[627] and may enhance adherence to continued home exercise. Involving patients in the design of their rehabilitation may result in better long-term outcome and forms the basis of this function-based group intervention.

Our systematic review identified no particular format of post-discharge physiotherapy associated with improved long-term patient outcomes. Addressing individualisation and patient preferences as described in the MRC framework,[94] we conducted a RCT to evaluate the feasibility of providing a 6-week postoperative activity-orientated rehabilitation programme for patients undergoing TKR. The objectives of the study were to determine uptake rates, reasons for non-attendance at classes, patient satisfaction with classes, patient-reported outcomes, and timing and suitability of the exercises and outcomes measures. The study also piloted a methodology to collect costs and outcomes to perform an economic evaluation.

Patients and methods

Ethics approval

Ethics approval for this study was provided by the South West – Cornwall and Plymouth Research Ethical Committee (NHS reference number 11/SW/0341), with study sponsorship and research and development approval provided from North Bristol NHS Trust (reference 2713). As a feasibility study of a RCT, the study was registered, UKCRN ID 12100.

Patient recruitment

Patients listed for primary TKR at the AOC were identified by a member of the clinical care team and invited to participate in this study. These patients were sent a study pack containing a patient information leaflet describing the nature and purpose of the study. When the patients attended their pre-assessment clinic, they were approached by a research nurse to discuss the study further and check eligibility. Patients wishing to participate in the study were asked to provide informed consent by signing the consent form. Patients not wishing to participate in the study were asked if they were willing to explain their reasons for not participating.

Inclusion criteria

Patients listed for primary TKR due to osteoarthritis.

Exclusion criteria

Patients listed for TKR for reasons other than osteoarthritis, patients listed for revision knee surgery including previous unicompartmental, tibial osteotomy or patellofemoral knee replacement surgery; patients unable to participate in exercise for any medical reason such as unstable cardiovascular or cardiorespiratory disease; patients with severe neurological disorders; patients unable to provide informed consent; and patients unable to understand written English, because not all the questionnaires have been validated in other languages.

Randomisation

Participants were allocated into either the intervention or usual care group, using Minim, by a member of administrative staff at the MRU not directly involved in the research study. Minimisation was used to ensure that each group had equal sex and age proportions. Patients were informed of the results of minimisation by telephone 2 weeks after their knee replacement by a member of the research team. Participants in the usual care group were instructed to continue with their current care and participants in the intervention group were invited to the AOC to participate in the exercise class. Prior to the exercise class, participants were asked to identify two functional goals that they would like to achieve following their knee replacement. Participants allocated to the exercise class were invited to bring a partner with them to the classes. Blinding of the research team or patients was not possible in this study because the intervention involved attending exercise classes run by the research physiotherapists.

Intervention: usual care

Usual physiotherapy care following TKR at the study centre consisted of a knee replacement booklet given out at a pre-operative education class. The booklet contained information about discharge planning, the pre-operative period, the operation day, early and later stage postoperative exercises, performing everyday functional activities, returning to work and hobbies, discharge goals, precautions, expectations and potential problems. Patients are advised on discharge to continue with the exercises in the booklet five times a day at home. Some patients could be referred to their local physiotherapy department for follow-up appointments and others may receive physiotherapy at home. This was at the discretion of the inpatient physiotherapy team or orthopaedic team. The patients may also be referred for physiotherapy by their GP or consultant.

Intervention: physiotherapy exercise class

The physiotherapy exercise class started 6 weeks after surgery and lasted for 6 weeks. Each class was 1 hour long and contained 14 separate 4-minute tasks-related exercise stations (*Table 99*) designed to address functional needs including muscle strength, balance, function and confidence. Participants were instructed to exercise at their own pace with a focus on performing quality movement rather than high quantity. In the first session, all the exercises were demonstrated to the participant by the physiotherapist and the two activity goals were discussed. These activity goals then formed the basis of individualised exercises incorporated into remaining exercise sessions. Two experienced physiotherapists supervised the class and participants were encouraged to discuss progression of exercise with the physiotherapists during the class. On completion of the class, participants were given a list of exercises, including their individual exercises, to continue with at home on a regular basis at their leisure. All travel and parking cost incurred by participants were refunded. Taxis were provided for patients unable to get to and from the class by public or personal transport.

Assessment times and outcome measures

All participants were asked to complete study questionnaires before surgery and at 2 weeks, 3 months and 6 months after surgery. In addition, participants were contacted at 6 weeks and 3 months after surgery to complete a MYMOP2 questionnaire. A study evaluation was completed by all participants at 3 months after surgery. Participants in the physiotherapy exercise class were also asked to provide feedback about exercise classes by completing an exercise class evaluation following the final exercise session.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 99 Description of exercises in the physiotherapy exercise class

Exercise	Description	Task
Plinth exercises	This station is available for continuation of lower grade exercises such as ROM, quadriceps and hamstring strengthening and stretches. This can also be used for kicking practice and eccentric hamstrings	Maintain range and strength. Simulated kicking/swimming
Getting in/out of bed	Practise turning from back to side and to sitting. Then stand from sitting. Return to sitting then lying. Alternative exercise includes bridging then sit to stand. Plinth height can varied to increase level of difficulty	Getting in and out of bed. Sit-to-stand test
Balance tasks	Series of exercises including single-leg stance, wobble board, balance training, trampette, tandem walking. Exercises are progressed to include upper limb actions such as throwing and catching, reaching	Standing balance. Falls prevention
Treadmill	Practise straight line and inclined walking at various speeds	Walking on flat and uphill. Jogging
Squatting and crouching	Mini squat and semisquats. Progressing to full squat and crouching. Squats can be performed with the assistance of chairs, gym ball. Tasks can include cleaning floor, loading washing machine/dishwasher, DIY	Squatting down. Crouching down
Cycling	Static bike with variable levels of resistance	Cardiovascular fitness
Rowing and stepper machines	Optional cardiovascular station for those who may wish to return to gymnasium-based aerobic exercise machines	Gymnasium-based cardiovascular exercises
Individualised exercises (× 2)	Exercise designed specifically for individual patients	Individual task
Progressive kneeling	Kneeling at progressively increasing ranges of knee flexion on to cushioned or hard surfaces. Full kneeling and high kneeling. Kneeling to practise digging	Kneeling down. Gardening
Walking exercises	Walking over uneven surfaces. Walking carrying objects. Stepping into hoops over sticks	Walking. Falls prevention
Lunges	Mini lunges. Progressing depth of lunge. Lunge walking. Lunge to bowling or picking up objects	Picking up from floor. Bowling
Getting up from floor	Practise getting down and back up from a floor mat using chairs to assist	Getting off floor
Step up/down stairs	Stepping up and down on stairs of varying height	Stair ascent and descent

DIY, do it yourself.

Primary outcome measure

The main outcome measures for this study were the KOOS[273] and the LEFS.[294] The KOOS is an extended version of the WOMAC and contains information about knee pain and stiffness, knee function, sports and recreation, and the LEFS is a 20-item scoring system to measure lower limb function.

Additional outcome measures

The study questionnaire also contained additional outcome measures to determine completion rates for the following: MYMOP2,[287] University of California at Los Angeles (UCLA) Activity Score,[295] Activities-specific Balance Confidence Scale,[296] Self-efficacy for Rehabilitation,[297] Ab-IAP,[285] EQ-5D,[278] satisfaction with knee replacement and rehabilitation, service and resource usage, and adherence to home exercise.

Study and exercise class evaluation

Participants were asked to complete a study evaluation at 3 months following surgery. This included questions about study documentation, appropriateness of study questionnaires and assessment times.

Participants allocated to the physiotherapy exercise group were also asked to complete a class evaluation after completion of the exercise class. This included questions about the timing and duration of the exercise class, satisfaction with the class and exercises available and the opportunity to provide general comments on the class.

Reasons for non-attendance at classes

To assess adherence and any barriers to participation in the intervention, attendance and reasons for non-attendance at the exercise class were recorded.

Assessing non-participation

Ethical approval was provided to approach non-participants by telephone to ask their reasons for not taking part.

Statistical analysis

Descriptive statistics on study participants, recruitment and attrition rates, and physiotherapy outpatient referral rates were calculated. Participant feedback on the physiotherapy intervention was also explored. Analysis of return rates of study questionnaires and completion rates of outcome measures was calculated. Sample size calculations for future trials were calculated from selected outcome measures.

Results

Recruitment

A CONSORT flow diagram showing patient recruitment and retention in the study is shown in *Figure 55*. A total of 238 study packs were posted to potential participants, with 124 patients approached in the orthopaedic pre-assessment clinic. Of the 124 patients approached, 46 consented to participate in the study, giving a recruitment rate of 37.1%. Five patients were ineligible and one patient had surgery arranged outside the study period. Of the patients who declined to participate, 72 agreed to disclose their reasons for non-participation in this study. Baseline details of the 46 participants are summarised in *Table 100* and were similar between both groups.

Reasons for non-participation

Seventy-two patients (23 male and 49 female) agreed to disclose their reasons for non-participation in this study. The average age of patients not participating was 70.1 years (range 50–91 years). Fifteen reasons for no participation were reported; the most frequent issues for not participating in the study were related to travelling distance, transportation and commitment to attend the exercise class if allocated. These reasons accounted for 54% of the reported reasons why patients did not wish to participate in the study. Other reasons included concerns around existing comorbidities, caring for partners or family members, resistance to completion of questionnaires, planned vacations following surgery, uncomfortable about exercising in groups and anxiety about the forthcoming surgery.

Post-discharge referral for additional physiotherapy

Overall, 53.7% of participants in this study were referred for outpatient physiotherapy after their TKR. In the usual care group, 52.6% of participants were referred for outpatient physiotherapy, compared with 57.1% in the physiotherapy intervention group.

Attendance at the exercise class

A total of 23 participants were randomised into the physiotherapy intervention. Of the 23 participants randomised, two participants were excluded prior to starting the exercise class, three participants did not attend, and one participant attended a single exercise before admission for a manipulation under anaesthetic for joint pain and stiffness. Of the three participants who did not attend, reasons for non-attendance were a complication of medical condition, readmission for manipulation under anaesthetic and one participant decided to take a vacation overseas. Overall, the attendance rate was 73%, with 13 participants attending all six exercise classes and four participants missing only one exercise class.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

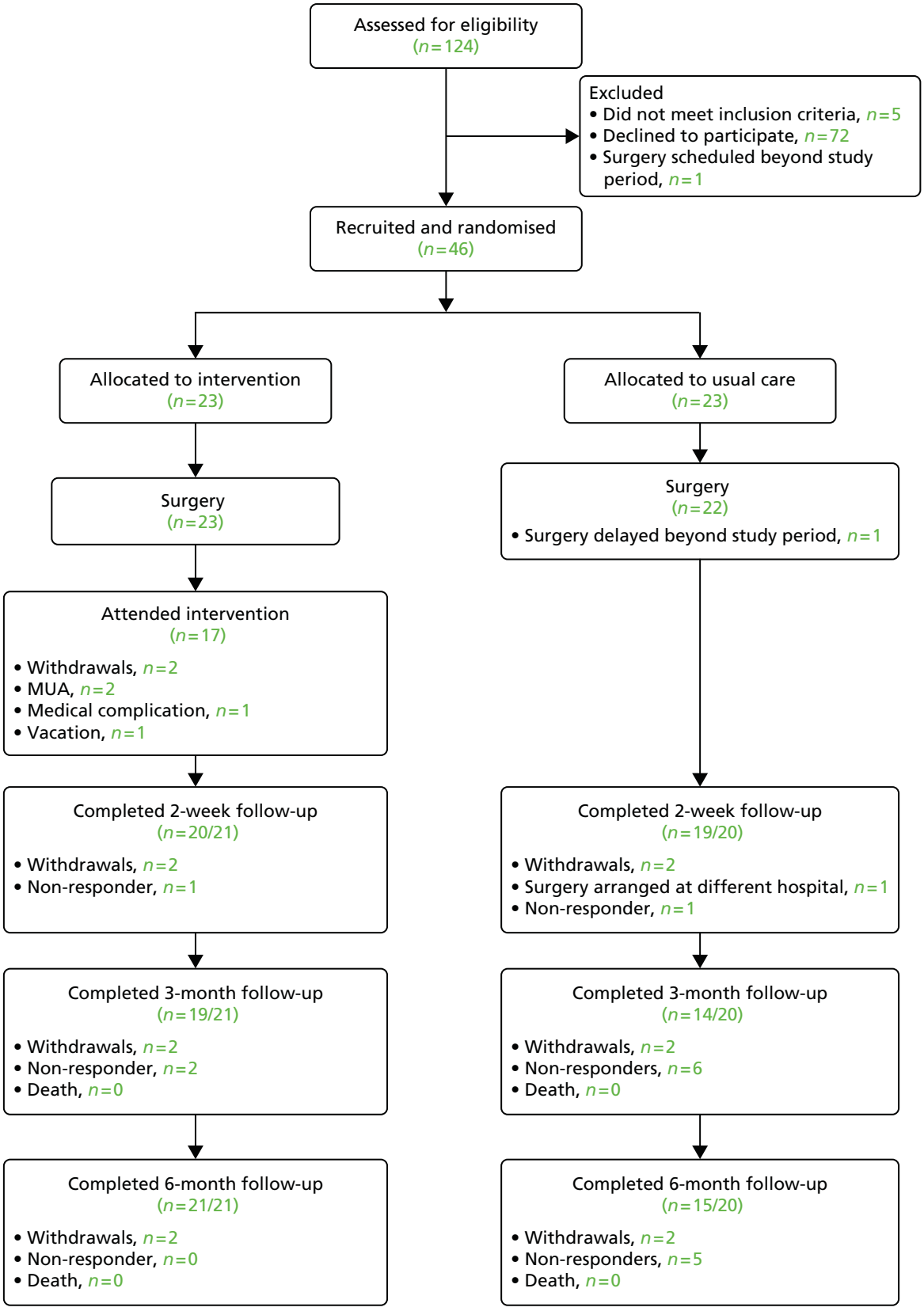


FIGURE 55 ARENA CONSORT flow diagram. MUA, manipulation under anaesthetic.

TABLE 100 Baseline demographics for participants in the ARENA study

Characteristic	All	Intervention group ($n = 23$)	Usual care group ($n = 23$)
Mean age, years (range)	68.6 (51–82)	70.0 (57–81)	67.2 (51–82)
Sex (male/female)	22/24	11/12	11/12
Laterality of implant (left/right)	19/27	9/14	10/13
Mean distance (miles) residing from hospital (range)	8.1 (1.3–18.6)	9.2 (1.7–17.7)	7.1 (1.3–18.6)
Living alone, %	27.7	17.3	38.1
Retired, %	71.3	82.6	60.0
Additional joint pains, %	85.7	100	71.4
Back pain, %	34.1	34.8	33.3
Diabetes, %	13.3	21.7	4.8
Angina, %	6.7	13.0	0.0
Mean KOOS pain score (95% CI)	42.4 (37.3 to 47.5)	40.5 (33.4 to 47.6)	44.5 (37.1 to 51.8)
Mean KOOS symptoms score (95% CI)	42.2 (37.1 to 47.3)	40.7 (33.6 to 47.8)	43.9 (36.4 to 51.3)
Mean KOOS ADL score (95% CI)	46.3 (40.7 to 51.8)	41.8 (34.2 to 49.3)	51.2 (43.3 to 59.1)
Mean KOOS sport/recreation score (SD)	14.9 (20.9)	12.2 (24.4)	18.1 (15.8)
Mean KOOS QoL score (SD)	15.6 (11.3)	12.5 (12.6)	18.4 (8.5)

The main non-medical reasons for non-attendance were that patients had arranged visits out of area on the day of the exercise class.

Evaluation of the exercise class

A total of 17 participants provided feedback on the exercise class. All participants felt that the duration of the session, at 1 hour, was the right amount of time to exercise. Three participants (18%) would have like to receive more than six sessions and one participant (6%) reported that the exercise class should have started sooner after surgery. Overall, all participants were satisfied with the range of exercises offered, with 15 (88%) participants reporting that they were very satisfied. The average usefulness of functional exercises and individual exercises within the class were scored as 9.6 out of 10 and 9.5 out of 10, respectively, on a numerical rating scale. All patients felt that the exercise class met their functional needs. For example:

> *coming to the class has been extremely useful. I felt the exercises were all relevant to everyday activities and really boosted my confidence on a day to day basis.*
>
> *Pt042*

> *there is no doubt that the sessions have expedited and enhanced my recovery. An extremely valuable experience.*
>
> *Pt031*

> *I think attending these sessions were very helpful emotionally and I felt better in that respect after the first session. Meeting other people to discuss problems with them and the staff was definitely a bonus.*
>
> *Pt030*

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Return of study questionnaires and resource-use logs

Study questionnaire return rates were high at 2 weeks after surgery with a 95% return rate in both groups. At 3 months after surgery, the rate of the questionnaire return was lower in the usual care group with 70.0% (14/20) returning the study questionnaire, compared with 90.5% (19/21) for the intervention group. Two participants in the usual care group were contacted by telephone to complete the KOOS. At 6 months, the questionnaire return rate in the usual care and intervention group was 75% (15/20) and 100% (21/21), respectively. Resource-use log return rate at 3 months was 55% (11/20) in the usual care group compared with 90.5% (19/21) in the intervention group. A slight increase in return rate was observed at 6 months after surgery with resource-use log return rates of 75% (14/20) and 100% (21/21) in the usual care and intervention groups, respectively.

Completion of KOOS and LEFS outcome measures

Completion rates of the KOOS and LEFS are shown in *Table 101*. Completion of the KOOS subsections and the LEFS at 2 weeks after surgery was high for both intervention groups. At the 3- and 6-month stages, completion rates were lower in the usual care for all KOOS subsections and the LEFS compared with the intervention group. Completion of the KOOS and LEFS was generally less likely at the 3-month post-operation stage for both intervention groups.

TABLE 101 Completion rates of the LEFS and KOOS subsections at 2 weeks, 3 months and 6 months after surgery in both the usual care and physiotherapy intervention groups

	2 weeks after surgery		3 months after surgery		6 months after surgery	
Outcome	Return, *n*/*N* (%)	Completion, x/*n* (%)	Return, *n*/*N* (%)	Completion, x/*n* (%)	Return, *n*/*N* (%)	Completion, x/*n* (%)
KOOS pain						
Usual care	19/20 (95)	19/19 (100)	14/20 (70)	14/14 (100)	15/20 (75)	14/15 (93)
Physiotherapy	20/21 (95)	20/20 (100)	19/21 (90)	19/19 (100)	21/21 (100)	21/21 (100)
KOOS symptoms						
Usual care	19/20 (95)	19/19 (100)	14/20 (70)	14/14 (100)	15/20 (75)	14/15 (93)
Physiotherapy	20/21 (95)	20/2 (100)	19/21 (90)	19/19 (100)	21/21 (100)	21/21 (100)
KOOS ADL						
Usual care	19/20 (95)	19/19 (100)	14/20 (70)	14/14 (100)	15/20 (75)	15/15 (100)
Physiotherapy	20/21 (95)	20/20 (100)	19/21 (90)	19/19 (100)	21/21 (100)	21/21 (100)
KOOS sport recreation						
Usual care	19/20 (95)	18/19 (95)	14/20 (70)	13/14 (93)	15/20 (75)	15/15 (100)
Physiotherapy	20/21 (95)	17/20 (85)	19/21 (90)	19/19 (100)	21/21 (100)	18/21 (86)
KOOS QoL						
Usual care	19/20 (95)	19/19 (100)	14/20 (70)	13/14 (93)	15/20 (75)	14/15 (93)
Physiotherapy	20/21 (95)	20/20 (100)	19/21 (90)	19/19 (100)	21/21 (100)	21/21 (100)
LEFS						
Usual care	18/20 (90)	17/18 (94)	12/20 (60)	11/12 (92)	15/20 (75)	14/15 (93)
Physiotherapy	20/21 (95)	19/20 (95)	19/21 (91)	19/19 (100)	21/21 (100)	19/21 (91)

n, number of outcome returned; *N*, total number of potential returnable outcomes; x, number completed.
Note
Completion rates (x/*n*) (%) of (*N*) returned questionnaires.

Completion of additional outcome measures

Completion rates of the additional outcome measures are shown in *Table 102*. Similarly to the LEFS and KOOS outcome measures, completion rates at 2 weeks were high in both groups. However, at 3 months after surgery, completion was poorer in the usual care group, with rates between 55% and 60%, than in the physiotherapy intervention group (76.2–90% completion). Similarly, at 6 months after surgery, completion rates were higher for the physiotherapy group than for the usual care group. Pain measured using a VAS demonstrated the poorest completion in both groups, with rates of 55% at 3 months and 50% at 6 months for the usual care group at 76.2% and 85.7%, respectively in the intervention group.

Completion of MYMOP2 questionnaires

Initial (6 weeks post operation) MYMOP2 scores were recorded for all participants that had surgery (41/41) and were not excluded from the study. At 3 months after surgery, the completion rate for the first follow-up MYMOP2 scores was 95% in the usual care group and 100% in the intervention group. At 6 months, the completion rates for the usual care and intervention groups were 85.7% and 95.2%, respectively.

Outcome data

Outcome scores for the KOOS subsections are shown in *Table 103* and those for the LEFS and additional measures are shown in *Table 104*. Improvements in score are observed for all measures in both intervention groups from 2 weeks to 6 months after surgery. There is a trend for higher scores in the exercise group for all KOOS subsections and LEFS scores, but no statistical analysis has been carried due to the feasibility nature of this study.

TABLE 102 Completion rate (%) of additional outcome measures at 2 weeks, 3 months and 6 months after surgery in both the usual care and physiotherapy intervention groups

Completion rates (%) of additional outcome measures	2 weeks after surgery	3 months after surgery	6 months after surgery
ABC scale			
Usual care	17/20 (85%)	12/20 (60%)	15/20 (75%)
Physiotherapy	20/21 (95%)	19/21 (91%)	21/21 (100%)
Pain (VAS)			
Usual care	17/20 (85%)	11/20 (55%	10/20 (50%)
Physiotherapy	20/21 (95%)	17/21 (76%)	18/21 (86%)
UCLA activity score			
Usual care	18/20 (90%)	12/20 (60%)	15/20 (75%)
Physiotherapy	20/21 (95%)	19/21 (91%)	20/21 (95%)
SER			
Usual care	18/20 (90%)	12/20 (60%)	14/20 (70%)
Physiotherapy	20/21 (95%)	19/21 (91%)	20/21 (95%)
Ab-IAP			
Usual care	17/20 (85%)	12/20 (60%)	15/20 (75%)
Physiotherapy	20/21 (95%)	19/21 (91%)	21/21 (100%)

ABC, activities-specific balance confidence; SER, self-efficacy for rehabilitation.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

TABLE 103 Mean (95% CI) scores for KOOS outcome data before surgery and at 2 weeks, 3 and 6 months after surgery

Outcome	Baseline surgery	2 weeks after surgery	3 months after surgery	6 months after surgery
KOOS pain				
Usual care	44.5 (36.7 to 52.2)	52.8 (44.1 to 61.5)	69.2 (57.9 to 80.5)	70.9 (60.4 to 81.4)
Physiotherapy	40.4 (33.3 to 47.5)	46.7 (40.4 to 53.0)	74.1 (64.6 to 83.8)	78.6 (70.1 to 87.2)
KOOS symptoms				
Usual care	43.9 (36.3 to 51.5)	42.9 (37.8 to 48.0)	54.8 (45.1 to 64.6)	56.7 (48.3 to 65.1)
Physiotherapy	40.6 (33.2 to 48.0)	52.2 (45.7 to 58.8)	59.6 (51.7 to 67.5)	58.5 (51.6 to 65.3)
KOOS ADL				
Usual care	51.1 (42.0 to 60.2)	58.1 (48.3 to 68.0)	76.1 (65.4 to 86.8)	73.5 (63.4 to 83.7)
Physiotherapy	40.9 (34.0 to 47.7)	53.6 (43.5 to 63.8)	81.2 (73.5 to 88.8)	79.6 (71.1 to 88.3)
KOOS sport recreation				
Usual care	18.0 (10.6 to 25.4)	12.9 (7.0 to 18.8)	27.9 (15.1 to 40.1)	37.1 (24.5 to 49.7)
Physiotherapy	12.2 (1.6 to 22.7)	16.8 (2.8 to 29.5)	39.2 (25.0 to 53.4)	46.3 (34.8 to 57.8)
KOOS QoL				
Usual care	19.0 (15.0 to 23.0)	16.7 (13.1 to 18.8)	36.1 (25.6 to 46.6)	45.1 (34.2 to 56.0)
Physiotherapy	12.4 (7.0 to 17.9)	23.9 (15.6 to 32.1)	52.4 (39.4 to 65.5)	61.5 (52.6 to 70.5)

TABLE 104 Mean (95% CI) for the LEFS and additional outcome measures before surgery and at 2 week and 3 months after surgery in both the physiotherapy intervention and usual care groups

Outcome	Before surgery	2 weeks after surgery	3 months after surgery	6 months after surgery
LEFS				
Usual care		30.1 (24.01 to 36.23)	48.8 (38.78 to 58.85)	45.0 (35.32 to 54.68)
Physiotherapy		26.1 (20.32 to 31.89)	55.8 (48.21 to 63.48)	57.8 (49.54 to 66.15)
ABC scale				
Usual care	62.9 (51.9 to 74.0)	60.5 (49.1 to 71.9)	79.0 (66.7 to 91.3)	80.6 (71.0 to 90.3)
Physiotherapy	48.2 (37.7 to 58.6)	43.7 (32.8 to 54.6)	84.3 (77.1 to 91.7)	84.1 (75.9 to 92.2)
Pain (VAS)				
Usual care	6.0 (5.0 to 7.1)	5.7 (4.6 to 6.8)	3.6 (2.2 to 5.0)	3.9 (1.7 to 6.0)
Physiotherapy	7.3 (6.4 to 8.2)	5.3 (4.1 to 6.5)	3.5 (1.8 to 5.2)	2.9 (1.3 to 4.6)
UCLA activity score				
Usual care	4.4 (3.6 to 5.3)	2.5 (2.2 to 2.9)	4.3 (3.7 to 5.0)	4.6 (3.7 to 5.6)
Physiotherapy	3.5 (3.1 to 4.0)	2.8 (2.4 to 3.1)	4.9 (4.1 to 5.7)	5.2 (4.4 to 5.9)
SER				
Usual care	91.9 (78.7 to 105.0)	91.2 (82.9 to 99.6)	101.5 (86.8 to 116.2)	103.8 (95.9 to 111.6)
Physiotherapy	86.5 (71.0 to 101.9)	87.3 (76.1 to 98.4)	108.7 (102.4 to 115.0)	110.7 (104.0 to 117.5)
Ab-IAP				
Usual care	17.2 (13.9 to 20.4)	20.8 (18.1 to 23.6)	13.9 (10.0 to 17.8)	15.4 (11.9 to 18.9)
Physiotherapy	18.7 (15.4 to 21.9)	19.5 (16.1 to 22.9)	11.5 (9.5 to 13.5)	10.9 (7.8 to 14.0)

ABC, activities-specific balance confidence; SER, self-efficacy for rehabilitation.

Sample size calculation

The minimal clinically important difference for the LEFS is nine scale points.[294] In our feasibility study, we observed a mean LEFS score of 45.0 points (SD 18.4 points). We have also allowed for a 39% missing data rate but we will implement measures in the definitive trial to improve LEFS completion rates. For the purposes of the sample size calculation we have assumed a similar SD for the LEFS at 12 months post operation, owing to the lack of published data on LEFS scores at this time point. We have also accounted for a missing data rate of 39%, although we will implement measures in the definitive trial to improve LEFS completion rates. Therefore, we have calculated that we will need to recruit a sample of 256 patients to allow us to detect a minimal clinically important difference on the LEFS between trial arms at 12 months post operation, assuming a power of 80%, a two-sided 5% significance level and accounting for up to 39% missing data or attrition.

Discussion

This study was designed to evaluate the feasibility of implementing a RCT comparing a physiotherapy exercise class with usual care for patients after TKR. We recruited 46 participants from 124 patients approached in an orthopaedic clinic, giving a recruitment rate of 37.1%. This rate is similar to that of a recent feasibility trial by Minns Lowe and colleagues[595] with a recruitment rate of 34%, but lower than previous RCTs where recruitment rates range from 47% to 63%.[520,597] Recruitment into trials can be difficult and investigations to evaluate barriers in the recruitment process are important to optimise participant uptake. The main reasons for non-participation in our study were travel-related issues and the inability to commit to the intervention if allocated to this group. Issues with transportation have been highlighted in a previous feasibility study in which 43% of non-participation was due to travel and parking issues,[595] indicating that provision of independent travel to study appointments could potentially increase recruitment rates. However, in our study participants were offered transport if allocated to the intervention group and reimbursement of travel costs. Greater emphasis on the provided travel arrangements in future trials may also be beneficial for patients considering participation in studies involving travelling to additional appointments.

Despite the burden of attending six additional physiotherapy appointments, the group physiotherapy exercise class was generally well received and attendance was high. The attendance rate of 73% is similar to that of other studies that involve repeated appointments for a physiotherapy intervention.[590] Harmer and colleagues compared land-based with water-based rehabilitation after TKR and reported an 81% attendance rate when participants attended more than eight treatment sessions.[590] Feedback from participants allocated to the intervention group in our study was generally positive and supportive of the exercise class, with 84% of participants reporting that they were satisfied. Participants reported that the class was of adequate duration and included exercises that met their needs. Although satisfaction following knee replacement is high,[628] levels of physical function are lower in TKR patients,[629] who often require more physiotherapy input than patients with other arthroplasties.[618] Several ongoing difficulties are reported after surgery.[618,630] Wright and colleagues[630] reported that the most common functional complaints do not improve after knee replacement, the complaints include difficulty kneeling and crouching, and impaired ability to walk up and down stairs. Rogers and colleagues[629] also found bending/stooping and walking 1 km a frequently reported difficulty after TKR. The aim of the exercise class was to provide patients with a series of different exercises, including kneeling, stairs and treadmill walking, to address these common difficulties and that can be transferable into normal daily life. Unfortunately, this study was not powered to determine whether or not such improvements can occur with the provision of our physiotherapy exercise class design and a larger-scale RCT is required.

It was also noted that the class was beneficial on an emotional level by increasing confidence and having regular contact with other patients, and access to professionals with expertise in rehabilitation was valued. Health professional support and engagement with peers is important for patients after joint replacement[626] and can have a positive impact on functional attainment and QoL.[631] Group-based physiotherapy can be enjoyable for patients,[628] allows patients to compare their progress with that of their peers and offers interaction between patients who have experienced knee replacement surgery.[628] Involving participants

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

with designing their own rehabilitation was well received with the individualised exercise component scoring 9.5 out of 10 for usefulness. Thus, offering a one-to-one component, albeit in the initial stages of the class, and devising strategies to involve patients in their own rehabilitation is important to assist in adherence, empowerment and self-efficacy.[626,627] The concept of incorporating one-to-one physiotherapy within the group setting has been highlighted by Naylor and colleagues[628] as potentially beneficial in allowing identification of persistent postoperative problems and by influencing adherence. Our study indicates that patients were satisfied with the nature of the exercise class and individualised component offered, suggesting that this is a feasible design for future large-scale RCTs.

In addition to developing an exercise intervention, we evaluated the use of a postal study questionnaire and resource-use log. Questionnaire return rates were found to be higher in the intervention group than the usual care group, particularly at 3 and 6 months after surgery. Additional telephone contact to collect the primary outcome measure increased the number KOOS scores recorded. Reasons for this low return rate in the usual care group were not explored in this study but this highlights the limitations of using postal questionnaires. The higher return rates in the intervention group are not unexpected and may reflect closer relationships developed between participants attending the group and the research team/physiotherapists compared with those not invited to attend the class. One participant in the usual care group quoted in the study evaluation document that 'if I was in the group (referring to the exercise class) I would have probably filled out the forms'.

Another key part of this feasibility study was to investigate the use of different outcome measures for patients after TKR. It has been suggested that there is a need for newer measures to evaluate rehabilitation outcome in patients with TKR[595] and part of this study was to look at the return and completion rates of study outcome measures. Of particular interest were the KOOS and LEFS. Although the return rates were higher in the physiotherapy intervention group than in the usual care group, the completion rates of those measures returned were similar between groups at both 3 and 6 months after surgery. Completion rates were lowest for the KOOS sport and recreation subsection at 6 months following surgery, particularly with questions related to running, jumping, kneeling and squatting, indicating that participants may have found these specific questions irrelevant and this should be a consideration for the use of this outcome measure in future trials.

Sample size

Using the LEFS as a functional outcome measure to generate a sample size calculation demonstrated that a total of 256 participants would be required to run a full-scale RCT powered at 80%. Using the LEFS as an outcome measure may provide a more feasible method of delivering a RCT comparing our physiotherapy intervention with usual care in a timely manner at our centre. The LEFS is a validated 20-item questionnaire that assesses lower limb functional impairment and difficulty in performing everyday tasks. The LEFS has been recommended as the outcome measure of choice to measure physical functioning in patients with knee osteoarthritis because of its good psychometric properties and minimal floor and ceiling effects,[497] and has more recently been used in trials to compare physiotherapy interventions after TKR.[589,600] In the study by Fung and colleagues[589] the LEFS was used as an outcome measure to compare the effects of additional Wii-Fit (Nintendo Wii™; Nintendo of America, Redmond, WA, USA) exercises with outpatient physiotherapy after TKR. The study included 50 participants and had a medium effect size. A sample size of 80 would be required for a fully powered trial. Other authors report varying sample sizes depending on outcome measures used. Minns Lowe and colleagues[595] used the OKS to demonstrate that 521 participants would be required in each arm (90% power, level of significance 0.05) to run a RCT comparing usual care with home physiotherapy after TKR. Furthermore, Frost and colleagues[588] reported that, depending on the outcome measure used, between 100 and 550 participants would be required to compare the effects of traditional and functional exercises in patients after TKR. Thus, the use of the LEFS in the present study would allow acceptable recruitment numbers and sufficient power to run a fully powered RCT comparing the physiotherapy group exercise with usual care.

Conclusion

The implementation of a RCT to compare a 6-week functional exercise group with usual care for patients after TKR is a feasible and acceptable design in a large orthopaedic centre. In order to run fully powered trial, a total of 256 participants would need to be recruited for the LEFS to be used as a primary outcome measure.

Physiotherapy exercise general discussion

We conducted a survey in 2011 of physiotherapy provision after total hip and knee replacement at high-volume orthopaedic centres in England and Wales. We found that physiotherapy following discharge after TKR was a more common practice than after THR, for which ongoing physiotherapy was provided depending on clinical need. Group exercises were the favoured destination for patients following TKR in high-volume centres with focus on knee-specific strengthening, stretching and functional exercises.

After THR, no high-volume orthopaedic centres offered routine physiotherapy unless patients were considered in clinical need of additional physiotherapy support.

In our studies of evaluations of physiotherapy exercise we focused on patients with TKR. We were aware of a systematic review in progress that was updating the review of physiotherapy exercise by Minns Lowe and colleagues,[85] which is now published.[632] Although the authors concluded that published studies support some potential benefit for physiotherapy exercise in relation to patient function, walking and muscle strengthening, there is a need for further high-quality studies with adequate statistical power and long-term follow-up.

In our systematic review and meta-analysis of studies including patients with TKR, there was a suggestion that patients who received a programme of physiotherapy exercise achieved short-term improvements in physical function and pain compared with controls. However, this was based on a small number of studies with small numbers of patients randomised. Again based on limited evidence, there was no benefit suggested in relation to longer-term recovery.

There were insufficient studies with adequate patient numbers to provide conclusive evidence on different methods of provision. To evaluate the clinical effectiveness of home-based provision compared with physiotherapy exercise in an outpatient setting would require large studies, as the objective would be to show equivalence. On the basis of their pilot study, Minns Lowe and colleagues[595] concluded that a more definitive evaluation of home-based compared with outpatient provision would require randomisation of 1271 patients with TKR.

In developing a new physiotherapy exercise intervention for evaluation in patients with TKR, we recognised the importance of individual patient concerns and the need to focus on activities that they consider important. This formed the basis of an individualised and task-orientated exercise class developed for evaluation in the ARENA study. Group physiotherapy is a cost-effective method of delivery and allows patients to participate in exercise within a supported environment in the company of other patients with similar problems. The inclusion of individualised exercises specific to each patient's problems aimed to increase self-efficacy and to empower patients to take an active role in their rehabilitation.

We conducted a RCT to evaluate the feasibility of providing a 6-week postoperative activity-orientated rehabilitation programme for patients undergoing TKR. The group physiotherapy exercise class was generally well received and attendance was high, with 84% of participants reporting that they were satisfied. Participants reported that the class was of adequate duration and included exercises that met their needs. The main reasons for non-participation in the study were travel related and the inability to commit to the intervention.

In order to run a fully powered trial, we estimate that 256 participants would need to be recruited with the LEFS used as a primary outcome measure.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Chapter 12 Discussion and conclusions

The RESTORE programme

Well-conducted studies in representative populations of patients with total hip and knee joint replacement suggest that many people continue to have painful joints after surgery. The proportion of people with an unfavourable long-term pain outcome ranges from about 7% to 23% after hip replacement and 10% to 34% after knee replacement. Similarly, about 10% of patients with hip replacement and 30% with knee replacement do not have a long-term functional improvement that is clinically or statistically significant. The amount of improvement in walking performance is rarely large.

Improving the experience and outcome of joint replacement has the potential to impact on patients and services. The RESTORE programme was designed to deliver high-quality research focusing on understanding the experience of joint replacement and to identify ways to improve the experience and outcomes of people undergoing total hip or knee replacement for osteoarthritis.

We conducted research into care at key times in the patient pathway from being referred for total hip or knee replacement to the time after surgery when an optimal outcome should be achieved. We have used appropriate research methods to synthesise evidence from previous research, to explore the patient experience of surgery, to evaluate the clinical effectiveness, cost-effectiveness and acceptability of a perioperative pain management strategy, to compare the properties and responsiveness of outcome measures, and to assess the feasibility of new interventions before and after joint replacement. Approaches used were systematic reviews, cohort studies, fully powered RCTs and smaller feasibility randomised trials, a survey of current practice and qualitative studies. To ensure PPI throughout the programme, all studies were discussed and developed in collaboration with patient representatives and a patient forum.

Originally we had aimed to focus our ADAPT study on the development of new outcome measures relating to the pain and functional problems experienced by people with osteoarthritis, specifically ICOAP and Ab-IAP. Our patient group argued strongly that we should avoid using questionnaires that repeated themselves and we are aware of the fatigue experienced by study participants completing multiple questionnaires with associated poor-quality and incompleteness of data. Thus, in ADAPT, we studied key patient-reported outcomes, performance tests and movement analysis.

Another change from our original objectives relates to the design of a complex package of care supporting patients throughout the joint replacement pathway. We identified five possible elements: pre-surgical education, optimisation of pre-surgical health, occupational therapy and home modifications provided before surgery, physical therapy, and pain control. Preliminary systematic reviews by us as well as others did not identify evidence-based interventions to fulfil the specific elements. This indicated the need for feasibility studies as conducted in the RESTORE programme and ultimately fully powered RCTs. One of these, the ARENA randomised trial of physiotherapy exercise after TKR commenced in March 2015.[633]

Ultimately, we aim to develop consensus statements and the conclusions of the RESTORE programme will be a cornerstone of these along with new studies based on these research findings and information from the National Joint Registry.

To draw together the conclusions from the separate research strands we now consider our findings in the context of research practice and the patient pathway from waiting for total hip or knee replacement through surgery and rehabilitation to long-term recovery.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Research practice

Numerous methods are available to assess general health and functional outcomes after hip and knee replacement. A limitation to several of our studies was the need for questionnaires to be completed in English by participants or carers. Validated translations of several questionnaires are now available and this should be a factor considered in future research.

In our ADAPT cohort study, we compared different measures used to assess function in people undergoing hip and knee replacement. The strongest correlations were between the different self-assessment measures and between the different performance tests. However, the correlations between self-assessment measures and performance tests were much lower, highlighting the importance of using both a self-assessment measure and a performance test to obtain a comprehensive assessment of function. Furthermore, associations between functional measures and other patient factors suggest that age, pain and psychological health should be considered as covariates in future analyses.

Ceiling effects were noted for self-assessment measures such as WOMAC and to a lesser extent for the clinician-administered scores. Some objective measures and gait analyses were still improving after surgery at a time when WOMAC function scores were reaching a plateau. However, other objective measures had a similar pattern of improvement, suggesting that the WOMAC function score provides a reasonable reflection of functional change.

Range of motion is commonly used to evaluate joint replacement outcome in clinical practice after hip and knee replacement and forms part of widely used outcome scores. In the ADAPT study, ROM did not correlate well with other measures of function and seemed to add little value to the assessment of functional impairment.

In our systematic review looking at pain outcome assessment in published research in TKR, we found that assessment has been inconsistent with extensive variation in measures used. The most commonly used outcome measure relied on clinician assessment with a single question about pain. Despite the availability of many validated pain-related instruments, few studies had attempted to capture the incidence, character and impact of chronic pain after TKR. Our review showed a reduction over time in the use of the AKSS, accompanied by an increase in the use of the WOMAC index, an established PROM. Future research is needed to develop consensus and standardisation on which pain domains should be assessed after TKR.

In evaluating the clinical effectiveness of interventions, RCTs and ultimately their systematic review and meta-analysis provide the most reliable evidence on the clinical effectiveness of interventions. In our APEX randomised trials investigating the clinical effectiveness and cost-effectiveness of wound infiltration anaesthesia in reducing chronic pain after hip and knee replacement, we achieved a recruitment rate of > 50%. Within the trials, research nurses used peer-review methods to support training and optimise recruitment practice. In qualitative interviews, patients and health-care professionals reported that they had weighed up the benefit and cost of involvement. They were interested in involvement in the APEX trials because they considered the trials to be important and relevant. Patients expressed their desire to help others by contributing to the furthering of clinical knowledge and many patients thought that they might benefit physically and psychologically from taking part.

Qualitative studies including APEX participants and health-care professionals also demonstrated the importance of clinical trials placing minimal burden on patients and health-care professionals. Health-care professionals wanted the trial to have minimal impact on daily clinical practice and patients wanted data collection and participation to be as easy as possible.

Waiting for total hip or knee replacement

In the APEX cohort we compared radiographic assessment of osteoarthritis severity with patient-reported function and pain severity. For patients with hip osteoarthritis, there was no strong association but in patients with knee osteoarthritis, those with less severe radiographic osteoarthritis had more severe pain and functional problems. This suggests that some patients may have pain that is driven predominantly by central pain sensitisation rather than peripheral changes within the joint.

Comparisons of recovery trajectories in hip and knee replacement show different inter-relationships between pain and function. In the APEX cohort, chronic pain after THR was driven predominantly by pain at rest while chronic pain after TKR was driven predominantly by pain on movement. These findings suggest different pain mechanisms within hip and knee osteoarthritis and highlight the importance of future work to identify the sources and potential treatment options for these different pain mechanisms.

Interviews with patients found that delays for surgery are a common occurrence in the NHS for patients awaiting orthopaedic intervention. Patients can experience a range of emotional reactions if their surgery is delayed or cancelled and the wait for surgery can have detrimental physical and emotional consequences. It is important that health professionals identify those at increased risk and work towards minimising delay and cancellation of operation dates where possible.

In our review of longitudinal studies, patients with better physical function and lower pain before total hip and knee replacement generally achieved a better recovery in terms of joint specific pain and function. Patients with poor physical function before surgery may have greater absolute improvement. This was also noted in the ADAPT study, in which patients with very severe disease at the time of surgery were more likely to have substantially improved long-term function. However, in patients receiving TKR, functional levels achieved were related to the levels of function before surgery. This suggests that delays to surgery with associated functional decline may lead to worse outcomes for patients with knee osteoarthritis.

In the longitudinal studies identified in the review, patients with depression before surgery had poorer long-term pain and functional outcomes. For patients receiving TKR, there was evidence of a relationship between anxiety and poor general psychological health before surgery and poorer long-term pain and functional outcomes. In the APEX cohort study, we found that pre-operative widespread pain sensitisation was not predictive of the amount of pain relief that patients gained from total hip or TKR.

Patients with a broad range of BMIs benefited from total hip and knee replacement but those with the highest BMIs may not achieve good long-term levels of function and pain control.

Our qualitative research, cohort study, feasibility trials and systematic review of longitudinal studies suggest that interventions before surgery to optimise a patient's physical function, pain levels and psychological health merit further study. In the context of advanced osteoarthritis in which conservative treatments have not controlled symptoms, an exercise and education intervention may aim to maintain functional levels or prevent further decline. Alternatively, reduction of surgery waiting times may mean that patients do not experience further worsening of symptoms and thus poorer long-term functional outcomes.

In randomised evaluations of pre-surgical exercise and education identified in our systematic review, there was a suggestion that physical function can be enhanced and pain reduced before surgery in patients waiting for hip replacement. Studies in patients with knee replacement did not provide strong evidence for benefit. Interventions were associated with reduced anxiety during the hospital admission and quicker mobilisation. The value of specific exercise content was unclear, which may reflect the aims of pre-surgical exercise to maintain functional ability and prevent decline whereas post-surgical rehabilitation is substantially based on adjustment to physical changes associated with the prosthesis.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Pain management before surgery is important, particularly in the context of prolonged waiting times. In our feasibility randomised trial of a group-based pain self-management intervention for patients undergoing THR, the recruitment rate was 23%. Barriers to participation related to patient views of the course, satisfaction with current self-management and difficulty getting to the study centre. An issue in evaluation of pre-surgical interventions may be the perception of patients that conservative strategies have been exhausted and that only surgery can relieve pain. However, among those who attended, the group-based pain self-management intervention was acceptable and well received.

Conventionally, aids and home modifications to support independence are provided after surgery. Other aspects of occupational therapy, such as hip precautions, which aim to reduce the risk of dislocation, may be provided at pre-operative classes, in written material and reinforced during the hospital stay. In our systematic review (see *Chapter 10*), we found some evidence from a few small studies for benefit for occupational therapy in improving physical function, usually when provided in combination with physiotherapy exercise. Improvements to physical function and pain were only short-term. In the PROOF-THR study, we conducted a feasibility randomised trial of a pre-operative occupational therapy home visit with provision and instruction in use of compensatory devices, education and counselling. The successful recruitment, randomisation of participants and delivery of the intervention, plus the reasonable attrition rate, suggested that this trial design would be feasible to take forward into a large definitive trial.

Perioperative pain management

Our systematic review suggested that local anaesthetic infiltration before wound closure was effective in reducing short-term pain after total hip and knee replacement. Pain was further reduced with the addition of post-closure analgesia and, in TKR, with inclusion of ketorolac in the infiltrate. In TKR, there was little evidence to suggest additional benefit to that provided by FNB. Few studies explored the potential long-term impact of perioperative pain management with local anaesthetic infiltration.

Our APEX RCTs were fully powered evaluations including 322 patients receiving THR and 316 patients receiving TKR. Patients were randomised to an intervention of local anaesthetic wound infiltration or to a control group receiving usual care. In patients with THR, there was little benefit for local infiltration anaesthesia in reducing pain during the first 3 days after surgery. In our meta-analysis of previous studies, benefit for the specific regimen evaluated in the APEX trials was apparent only at rest at 24 hours with no benefit during activity or at 48 hours. Only when additional post-closure anaesthesia was provided through a catheter or injection was there benefit at 48 hours and during activity. Few previous studies reported long-term outcomes. In our APEX hip trial, local anaesthetic infiltration was associated with reduced incidence of long-term pain after THR.

In the APEX trial in patients with TKR, all patients had a FNB sited during surgery, a recognised method of providing analgesia after TKR. In the first 48 hours after surgery there was little suggestion of improvement in pain control in patients receiving local anaesthetic infiltration compared with controls. This was consistent with short-term results from systematic review in trials in which FNB was provided. There was no strong evidence for improved long-term pain control in patients receiving local anaesthetic infiltration in the APEX knee trial.

In the absence of FNB, our systematic review showed short-term benefit for local anaesthetic infiltration in patients receiving TKR, particularly if additional analgesia was provided through a catheter or injection after wound closure. In developing the protocol for the APEX trials, we decided against the use of extra delivery of anaesthesia. The use of catheters generally in health care is associated with a risk of infection. In the studies we reviewed, the rate of deep infection after hip or knee replacement was low and it is not possible to state conclusively that use of a catheter was associated with increased risk of infection. However, there were six infections in 505 patients who received an active catheter (1.19%), compared with a total of eight infections in all 2348 patients randomised (0.34%). Further cohort or registry studies may provide more definitive evidence on the safety of additional analgesia provided through catheters after wound closure.

From the perspective of the NHS and PSS, the addition of local anaesthetic infiltration to the usual analgesia regimen was a cost-effective treatment option in primary THR. Our findings also indicate positive health benefits and cost savings in TKR, but with considerably more uncertainty around the cost-effectiveness result.

Qualitative interviews with patients in the APEX study showed that the experience of joint replacement can temporarily alter patients' views of the acceptability, necessity and value of pain relief medication around the time of surgery. Once recovery from surgery has started, then long-standing beliefs about appropriate use of pain relief medications may take prominence. This alteration is related to views about pain due to surgical intervention in contrast with interpretation of pain from living with long-term osteoarthritis. Importantly, views about pain medication use are influenced by interactions with health-care professionals.

Rehabilitation

Interviews highlighted how patients value the offer of postoperative physiotherapy shortly after surgery as well as longer-term follow-up in secondary care. The latter may be of particular value for those patients who experience complications after surgery or who lack confidence in their prosthesis.

In our survey of physiotherapy provision at high-volume orthopaedic centres in England and Wales, we found that physiotherapy following discharge after TKR was a more common practice than after THR. For patients following TKR, the focus was on knee-specific strengthening, stretching and functional exercises provided in a group setting.

In our systematic review and meta-analysis there was a suggestion that patients who received a programme of post-discharge physiotherapy exercise after TKR achieved short-term improvements in physical function and pain compared with controls (see *Chapter 11*).[585] However, this was based on a small number of studies with low numbers of patients randomised. There was no evidence, again from a few small studies, for better longer-term recovery in patients receiving physiotherapy exercise. Regarding provision at home, further research is needed to establish equivalence or additional benefit in comparison with that provided in an outpatient setting.

In the ARENA study, we assessed the feasibility of a randomised trial to evaluate a 6-week individualised and task-orientated exercise class. The inclusion of individualised exercises specific to each patient's own concerns aimed to increase self-efficacy and to empower patients to take an active role in their rehabilitation. The group physiotherapy exercise class was generally well received and attendance and satisfaction were high. The main reasons for non-participation in the study were travel related and the inability to commit to the intervention. The ARENA study suggested that a fully powered RCT of individualised and task-orientated exercises would be feasible in patients with TKR.

Potential value of a complex package of care

In the RESTORE programme we have identified key time points when specific interventions merit evaluation in fully powered RCTs. Once there is evidence in place about the clinical effectiveness and cost-effectiveness of specific interventions, their value may be greatest if implemented as a complex intervention.

In the care of older people, a complex intervention can be regarded as 'a combination of interdisciplinary teamwork for health and social problems'.[634] According to the UK MRC framework, a complex intervention has a number of interacting components, a number of behaviours and level of difficulty required by those delivering or receiving the intervention, a number of groups or organisational levels targeted, and a number and variability of outcomes.[94] A degree of flexibility or tailoring of the intervention can be incorporated.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Some published interventions have covered both the pre- and post-surgical rehabilitation periods. For example, Gilbey and colleagues[494] and Mitchell and colleagues[520] demonstrated the feasibility of physiotherapy exercise in total hip and knee replacement patients, respectively.

Our research suggests potential value for a number of components for incorporation in a complex intervention:

- pre-surgical education on the patient pathway, pain management, psychological counselling and advice or interventions relating to maintenance or improvement of physical function
- pre-surgical health check to ensure appropriate management of health conditions
- occupational therapy provided before surgery at home visit
- evidence-based perioperative pain management
- post-discharge physiotherapy with a patient choice element.

For patients, interventions embedded within a care pathway might be more acceptable than those provided exclusively before surgery when the perception is that little can be achieved, or after a care pathway when, for the majority of patients, a degree of improved function and pain relief have been achieved by the joint replacement itself.

Conclusions and recommendations

Future research is needed to develop consensus and standardisation on which pain domains should be assessed after TKR. For assessment of functional outcomes, researchers should consider a patient-reported outcome and a performance test.

Large-scale randomised evaluations in patients receiving total hip and knee replacements are feasible and their value is recognised by patients and health-care professionals. Health-care professionals want randomised trials to have minimal impact on daily clinical practice and patients want data collection and participation to be as easy as possible.

Local anaesthetic infiltration as evaluated in the APEX RCT is effective in reducing the incidence of long-term pain after THR and is also cost-effective. In TKR, there may be limited benefit for improved pain control if a FNB has already been sited.

We have shown that a group-based activity-orientated physiotherapy intervention is both feasible and acceptable to patients who have received a TKR. Further research is indicated to evaluate its clinical effectiveness and cost-effectiveness in an appropriately powered randomised evaluation.

Future research should evaluate the clinical effectiveness and cost-effectiveness of providing aids, home modifications and other aspects of occupational therapy to patients before their hospital admission for THR. We have shown this to be both feasible and acceptable to patients. Background research is required to support similar interventions in TKR.

Research should explore the possibility that optimising management of comorbid health conditions may improve outcomes for patients with total hip and knee replacement. In the first instance, this will require up-to-date systematic reviews of health management interventions and ultimately RCTs to evaluate the clinical effectiveness and cost-effectiveness of optimising the treatment of comorbid conditions. Provision of education, exercise and counselling before surgery may not be acceptable to a large proportion of patients waiting for total hip or knee replacement.

Ultimately, the optimal care for patients receiving total hip and knee replacement may be a complex intervention covering all stages of the patient pathway with the incorporation of patient choice and individualisation of therapies.

Acknowledgements

Management of the RESTORE programme

Ultimate responsibility for management of the programme lay with the PI, Professor Ashley Blom. Professor Paul Dieppe and Dr Rachael Gooberman-Hill were deputy PIs for the programme and provided significant input into the management, co-ordination and strategic development of all the work packages. Most of the staff recruitment was led by Dr Rachael Gooberman-Hill with input from North Bristol Research and Innovation into all NHS posts. The programme was co-ordinated by Dr Vikki Wylde with the help of Mrs Louise Hawkins. Three monthly programme meetings were held for all the coapplicants. The entire programme was hosted by North Bristol NHS Trust with the exception of the occupational therapy work package which was undertaken in two hospitals in the West Midlands. Subcontracts with the Universities of Bristol, Exeter, Birmingham and East Anglia facilitated shared working between the NHS and University academia. Individual work packages were led by Mr Andrew Beswick (systematic review), Dr Rachael Gooberman-Hill (qualitative studies and public/patient involvement), Professor Ashley Blom (APEX and ADAPT), Dr Vikki Wylde (pain management), Dr Neil Artz (physiotherapy), Professor Catherine Sackley (occupational therapy) and Dr Sian Noble (health economics). Assembly and writing of the final programme report was co-ordinated by Mr Andrew Beswick.

All trials were monitored regularly by the Research and Innovation department and APEX was inspected by the Medicines and Healthcare products Regulatory Agency as part of the routine inspection of North Bristol NHS Trust. Furthermore, all trials were monitored by independent Trial Steering Committees and APEX was additionally monitored by an independent data monitoring committee. Regular meetings were held for each separate trial by the research staff involved. In addition, we circulated monthly reports of progress in patient recruitment and outcomes.

Contributions of authors

Ashley W Blom (Professor, Orthopaedic Surgery) was the PI of this research programme and research lead for APEX and ADAPT. Contributed to all aspects of the research from inception to writing of the report.

Neil Artz (Lecturer, Physiotherapy) was the research lead for ARENA and the physiotherapy survey.

Andrew D Beswick (Research Fellow, Systematic Reviews) was a coapplicant on the grant application and research lead for the systematic reviews. Supervised design, conduct and analysis of studies within the research programme. Coordinated writing of the final report.

Amanda Burston (Research Assistant, PPI) contributed to all aspects of PPI.

Paul Dieppe (Professor, Health Services Research) was a coapplicant on the grant application and contributed to the research programme, particularly the ADAPT study, from inception to writing of the report.

Karen T Elvers (Research Associate, Systematic Reviews) contributed to the design, conduct and analysis of the systematic reviews.

Rachael Gooberman-Hill (Reader, Health Services Research) was a coapplicant on the grant application and research lead for the qualitative studies and PPI. Supervised design, conduct and analysis of studies within the research programme.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Jeremy Horwood (Senior Research Fellow, Qualitative Research) was a coapplicant on the grant application and contributed to the design, conduct and analysis of the qualitative studies.

Paul Jepson (Clinical Tutor in Physiotherapy, Physiotherapy) contributed to the design, conduct and analysis of the PROOF-THR study and occupational therapy systematic review.

Emma Johnson (Research Associate, Qualitative Research) contributed to the design, conduct and analysis of the qualitative studies.

Erik Lenguerrand (Research Fellow, Statistics) contributed to the statistical analysis of studies.

Elsa Marques (Research Associate, Health Economics) contributed to the design, conduct and analysis of the health economics work and systematic reviews.

Sian Noble (Senior Lecturer, Health Economics) was a coapplicant on the grant application and research lead for health economics.

Mark Pyke (Consultant Anaesthetist, Anaesthetics) was a coapplicant on the grant application and contributed to the design, conduct and interpretation of studies within the research programme.

Catherine Sackley (Professor, Rehabilitation) was a coapplicant on the grant application and research lead for PROOF-THR.

Gina Sands (Senior Research Associate, Rehabilitation) contributed to the conduct and analysis of the PROOF-THR study.

Adrian Sayers (Research Fellow, Statistics) contributed to the statistical analysis of data.

Victoria Wells (Former Patient) contributed patient and public perspective to all the research studies.

Vikki Wylde (Research Fellow, Health Services Research) was a coapplicant on the grant application, overall programme co-ordinator, research lead for SPIRAL and trial manager for APEX. Contributed to the design, conduct and analysis of studies within the research programme.

All authors contributed to the writing of the report.

Thanks to collaborators and contributors

Particular thanks go out to the patients who participated in the RESTORE RCTs and cohort studies, and to the patients and health-care professionals who we interviewed.

We would like to give special thanks for contributions to the RESTORE programme to Andy Judge, Anthony Sack, Avril Drummond, Bernd Grimm, Beverley Evanson, Caroline Roper, Catherine Minns Lowe, Cindy Mann, Constance Jamera, David Rea, Debbie Delgado, Diana Pratt, Ed Davies, Emma Clark, Emma Gendall, Hayley Jones, Ian Learmonth, James Berstock, Jennifer Tyler, Jon Tobias, Julia Edwards, Julie Bruce, Koye Odutola, Laura Miller, Leigh Morrison, Louise Hawkins, Luke Brunton, Mike Whitehouse, Natalija Stefanovich-Lawbuary, Nick Howells, Phil Baker, Pippa English-Penfold, Rachel Haynes, Samantha Dixon, Sara Brooks, Sharon Nolan, Sophie Whitcombe, Stijn Bolink, Sue Bowman, Sue Evans, Tim Peters, Toby Smith and Will Hollingsworth.

We would like to express particular thanks to the patient partners who have contributed to the PEP-R group and ultimately to the successful delivery of the RESTORE programme.

We acknowledge the support of the NIHR, through the Comprehensive Clinical Research Network.

Thanks also go to all the consultant orthopaedic surgeons and anaesthetists who contributed to the RESTORE programme, with special thanks to Gordon Bannister, John Church, Steve Eastaugh-Waring, Alan Gibson, Williams Harries, Paul Harvie, Katherine Jenkins, Michael Kelly, Nick Koehli, John Leigh, Sanchit Mehendale, Ronelle Mouton, Andrew Porteous and Jason Webb.

We would like to thank members of the APEX data monitoring committee (Paul Ewings, Neville Goodman and Adrian Taylor), APEX trial steering committee (Alan Montgomery, David Marsh, Julie Chappell and Cathy Stannard) and ADAPT steering committee (Shea Palmer and John Collins).

We would also like to thank Nigel Arden and the COAST programme team.

We are grateful for the support of Nicola Williams and colleagues at Research and Innovation, North Bristol NHS Trust, and also to the University of Bristol, University of Birmingham, University of East Anglia and the University of Exeter.

We would like to thank the authors of research studies who provided additional information for our systematic reviews: Aleksandra Vukomanovic, Alison Harmer, Alison McGregor, Ann Swank, Anna-Maija Kauppila, Brian Mockford, Carol Mancuso, Caroline Mitchell, Clare Sandell, Constant Busch, Daniel Rooks, Damien Bennett, Damien Byrne, Deborah McDonald, Gary Minto, Georgios Evgeniadis, Helen Frost, In Jun Koh, Janine-Sophie Giraudet LeQuintrec, Karen Toftdahl Bjørnholdt, Kirsi Johansson, Martin Thorsell, Michael Dewey, Michel Tousignant, Montserrat Núñez, Osamu Aoki, Per Essving, Per Wretenberg, Peiliang Fu, Rohan Rajan, Sara Piva, Simona Ferrante, Thomas Hoogeboom, Thoralf Leibs, Tim Ackland, Torben Bæk Hansen, Vera Fung, Yi ChenYun-Li Zhu and Yvette Bulthius.

Publications

APEX[364,365,367,472,473]

Wylde V, Gooberman-Hill R, Horwood J, Beswick A, Noble S, Brookes S, *et al.* The effect of local anaesthetic wound infiltration on chronic pain after lower limb joint replacement: a protocol for a double-blind randomised controlled trial. *BMC Musculoskelet Disord*; 2011;**12**:53.

Wylde V, Lenguerrand E, Gooberman-Hill R, Beswick AD, Marques E, Noble S, *et al.* Effect of local anaesthetic infiltration on chronic postsurgical pain after total hip and knee replacement: the APEX randomised controlled trials. *Pain* 2015;**156**:1161–70.

Wylde V, Sayers A, Lenguerrand E, Gooberman-Hill R, Pyke M, Beswick AD, *et al.* Preoperative widespread pain sensitization and chronic pain after hip and knee replacement: a cohort analysis. *Pain* 2015;**156**:47–54.

Marques E, Blom AW, Lenguerrand E, Wylde V, Noble SM. Local anaesthetic wound infiltration in addition to standard anaesthetic regimen in total hip and knee replacement: long-term cost-effectiveness analyses alongside the APEX randomised controlled trials. *BMC Med* 2015;**13**:151.

Sayers A, Wylde V, Lenguerrand E, Beswick AD, Gooberman-Hill R, Pyke M*, et al.* Rest pain and movement-evoked pain as unique constructs in hip and knee replacements. *Arthritis Care Res* 2016;**68**:237–45.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

ADAPT[262–265]

Wylde V, Blom AW, Bolink S, Brunton L, Dieppe P, Gooberman-Hill R, *et al.* Assessing function in patients undergoing joint replacement: a study protocol for a cohort study. *BMC Musculoskelet Disord* 2012;**13**:220.

Wylde V, Lenguerrand E, Brunton L, Dieppe P, Gooberman-Hill R, Mann C, *et al.* Does measuring the range of motion of the hip and knee add to the assessment of disability in people undergoing joint replacement? *Orthop Traumatol Surg Res* 2014;**100**:183–6.

Bolink SAAN, Brunton LR, van Laarhoven S, Lipperts M, Heyligers IC, Blom AW, *et al.* Frontal plane pelvic motion during gait captures hip osteoarthritis related disability. *Hip Int* 2015;**25**:413–19.

Lenguerrand E, Wylde V, Gooberman-Hill R, Sayers A, Brunton L, Beswick AD, *et al.* Trajectories of Pain and Function after Primary Hip and Knee Arthroplasty: the ADAPT Cohort Study. *PLOS ONE* 2016;**11**:e0149306.

Patient experience[229,230,363]

Johnson E, Horwood J, Gooberman-Hill R. Patients' journeys through total joint replacement: patterns of medication use. *Musculoskeletal Care* 2014;**12**:92–102.

Johnson EC, Horwood J, Gooberman-Hill R. Conceptualising time before surgery: the experience of patients waiting for hip replacement. *Soc Sci Med* 2014;**116**:126–33.

Horwood J, Johnson E, Gooberman-Hill R. Understanding involvement in surgical orthopaedic randomized controlled trials: a qualitative study of patient and health professional views and experiences. *Int J Orthop Trauma Nurs* 2016;**20**:3–12.

Systematic reviews[18,95,366,585,635]

Beswick A, Wylde V, Gooberman-Hill R, Blom A, Dieppe P. What proportion of patients report pain after hip and knee replacement for osteoarthritis? A systematic review of prospective studies in unselected patients. *BMJ Open* 2012;**2**:e000435.

Wylde V, Bruce J, Beswick A, Elvers K, Gooberman-Hill R. The assessment of chronic post-surgical pain after knee replacement: a systematic review. *Arthritis Care Res* 2013;**65**:1795–803.

Marques E, Jones H, Elvers K, Pyke M, Blom AW, Beswick A. Local anaesthetic infiltration for perioperative pain control in total hip and knee replacement: systematic review and meta-analyses of short- and long-term effectiveness. *BMC Musculoskelet Disord* 2014;**15**:220.

Jepson P, Beswick A, Smith TO, Sands G, Drummond A, Davis ET, *et al.* Assistive devices, hip precautions, environmental modifications and training to prevent dislocation and improve function after hip arthroplasty (protocol). *Cochrane Database Syst Rev* 2013;**11**:CD010815.

Artz N, Elvers KT, Lowe CM, Sackley C, Jepson P, Beswick AD. Effectiveness of physiotherapy exercise following total knee replacement: systematic review and meta-analysis. *BMC Musculoskelet Disord* 2015;**16**:15.

SPIRAL[536]

Wylde V, Marques E, Artz N, Blom AW, Gooberman-Hill. Effectiveness and cost-effectiveness of a group-based pain self-management intervention for patients undergoing total hip replacement: feasibility study for a randomised controlled trial. *Trials* 2014;**15**:176.

ARENA/physiotherapy survey[78,586]

Artz N, Dixon S, Wylde V, Beswick A, Blom AW, Gooberman-Hill R. Physiotherapy provision following discharge after total hip and total knee replacement: a survey of current practice at high volume NHS hospitals in England and Wales. *Musculoskeletal Care* 2013;**11**:31–8.

Artz N, Dixon S, Wylde V, Marques E, Beswick AD, Lenguerrand E, *et al.* Comparison of group-based outpatient physiotherapy with usual care after total knee replacement: a feasibility study for a randomized controlled trial. *Clin Rehabil* 2016;**10**:epub ahead of print 11 April.

PROOF-THR[562]

Jepson P, Sands G, Beswick AD, Davis ET, Blom AW, Sackley CM. A feasibility randomised controlled trial of pre-operative occupational therapy to optimise recovery for patients undergoing primary total hip replacement for osteoarthritis (PROOF-THR). *Clin Rehabil* 2015;**30**:156–66.

Research methods[368]

Mann C, Delgado D, Horwood J. Discussion and qualitative evaluation of internal peer-review to train nurses recruiting to a randomised controlled trial – internal peer-review for recruitment training in trials (InterPReTiT). *J Adv Nurs* 2014;**70**:777–90.

Health economic studies[432]

Marques E, Johnson EC, Gooberman-Hill R, Blom AW, Noble S. Using resource use logs to reduce the amount of missing data in economic evaluations alongside trials. *Value Health* 2013;**16**:195–201.

Patient and public involvement[636]

Gooberman-Hill R, Burston A, Clark E, Johnson E, Nolan S, Wells V, *et al.* Involving patients in research: considering good practice. *Musculoskeletal Care* 2013;**11**:187–90.

Others[637–639]

Wylde V, Jeffery A, Dieppe P, Gooberman-Hill R. The assessment of persistent pain after joint replacement. *Osteoarthritis Cart* 2012;**20**:102–5.

Brunton L, Wylde V, Dieppe P. Assessing the health status of people with arthritis: does the research help the clinician? The example of osteoarthritis of the knee. *Rheumatology* 2012;**51**:1143–4.

Marques E, Noble S, Blom AW, Hollingworth W. Disclosing total waiting times for joint replacement: Evidence from the English NHS using linked HES data. *Health Econ* 2014;**23**:806–20.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Conference presentations and posters

APEX

Wylde V, Lenguerrand E, Gooberman-Hill R, Beswick A, Marques E, Noble S, *et al.* The effect of intra-operative local wound infiltration on chronic pain after total hip replacement: a randomised controlled trial. Paris: OARSI conference; April 2014.

Wylde V, Lenguerrand E, Gooberman-Hill R, Beswick A, Marques E, Noble S, *et al.* The effect of local anaesthetic infiltration on chronic post-surgical pain after total hip and knee replacement: the APEX randomised controlled trials. Milan: European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis; March 2015.

ADAPT

Lenguerrand E, Wylde V, Brunton L, Gooberman-Hill R, Dieppe P, Blom AW. Measuring physical function among patients with lower limb joint impairment. Bristol: Population Health Early Career Researchers' Event; June 2013.

Brunton L, Bolink S, Grimm B, Blom A. A novel gyrometer based assessment of the clinical orthopaedic single leg stance 'trendelenburg test'. Glasgow: Second International Conference on Ambulatory Monitoring of Physical Activity and Movement; May 2011.

Bolink S, Brunton L, van Laarhoven, Lipperts M, Grimm B, Heyligers IC, et al. Inertial sensor based gait analysis: a clinical application in patients with osteoarthritis. Barcelona: Osteoarthritis Research Society International; April 2012.

Lenguerrand E, Wylde V, Brunton L, Gooberman-Hill R, Blom AW, Dieppe P. The need for caution in the selection and interpretation of measures of function for patients with severe hip and knee problems. Paris: Osteoarthritis Research Society International conference; April 2014.

Lenguerrand E, Wylde V, Sayers A, Beswick AD, Brunton L, Gooberman-Hill R, *et al.* Pain recovery after hip and knee replacement: a longitudinal study. Milan: European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis; March 2015.

Patient experience

Johnson E, Horwood J, Gooberman-Hill R. 'I don't like pill popping': changes in patients' attitudes and behaviours towards pain relief medication at the time of total joint replacement. Edinburgh: British Pain Society conference; June 2011.

Johnson E, Gooberman-Hill R, Horwood J. 'I might as well, better than doing a crossword': patients' motivations for, and experience of, participation in an orthopaedic randomised controlled trial (RCT). Bristol: North Bristol Trust Research Day; November, 2011.

Johnson E, Gooberman-Hill R, Horwood J. 'I might as well, better than doing a crossword': patients' motivations for, and experience of, participation in an orthopaedic randomised controlled trial (RCT). Bristol: Population Health Symposium; November 2011.

Johnson E, Horwood J, Gooberman-Hill R. Experiences of delay and cancellation in the secondary care pathway to total hip replacement: a qualitative study. Bristol: Population Health Annual Symposium; November 2012.

Johnson E, Horwood J, Gooberman-Hill R. Understanding the experience of time while waiting for hip replacement surgery. Liverpool: British Rheumatology Society Conference; April 2014.

Gooberman-Hill R, Horwood J, Johnson E. Waiting for hip replacement: patients' experiences of time. Paris: Osteoarthritis Research Society International conference; April 2014.

Gooberman-Hill R, Horwood J, Johnson E. Psychological aspects of hip replacement: a longitudinal qualitative study of patients' experiences. Milan: European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis; March 2015.

Systematic reviews

Beswick A, Dieppe P, Wylde V, Gooberman-Hill R, Blom A. What proportion of patients report pain after total hip or knee arthroplasty for osteoarthritis? A systematic review of prospective studies in unselected patients. Chicago, IL: American College of Rheumatology Annual Scientific Meeting; November 2011.

Elvers K, Stefanovich-Lawbuary N, Artz N, Gooberman-Hill R, Blom AW, Beswick A. Pre-surgical interventions to optimise functional health before hip and knee arthroplasty. A systematic review of randomised controlled trials. Berlin: European Federation of National Associations of Orthopaedics and Traumatology; May 2012.

Beswick A, Wylde V, Gooberman-Hill R, Blom AW, Dieppe P. What proportion of patients report long-term pain after total hip or knee arthroplasty for osteoarthritis? A systematic review of prospective studies in unselected patients. Berlin: European Federation of National Associations of Orthopaedics and Traumatology; May 2012.

Wylde V, Bruce J, Beswick A, Elvers K, Gooberman-Hill R. The assessment of chronic pain after knee replacement: a systematic review. Bournemouth: British Pain Society Annual Scientific Conference; April 2013.

Wylde V, Bruce J, Beswick A, Elvers K, Gooberman-Hill R. The assessment of chronic pain after knee replacement: a systematic review. Bristol: Population Health Early Career Researchers' Event; June 2013.

Wylde V, Bruce J, Beswick A, Elvers K, Gooberman-Hill R. The assessment of chronic pain after knee replacement: a systematic review. Manchester: COMET conference; June 2013.

SPIRAL

Wylde V and Gooberman-Hill R. A pain management intervention for postoperative pain after hip replacement: barriers to trial participation. Bristol: Population Health Early Career Researchers Event; June 2012.

Wylde V and Gooberman-Hill R. A pain management intervention for postoperative pain after hip replacement: barriers to trial participation. Bristol: Population Health Annual Symposium; November 2012.

Wylde V, Marques E, Artz N, Blom AW, Gooberman-Hill R. Effectiveness and cost-effectiveness of a group-based pain self-management intervention for patients undergoing total hip replacement: feasibility study for a randomised controlled trial. Manchester: British Pain Society Annual Scientific Meeting; April 2014.

Wylde V, Marques E, Artz N, Blom AW, Gooberman-Hill R. Effectiveness and cost-effectiveness of a group-based pain self-management intervention for patients undergoing total hip replacement: feasibility study for a randomised controlled trial. Paris: Osteoarthritis Research Society International conference; April 2014.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

ARENA/physiotherapy survey

Wylde V, Artz N, Dixon S, Marques E, Lenguerrand E, Blom AW, *et al.* Effectiveness and cost-effectiveness of a group-based outpatient physiotherapy intervention following knee replacement for osteoarthritis: feasibility study for a randomised controlled trial. Paris: Osteoarthritis Research Society International conference; April 2014.

Dixon S, Artz N, Wylde V, Beswick A, Blom AW, Gooberman-Hill R. Physiotherapy provision following discharge after total hip and total knee replacement: a survey of current practice at high volume NHS hospitals in England and Wales. Bristol: Population Health Early Career Researchers Event; June 2014.

Artz, N. Rehabilitation following total knee replacement. Bristol: Arthroplasty Care Practitioner's Association annual conference; February 2013.

PROOF-THR

Jepson P, Hoppitt T, Beswick A, Wylde V, Sackley C. A pilot randomised controlled trial of pre-surgery occupational therapy intervention versus usual care to optimise recovery for patients undergoing primary total hip replacement for osteoarthritis. South West Society for Academic Primary Care Annual meeting, Devon: Society for Academic Primary Care Annual meeting, March 2012.

Jepson P, Sands G, Beswick A, Wylde V, Gravelle R, Sackley C. A pilot randomised controlled trial of occupational therapy to optimise recovery for patients undergoing primary total hip replacement for osteoarthritis (PROOF). Glasgow: Society for Research in Rehabilitation conference; June 2014.

Research methods

Gooberman-Hill R, Beswick A, Mann C, Johnson E, Horwood J, Blom A, *et al.* Enhancing the process of a clinical trial in osteoarthritis with embedded qualitative approaches. Belgium: Osteoarthritis Research Society International; September 2010.

Delgado D, Mann C. The importance of effective interpersonal and communication skills in order to maximise the buy-in of clinical staff: an experience of running a large RCT in a hospital setting. Harrogate: Annual Royal College of Nursing International Research Conference; May 2011.

Mann C, Gendall E, Morrison L, Delgado D. Peer review to enhance recruitment procedures in a large randomised controlled trial. Harrogate: Annual Royal College of Nursing International Research Conference; May 2011.

Mann C, Gendall E, Morrison L, Delgado D. Peer review to enhance recruitment procedures in a large randomised controlled trial (APEX). Bristol: North Bristol Trust Research Day; November 2011.

Lenguerrand E, Wylde V, Gooberman-Hill R, Noble S, Marques E, Dieppe P, *et al.* Trial data management: lessons from a large orthopaedic trial. Edinburgh: Second Clinical Trials Methodology Conference; November 2013.

Health economic methods

Noble S, Marques E, Johnson E, Blom A. The use of participant resource use logs in reducing the amount of missing data in resource use questionnaires. Toronto, ON: iHEA 8th World Congress on Health Economics; July 2011.

Noble S, Marques E, Johnson E, Blom A. The use of participant resource use logs in reducing the amount of missing data in resource use questionnaires. Bristol: MRC Clinical Trials Methodology Conference; October 2011.

Marques E, Johnson E, Gooberman-Hill R, Blom AW, Noble S. Using resource use logs to reduce the amount of missing data in economic evaluations alongside trials. Bristol: South West Health economists meeting; May 2012.

Patient and public involvement

Gooberman-Hill R, Burston A, Lenguerrand E, Clark E, Johnson E, PEP-R group. Patient involvement in clinical research: a qualitative evaluation of impact. Edinburgh: Second Clinical Trials Methodology Conference; November 2013.

Gooberman-Hill R, Burston A, Clark E, Johnson E, Nolan S, Wells V, *et al.* Evaluation of a patient involvement activity in musculoskeletal health research: impact on patients and researchers. Exeter: Consolidating the evidence base for public involvement in health services research event; November 2013.

Burston A, Gooberman-Hill R, Johnson E, Wells V, Clark E, Nolan S, *et al.* Patient involvement in musculoskeletal health research: a qualitative evaluation of impact. Liverpool: British Rheumatology Society Conference; April 2014.

Burston A. Panel member for workshop 'Public involvement beyond health research'. Bristol: National Co-ordinating centre for Public Engagement Annual conference; November 2013.

Others

Marques E, Noble S, Blom A, Hollingworth W. Disclosing total waiting times: clinical pathways for patients awaiting total joint replacement. York: Health Economists Study Group; January 2011.

Marques E, Noble S, Blom A.W. and Hollingworth W. Hidden waiting times for total joint replacement: a study of linked HES data. Bristol: Population Health Symposium; November 2011.

Beswick A, Gooberman-Hill R, Horwood J, Wylde V, Marques E, Blom A, on behalf of the RESTORE study group. The RESTORE programme. Bristol: Population Health Symposium; September 2010.

Beswick A, Elvers K, Gooberman- Hill R, Smith A, Blom A. What is the evidence to guide surgical treatment of infected hip prostheses? Bath: Bath biomechanics symposium; September 2011.

RESTORE team. The RESTORE programme. Amsterdam: European Orthopaedic Research Society Conference; September 2012.

Gooberman-Hill, R. Arthritis Care working with The Musculoskeletal Research Unit. Bristol: Arthritis Care AGM; June 2011.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Horwood J, on behalf of the RESTORE group. The RESTORE programme. Bristol: WLCRN Musculoskeletal specialty meeting; October 2011.

Wylde V. Orthopaedic health services research at the Musculoskeletal Research Unit. Bristol: School of Clinical Sciences Showcase Event; May 2013.

Study feedback reports for patients

Study feedback reports for patients are included in *Appendix 38*.

Data sharing statement

Requests for research collaborations based on data collected in the RESTORE programme should be addressed to the programme corresponding author. Subject to ethical approval when required, and the appropriateness of analyses proposed, the authors are committed to the sharing of data, statistical code and research methods.

References

1. Peat G, McCarney R, Croft P. Knee pain and osteoarthritis in older adults: a review of community burden and current use of primary health care. *Ann Rheum Dis* 2001;**60**:91–7. http://dx.doi.org/10.1136/ard.60.2.91
2. Woolf AD, Pfleger B. Burden of major musculoskeletal conditions. *Bull World Health Organ* 2003;**81**:646–56.
3. National Joint Registry for England and Wales. *National Joint Registry for England and Wales: 10th Annual Report*. Hemel Hempstead: NJR Centre; 2013.
4. Thorstensson C, Gooberman-Hill R, Adamson J, Williams S, Dieppe P. Help-seeking behaviour among people living with chronic hip or knee pain in the community. *BMC Musculoskelet Disord* 2009;**10**:153. http://dx.doi.org/10.1186/1471-2474-10-153
5. Sanders C, Donovan J, Dieppe P. The significance and consequences of having painful and disabled joints in older age: co-existing accounts of normal and disrupted biographies. *Sociol Health Illn* 2002;**24**:227–53. http://dx.doi.org/10.1111/1467-9566.00292
6. Gignac MA, Davis AM, Hawker G, Wright JG, Mahomed N, Fortin PR, *et al.* 'What do you expect? You're just getting older': a comparison of perceived osteoarthritis-related and aging-related health experiences in middle- and older-age adults. *Arthritis Rheum* 2006;**55**:905–12. http://dx.doi.org/10.1002/art.22338
7. Jordan K. *What do general practitioners see? Musculoskeletal Matters Bulletin 1*. Staffordshire: Arthritis Research UK Primary Care Centre; 2009.
8. Neogi T, Zhang Y. Epidemiology of osteoarthritis. *Rheum Dis Clin North Am* 2013;**39**:1–19. http://dx.doi.org/10.1016/j.rdc.2012.10.004
9. Kadam UT, Jordan K, Croft PR. Clinical comorbidity in patients with osteoarthritis: a case–control study of general practice consulters in England and Wales. *Ann Rheum Dis* 2004;**63**:408–14. http://dx.doi.org/10.1136/ard.2003.007526
10. Reeuwijk KG, de Rooij M, van Dijk GM, Veenhof C, Steultjens MP, Dekker J. Osteoarthritis of the hip or knee: which coexisting disorders are disabling? *Clin Rheumatol* 2010;**29**:739–47. http://dx.doi.org/10.1007/s10067-010-1392-8
11. Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, *et al.* OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cart* 2008;**16**:137–62. http://dx.doi.org/10.1016/j.joca.2007.12.013
12. Jordan KM, Arden NK, Doherty M, Bannwarth B, Bijlsma JWJ, Dieppe P, *et al.* EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: report of a task force of the standing committee for international clinical studies including therapeutic trials (ESCISIT). *Ann Rheum Dis* 2003;**62**:1145–55. http://dx.doi.org/10.1136/ard.2003.011742
13. Zhang W, Doherty M, Arden N, Bannwarth B, Bijlsma J, Gunther K-P, *et al.* EULAR evidence based recommendations for the management of hip osteoarthritis: report of a task force of the EULAR standing committee for international clinical studies including therapeutics (ESCISIT). *Ann Rheum Dis* 2005;**64**:669–81. http://dx.doi.org/10.1136/ard.2004.028886
14. National Institute for Health and Care Excellence (NICE). *Osteoarthritis: National Clinical Guideline for Care and Management in Adults*. London: NICE; 2008.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

15. Liang MH, Cullen KE, Larson MG, Thompson MS, Schwartz JA, Fossel AH, *et al.* Cost-effectiveness of total joint arthroplasty in osteoarthritis. *Arthritis Rheum* 1986;**29**:937–43. http://dx.doi.org/10.1002/art.1780290801

16. Chang RW, Pellisier JM, Hazen GB. A cost-effectiveness analysis of total hip arthroplasty for osteoarthritis of the hip. *JAMA* 1996;**275**:858–65. http://dx.doi.org/10.1001/jama.1996.03530350040032

17. Dreinhofer KE, Dieppe P, Sturmer T, Grober-Gratz D, Floren M, Gunther KP, *et al.* Indications for total hip replacement: comparison of assessments of orthopaedic surgeons and referring physicians. *Ann Rheum Dis* 2006;**65**:1346–50. http://dx.doi.org/10.1136/ard.2005.047811

18. Beswick AD, Wylde V, Gooberman-Hill R, Blom A, Dieppe P. What proportion of patients report long-term pain after total hip or knee replacement for osteoarthritis? A systematic review of prospective studies in unselected patients. *BMJ Open* 2012;**2**:e000435. http://dx.doi.org/10.1136/bmjopen-2011-000435

19. Health and Social Care Information Centre. *Hospital Episode Statistics, Main procedures and interventions: 4 character Table 2001–02*; 2002. URL: www.hscic.gov.uk/article/2021/Website-Search?productid=3651&q=4+character+table+2001-02&sort=Relevance&size=10&page=1&area=both#top (accessed 21 July 2016).

20. Health and Social Care Information Centre. *Hospital Episode Statistics, Main procedures and interventions: 4 character Table 2011–12*; 2012. URL: www.hscic.gov.uk/catalogue/PUB08288 (accessed 21 July 2016).

21. Dixon T, Shaw M, Ebrahim S, Dieppe P. Trends in hip and knee joint replacement: socioeconomic inequalities and projections of need. *Ann Rheum Dis* 2004;**63**:825–30. http://dx.doi.org/10.1136/ard.2003.012724

22. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am* 2007;**89–A**:780–5. http://dx.doi.org/10.2106/JBJS.F.00222

23. Torjesen I. NHS is unlikely to meet Nicholson challenge to deliver £20bn in efficiency savings, says King's Fund. *BMJ* 2012;**345**:e6496. http://dx.doi.org/10.1136/bmj.e6496

24. Gooberman-Hill R, Woolhead G, Mackichan F, Ayis S, Williams S, Dieppe P, *et al.* Assessing chronic joint pain: lessons from a focus group study. *Arthritis Rheum* 2007;**57**:666–71. http://dx.doi.org/10.1002/art.22681

25. Gooberman-Hill R, French M, Dieppe P, Hawker G, Gooberman-Hill R, French M, *et al.* Expressing pain and fatigue: a new method of analysis to explore differences in osteoarthritis experience. *Arthritis Rheum* 2009;**61**:353–60. http://dx.doi.org/10.1002/art.24273

26. Sale JE, Gignac M, Hawker G. How 'bad' does the pain have to be? A qualitative study examining adherence to pain medication in older adults with osteoarthritis. *Arthritis Rheum* 2006;**55**:272–8. http://dx.doi.org/10.1002/art.21853

27. Milder TY, Lipworth WL, Williams KM, Ritchie JE, Day RO. 'It looks after me': how older patients make decisions about analgesics for osteoarthritis. *Arthritis Care Res* 2011;**63**:1280–6. http://dx.doi.org/10.1002/acr.20514

28. O'Neill T, Jinks C, Ong B. Decision-making regarding total knee replacement surgery: a qualitative meta-synthesis. *BMC Health Serv Res* 2007;**7**:52. http://dx.doi.org/10.1186/1472-6963-7-52

29. Sansom A, Donovan J, Sanders C, Dieppe P, Horwood J, Learmonth I, *et al.* Routes to total joint replacement surgery: patients' and clinicians' perceptions of need. *Arthritis Care Res* 2010;**62**:1252–7. http://dx.doi.org/10.1002/acr.20218

30. Woolhead GM, Donovan JL, Dieppe PA. Outcomes of total knee replacement: a qualitative study. *Rheumatology* 2005;**44**:1032–7. http://dx.doi.org/10.1093/rheumatology/keh674

31. Judge A, Cooper C, Arden NK, Williams S, Hobbs N, Dixon D, *et al.* Pre-operative expectation predicts 12-month postoperative outcome among patients undergoing primary total hip replacement in European orthopaedic centres. *Osteoarthritis Cart* 2011;**19**:659–67. http://dx.doi.org/10.1016/j.joca.2011.03.009

32. McHugh GA, Luker KA. Individuals' expectations and challenges following total hip replacement: a qualitative study. *Disabil Rehabil* 2012;**34**:1351–7. http://dx.doi.org/10.3109/09638288.2011.644022

33. Aamodt A, Nordsletten L, Havelin LI, Indrekvam K, Utvåg SE, Hviding K. Documentation of hip prostheses used in Norway: A critical review of the literature from 1996–2000. *Acta Orthop Scand* 2004;**75**:663–76. http://dx.doi.org/10.1080/00016470410004021

34. National Institute for Health and Care Excellence (NICE). *Guidance on the Selection of Prostheses for Primary Total Hip Replacement*. London: NICE; 2000.

35. Havelin LI, Fenstad AM, Salomonsson R, Mehnert F, Furnes O, Overgaard S, *et al.* The Nordic arthroplasty register association: a unique collaboration between 3 national hip arthroplasty registries with 280,201 THRs. *Acta Orthop* 2009;**80**:393–401. http://dx.doi.org/10.3109/17453670903039544

36. Jain NB, Guller U, Pietrobon R, Bond TK, Higgins LD. Comorbidities increase complication rates in patients having arthroplasty. *Clin Orthop Relat Res* 2005;**435**:232–8. http://dx.doi.org/10.1097/01.blo.0000156479.97488.a2

37. Blom AW, Rogers M, Taylor AH, Pattison G, Whitehouse S, Bannister GC. Dislocation following total hip replacement: the Avon Orthopaedic Centre experience. *Ann R Coll Surg Engl* 2008;**90**:658–62. http://dx.doi.org/10.1308/003588408X318156

38. Blom AW, Taylor AH, Pattison G, Whitehouse S, Bannister GC. Infection after total hip arthroplasty: The Avon experience. *J Bone Joint Surg Br* 2003;**85–B**:956–9. http://dx.doi.org/10.1302/0301-620X.85B7.14095

39. Blom AW, Brown J, Taylor AH, Pattison G, Whitehouse S, Bannister GC. Infection after total knee arthroplasty. *J Bone Joint Surg Br* 2004;**86**:688–91. http://dx.doi.org/10.1302/0301-620X.86B5.14887

40. Berry DJ. Epidemiology: hip and knee. *Orthop Clin North Am* 1999;**30**:183–90. http://dx.doi.org/10.1016/S0030-5898(05)70073-0

41. Lapidus L, Ponzer S, Pettersson H, de Bri E. Symptomatic venous thromboembolism and mortality in orthopaedic surgery – an observational study of 45 968 consecutive procedures. *BMC Musculoskelet Disord* 2013;**14**:177. http://dx.doi.org/10.1186/1471-2474-14-177

42. Smith TO, Blake V, Hing CB. Minimally invasive versus conventional exposure for total hip arthroplasty: a systematic review and meta-analysis of clinical and radiological outcomes. *Int Orthop* 2011;**35**:173–84. http://dx.doi.org/10.1007/s00264-010-1075-8

43. Berstock JR, Beswick AD, Lenguerrand E, Whitehouse MR, Blom AW. Mortality after total hip replacement surgery: a systematic review. *Bone Joint Res* 2014;**3**:175–82. http://dx.doi.org/10.1302/2046-3758.36.2000239

44. Parry MC, Smith AJ, Blom AW. Early death following primary total knee arthroplasty. *J Bone Joint Surg Am* 2011;**93**:948–53. http://dx.doi.org/10.2106/JBJS.J.00425

45. Wylde V, Blom AW. The failure of survivorship. *J Bone Joint Surg Br* 2011;**93**:569–70. http://dx.doi.org/10.1302/0301-620X.93B5.26687

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

46. Lingard EA, Katz JN, Wright EA, Sledge CB, the Kinemax Outcomes Group. Predicting the outcome of total knee arthroplasty. *J Bone Joint Surg Am* 2004;**86**:2179–86.

47. Núñez M, Núñez E, del Val JL, Ortega R, Segur JM, Hernández MV, *et al.* Health-related quality of life in patients with osteoarthritis after total knee replacement: factors influencing outcomes at 36 months of follow-up. *Osteoarthritis Cart* 2007;**15**:1001–7. http://dx.doi.org/10.1016/j.joca.2007.02.019

48. Bachmeier CJM, March LM, Cross MJ, Lapsley HM, Tribe KL, Courtenay BG, *et al.* A comparison of outcomes in osteoarthritis patients undergoing total hip and knee replacement surgery. *Osteoarthritis Cart* 2001;**9**:137–46. http://dx.doi.org/10.1053/joca.2000.0369

49. Wylde V, Hewlett S, Learmonth ID, Dieppe P. Persistent pain after joint replacement: prevalence, sensory qualities, and postoperative determinants. *Pain* 2011;**152**:566–72. http://dx.doi.org/10.1016/j.pain.2010.11.023

50. Brander VA, Stulberg SD, Adams AD, Harden RN, Bruehl S, Stanos SP, *et al.* Predicting total knee replacement pain: a prospective, observational study. *Clin Orthop Relat Res* 2003;**416**:27–36. http://dx.doi.org/10.1097/01.blo.0000092983.12414.e9

51. Nikolajsen L, Brandsborg B, Lucht U, Jensen TS, Kehlet H. Chronic pain following total hip arthroplasty: a nationwide questionnaire study. *Acta Anaesthesiol Scand* 2006;**50**:495–500. http://dx.doi.org/10.1111/j.1399-6576.2006.00976.x

52. Judge A, Arden NK, Cooper C, Kassim Javaid M, Carr AJ, Field RE, *et al.* Predictors of outcomes of total knee replacement surgery. *Rheumatology* 2012;**51**:1804–13. http://dx.doi.org/10.1093/rheumatology/kes075

53. Hawker GA, Badley EM, Borkhoff CM, Croxford R, Davis AM, Dunn S, *et al.* Which patients are most likely to benefit from total joint arthroplasty? *Arthritis Rheum* 2013;**65**:1243–52. http://dx.doi.org/10.1002/art.37901

54. Judge A, Cooper C, Williams C, Dreinhoefer K, Dieppe P. Patient-reported outcomes one year after primary hip replacement in a European collaborative cohort. *Arthritis Care Res* 2010;**62**:480–8. http://dx.doi.org/10.1002/acr.20038

55. Toms AD, Mandalia V, Haigh R, Hopwood B. The management of patients with painful total knee replacement. *J Bone Joint Surg Br* 2009;**91**:143–50. http://dx.doi.org/10.1302/0301-620X.91B2.20995

56. Kassam A, Dieppe P, Toms AD. An analysis of time and money spent on investigating painful total knee replacements. *Br J Med Pract* 2012;**5**:a526.

57. Hawker GA, Stewart L, French MR, Cibere J, Jordan JM, March L, *et al.* Understanding the pain experience in hip and knee osteoarthritis – an OARSI/OMERACT initiative. *Osteoarthritis Cart* 2008;**16**:415–22. http://dx.doi.org/10.1016/j.joca.2007.12.017

58. Jones CA, Voaklander DC, Johnston DWC, Suarez-Almazor ME. Health related quality of life outcomes after total hip and knee arthroplasties in a community based population. *J Rheumatol* 2000;**27**:1745–52.

59. Bourne RB, Chesworth B, Davis A, Mahomed N, Charron K. Comparing patient outcomes after THA and TKA: is there a difference? *Clin Orthop Relat Res* 2010;**468**:542–6. http://dx.doi.org/10.1007/s11999-009-1046-9

60. Pollard B, Johnston M, Dieppe P. What do osteoarthritis health outcome instruments measure? Impairment, activity limitation, or participation restriction? *J Rheumatol* 2006;**33**:757–63.

61. Prince SA, Adamo KB, Hamel ME, Hardt J, Connor Gorber S, Tremblay M. A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review. *Int J Behav Nutr Phys Act* 2008;**5**:56. http://dx.doi.org/10.1186/1479-5868-5-56

62. Dolin SJ, Cashman JN, Bland JM. Effectiveness of acute postoperative pain management: I. Evidence from published data. *Br J Anaesth* 2002;**89**:409–23. http://dx.doi.org/10.1093/bja/89.3.409

63. Duggleby W, Lander J. Cognitive status and postoperative pain: older adults. *J Pain Symptom Manage* 1994;**9**:19–27. http://dx.doi.org/10.1016/0885-3924(94)90142-2

64. Chung F, Ritchie E, Su J. Postoperative pain in ambulatory surgery. *Anesth Analg* 1997;**85**:808–16.

65. Morrison RS, Magaziner J, McLaughlin MA, Orosz G, Silberzweig SB, Koval KJ, *et al.* The impact of postoperative pain on outcomes following hip fracture. *Pain* 2003;**103**:303–11. http://dx.doi.org/10.1016/S0304-3959(02)00458-X

66. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. *Lancet* 2006;**367**:1618–25. http://dx.doi.org/10.1016/S0140-6736(06)68700-X

67. Wilmore DW, Kehlet H. Management of patients in fast track surgery. *BMJ* 2001;**322**:473–6. http://dx.doi.org/10.1136/bmj.322.7284.473

68. Thomas DC, Kreizman IJ, Melchiorre P, Ragnarsson KT. Rehabilitation of the patient with chronic critical illness. *Crit Care Clin* 2002;**18**:695–715. http://dx.doi.org/10.1016/S0749-0704(02)00011-8

69. Reilly KA, Beard DJ, Barker KL, Dodd CAF, Price AJ, Murray DW. Efficacy of an accelerated recovery protocol for Oxford unicompartmental knee arthroplasty – a randomised controlled trial. *Knee* 2005;**12**:351–7. http://dx.doi.org/10.1016/j.knee.2005.01.002

70. Wylde V, Rooker J, Halliday L, Blom A. Acute postoperative pain at rest after hip and knee arthroplasty: severity, sensory qualities and impact on sleep. *Orthop Traumatol Surg Res* 2011;**97**:139–44. http://dx.doi.org/10.1016/j.otsr.2010.12.003

71. Capdevila X, Barthelet Y, Biboulet P, Ryckwaert Y, Rubenovitch J, d'Athis F. Effects of perioperative analgesic technique on the surgical outcome and duration of rehabilitation after major knee surgery. *Anesthesiology* 1999;**91**:8–15. http://dx.doi.org/10.1097/00000542-199907000-00006

72. Choi P, Bhandari M, Scott J, Douketis JD. Epidural analgesia for pain relief following hip or knee replacement. *Cochrane Database Syst Rev* 2003;**3**:CD003071. http://dx.doi.org/10.1002/14651858.cd003071

73. International Association for the Study of Pain (IASP). Classification of chronic pain. *Pain* 1986;(Suppl. 3):1–226.

74. Macrae W, Davies H. Chronic Postsurgical Pain. In Crombie I, editor. *Epidemiology of Pain*. Seattle: IASP Press; 1999. pp. 125–42.

75. Wylde V. *The Role of Pre-operative Pain Sensitisation in Chronic Pain after Total Knee Replacement*. Bristol: University of Bristol; 2010.

76. Macrae WA. Chronic pain after surgery. *Br J Anaesth* 2001;**87**:88–98. http://dx.doi.org/10.1093/bja/87.1.88

77. McMurray R, Heaton J, Sloper P, Nettleton S. Variations in the provision of occupational therapy for patients undergoing primary elective total hip replacement in the United Kingdom. *Br J Occup Ther* 2000;**63**:451–5. http://dx.doi.org/10.1177/030802260006300909

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

78. Artz N, Dixon S, Wylde V, Beswick A, Blom A, Gooberman-Hill R. Physiotherapy provision following discharge after total hip and total knee replacement: a survey of current practice at high-volume NHS hospitals in England and Wales. *Musculoskeletal Care* 2013;**11**:31–8. http://dx.doi.org/10.1002/msc.1027

79. Drummond A, Coole C, Brewin C, Sinclair E. Hip precautions following primary total hip replacement: a national survey of current occupational therapy practice. *Brit J Occup Ther* 2012;**75**:164–70. http://dx.doi.org/10.4276/030802212X13336366278059

80. World Health Organization (WHO). *International Classification of Functioning, Disability and Health*. Geneva: WHO; 2001.

81. Khan F, Ng L, Gonzalez S, Hale T, Turner-Stokes L. Multidisciplinary rehabilitation programmes following joint replacement at the hip and knee in chronic arthropathy. *Cochrane Database Syst Rev* 2008:2;CD004957. http://dx.doi.org/10.1002/14651858.cd004957.pub3

82. Ackerman IN, Bennell KL. Does pre-operative physiotherapy improve outcomes from lower limb joint replacement surgery? A systematic review. *Aust J Physiother* 2004;**50**:25–30. http://dx.doi.org/10.1016/S0004-9514(14)60245-2

83. McDonald S, Hetrick SE, Green S. Pre-operative education for hip or knee replacement. *Cochrane Database Syst Rev* 2004;**1**:CD003526. http://dx.doi.org/10.1002/14651858.cd003526.pub2

84. Minns Lowe CJ, Barker KL, Dewey M, Sackley CM. Effectiveness of physiotherapy exercise after knee arthroplasty for osteoarthritis: Systematic review and meta-analysis of randomised controlled trials. *BMJ* 2007;**335**:812–5. http://dx.doi.org/10.1136/bmj.39311.460093.BE

85. Minns Lowe C, Barker K, Dewey M, Sackley C. Effectiveness of physiotherapy exercise following hip arthroplasty for osteoarthritis: a systematic review of clinical trials. *BMC Musculoskelet Disord* 2009;**10**:1. http://dx.doi.org/10.1186/1471-2474-10-98

86. National Institute for Health and Care Excellence (NICE). *Guide to the Methods of Technology Appraisal*. London: NICE; 2013.

87. Pitimana-aree S, Visalyaputra S, Komoltri C, Muangman S, Tiviraj S, Puangchan S, *et al.* An economic evaluation of bupivacaine plus fentanyl versus ropivacaine alone for patient-controlled epidural analgesia after total-knee replacement procedure: a double-blinded randomized study. *Reg Anesth Pain Med* 2005;**30**:446–51. http://dx.doi.org/10.1097/00115550-200509000-00005

88. Colwell CW Jr, Morris BA. Patient-controlled analgesia compared with intramuscular injection of analgesics for the management of pain after an orthopaedic procedure. *J Bone Joint Surg Am* 1995;**77**:726–33.

89. Gonano C, Leitgeb U, Sitzwohl C, Ihra G, Weinstabl C, Kettner SC. Spinal versus general anesthesia for orthopedic surgery: anesthesia drug and supply costs. *Anesth Analg* 2006;**102**:524–9. http://dx.doi.org/10.1213/01.ane.0000194292.81614.c6

90. Demeere JL, Merckx C, Demeere N. Cost minimisation and cost effectiveness in anaesthesia for total hip replacement surgery, in Belgium? A study comparing three general anaesthesia techniques. *Acta Anaesthesiol Belg* 2006;**57**:145–51.

91. Strassels SA, Chen C, Carr DB. Postoperative analgesia: economics, resource use, and patient satisfaction in an urban teaching hospital. *Anesth Analg* 2002;**94**:130–7.

92. Kauppila A-M, Sintonen H, Aronen P, Ohtonen P, Kyllonen E, Arokoski JPA. Economic evaluation of multidisciplinary rehabilitation after primary total knee arthroplasty based on a randomized controlled trial. *Arthritis Care Res* 2011;**63**:335–41.

93. Tribe KL, Lapsley HM, Cross MJ, Courtenay BG, Brooks PM, March LM. Selection of patients for inpatient rehabilitation or direct home discharge following total joint replacement surgery: a comparison of health status and out-of-pocket expenditure of patients undergoing hip and knee arthroplasty for osteoarthritis. *Chronic Illness* 2005;**1**:289–302. http://dx.doi.org/10.1177/17423953050010041101

94. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ* 2008;**337**:a1655.

95. Wylde V, Bruce J, Beswick A, Elvers K, Gooberman-Hill R. The assessment of chronic post-surgical pain after knee replacement: A systematic review. *Arthritis Care Res* 2013;**65**:1795–803. http://dx.doi.org/10.1002/acr.22050

96. Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* (updated March 2011). The Cochrane Collaboration; 2011. URL: http://handbook.cochrane.org/ (accessed 21 July 2016).

97. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol* 2009;**62**:1006–12. http://dx.doi.org/10.1016/j.jclinepi.2009.06.005

98. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, *et al.* Meta-analysis of observational studies in epidemiology: a proposal for reporting. *JAMA* 2000;**283**:2008–12. http://dx.doi.org/10.1001/jama.283.15.2008

99. Richardson WS, Wilson MC, Nishikawa J, Hayward RS. The well-built clinical question: a key to evidence-based decisions. *ACP J Club* 1995;**123**:A12–3.

100. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Contr Clin Trials* 1986;**7**:177–88. http://dx.doi.org/10.1016/0197-2456(86)90046-2

101. Roberts VI, Esler CNA, Harper WM. A 15-year follow-up study of 4606 primary total knee replacements. *J Bone Joint Surg Br* 2007;**89–B**:1452–6. http://dx.doi.org/10.1302/0301-620X.89B11.19783

102. Quintana JM, Escobar A, Arostegui I, Bilbao A, Azkarate J, Goenaga JI, *et al.* Health-related quality of life and appropriateness of knee or hip joint replacement. *Arch Int Med* 2006;**166**:220–6. http://dx.doi.org/10.1001/archinte.166.2.220

103. Nilsdotter AK, Petersson IF, Roos EM, Lohmander LS. Predictors of patient relevant outcome after total hip replacement for osteoarthritis: A prospective study. *Ann Rheum Dis* 2003;**62**:923–30. http://dx.doi.org/10.1136/ard.62.10.923

104. Singh J, Lewallen D. Predictors of pain and use of pain medications following primary Total Hip Arthroplasty (THA): 5,707 THAs at 2-years and 3,289 THAs at 5-years. *BMC Musculoskelet Disord* 2010;**11**:90. http://dx.doi.org/10.1186/1471-2474-11-90

105. Baker PN, van der Meulen JH, Lewsey J, Gregg PJ. The role of pain and function in determining patient satisfaction after total knee replacement. Data from the National Joint Registry for England and Wales. *J Bone Joint Surg Br* 2007;**89–B**:893–900. http://dx.doi.org/10.1302/0301-620X.89B7.19091

106. Stephens MAP, Druley JA, Zautra AJ. Older adults' recovery from surgery for osteoarthritis of the knee: psychosocial resources and constraints as predictors of outcomes. *Health Psychol* 2002;**21**:377–83. http://dx.doi.org/10.1037/0278-6133.21.4.377

107. Lundblad H, Kreicbergs A, Jansson KA. Prediction of persistent pain after total knee replacement for osteoarthritis. *J Bone Joint Surg Br* 2008;**90–B**:166–71. http://dx.doi.org/10.1302/0301-620X.90B2.19640

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

108. Nilsdotter AK, Toksvig-Larsen S, Roos EM. Knee arthroplasty: are patients' expectations fulfilled? A prospective study of pain and function in 102 patients with 5-year follow-up. *Acta Orthop* 2009;**80**:55–61. http://dx.doi.org/10.1080/17453670902805007

109. Vuorenmaa M, Ylinen J, Kiviranta I, Intke A, Kautiainen HJ, Mälkiä E, *et al.* Changes in pain and physical function during waiting time and 3 months after knee joint arthroplasty. *J Rehabil Med* 2008;**40**:570–5. http://dx.doi.org/10.2340/16501977-0213

110. Czurda T, Fennema P, Baumgartner M, Ritschl P. The association between component malalignment and postoperative pain following navigation-assisted total knee arthroplasty: results of a cohort/nested case–control study. *Knee Surg Sports Traumatol Arthrosc* 2010;**18**:863–9. http://dx.doi.org/10.1007/s00167-009-0990-y

111. Bellamy N, Kirwan J, Boers M, Brooks P, Strand V, Tugwell P, *et al.* Recommendations for a core set of outcome measures for future phase III clinical trials in knee, hip, and hand osteoarthritis. Consensus development at OMERACT III. *J Rheumatol* 1997;**24**:799–802.

112. Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, *et al.* Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain* 2005;**113**:9–19. http://dx.doi.org/10.1016/j.pain.2004.09.012

113. Insall JN, Dorr LD, Scott RD, Scott WN. Rationale of the Knee Society clinical rating system. *Clin Orthop Relat Res* 1989;**248**:13–14. http://dx.doi.org/10.1097/00003086-198911000-00004

114. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol* 1988;**15**:1833–40.

115. Insall JN, Ranawat CS, Aglietti P, Shine J. A comparison of four models of total knee-replacement prostheses. *J Bone Joint Surg Am* 1976;**58**:754–65.

116. Ware JE Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;**30**:473–83. http://dx.doi.org/10.1097/00005650-199206000-00002

117. Dawson J, Fitzpatrick R, Murray D, Carr A. Questionnaire on the perceptions of patients about total knee replacement. *J Bone Joint Surg Br* 1998;**80**:63–9. http://dx.doi.org/10.1302/0301-620X.80B1.7859

118. Garratt AM, Brealey S, Gillespie WJ. Patient-assessed health instruments for the knee: a structured review. *Rheumatology* 2004;**43**:1414–23. http://dx.doi.org/10.1093/rheumatology/keh362

119. Riddle DL, Stratford PW, Bowman DH. Findings of extensive variation in the types of outcome measures used in hip and knee replacement clinical trials: a systematic review. *Arthritis Rheum* 2008;**59**:876–83. http://dx.doi.org/10.1002/art.23706

120. Kelly JC, Glynn RW, O'Briain DE, Felle P, McCabe JP. The 100 classic papers of orthopaedic surgery: a bibliometric analysis. *J Bone Joint Surg Br* 2010;**92**:1338–43. http://dx.doi.org/10.1302/0301-620X.92B10.24867

121. Darzi A. *High Quality Care for All: NHS Next Stage Review Final Report*. London: Department of Health; 2008.

122. Jha AK, Orav EJ, Zheng J, Epstein AM. Patients' perception of hospital care in the United States. *NEJM* 2008;**359**:1921–31. http://dx.doi.org/10.1056/NEJMsa0804116

123. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (MINORS): development and validation of a new instrument. *ANZ J Surg* 2003;**73**:712–6. http://dx.doi.org/10.1046/j.1445-2197.2003.02748.x

124. Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, *et al. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-analyses*. Ottawa Hospital Research Institute; 2013. URL: www.ohri.ca/programs/clinical_epidemiology/oxford.asp (accessed 20 May 2015).

125. Rolfson O, Dahlberg LE, Nilsson J-A, Malchau H, Garellick G. Variables determining outcome in total hip replacement surgery. *J Bone Joint Surg Br* 2009;**91–B**:157–61. http://dx.doi.org/10.1302/0301-620X.91B2.20765

126. Hajat S, Fitzpatrick R, Morris R, Reeves B, Rigge M, Williams O, *et al.* Does waiting for total hip replacement matter? Prospective cohort study. *J Health Serv Res Policy* 2002;**7**:19–25. http://dx.doi.org/10.1258/1355819021927638

127. Jones CA, Cox V, Jhangri GS, Suarez-Almazor ME. Delineating the impact of obesity and its relationship on recovery after total joint arthroplasties. *Osteoarthritis Cart* 2012;**20**:511–18. http://dx.doi.org/10.1016/j.joca.2012.02.637

128. Judge A, Arden NK, Batra RN, Thomas G, Beard D, Javaid MK, *et al.* The association of patient characteristics and surgical variables on symptoms of pain and function over 5 years following primary hip-replacement surgery: A prospective cohort study. *BMJ Open* 2013;**3**:e002453. http://dx.doi.org/10.1136/bmjopen-2012-002453

129. Stevens M, Paans N, Wagenmakers R, van Beveren J, van Raay JJAM, van der Meer K, *et al.* The influence of overweight/obesity on patient-perceived physical functioning and health-related quality of life after primary total hip arthroplasty. *Obesity Surgery* 2012;**22**:523–9. http://dx.doi.org/10.1007/s11695-011-0483-1

130. Anakwe RE, Jenkins PJ, Moran M. Predicting dissatisfaction after total hip arthroplasty: a study of 850 patients. *J Arthroplasty* 2011;**26**:209–13. http://dx.doi.org/10.1016/j.arth.2010.03.013

131. Clement ND, Muzammil A, Macdonald D, Howie CR, Biant LC. Socioeconomic status affects the early outcome of total hip replacement. *J Bone Joint Surg Br* 2011;**93**:464–9. http://dx.doi.org/10.1302/0301-620X.93B4.25717

132. Davis AM, Wood AM, Keenan ACM, Brenkel IJ, Ballantyne JA. Does body mass index affect clinical outcome post-operatively and at five years after primary unilateral total hip replacement performed for osteoarthritis? A multivariate analysis of prospective data. *J Bone Joint Surg Br* 2011;**93**:1178–82. http://dx.doi.org/10.1302/0301-620X.93B9.26873

133. Gandhi R, Dhotar H, Davey JR, Mahomed NN. Predicting the longer-term outcomes of total hip replacement. *J Rheumatol* 2010;**37**:2573–7. http://dx.doi.org/10.3899/jrheum.100149

134. Garbuz DS, Xu M, Duncan CP, Masri BA, Sobolev B. Delays worsen quality of life outcome of primary total hip arthroplasty. *Clin Orthop Relat Res* 2006;**447**:79–84. http://dx.doi.org/10.1097/01.blo.0000203477.19421.ed

135. Moran M, Walmsley P, Gray A, Brenkel IJ. Does body mass index affect the early outcome of primary total hip arthroplasty? *J Arthroplasty* 2005;**20**:866–9. http://dx.doi.org/10.1016/j.arth.2005.02.008

136. Xu M, Garbuz DS, Kuramoto L, Sobolev B. Classifying health-related quality of life outcomes of total hip arthroplasty. *BMC Musculoskelet Disord* 2005;**6**:48. http://dx.doi.org/10.1186/1471-2474-6-48

137. Workgroup of the American association of hip and knee surgeons evidence based committee. Obesity and total joint arthroplasty: a literature based review. *J Arthroplasty* 2013;**28**:714–21. http://dx.doi.org/10.1016/j.arth.2013.02.011

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

138. Liu B, Balkwill A, Banks E, Cooper C, Green J, Beral V. Relationship of height, weight and body mass index to the risk of hip and knee replacements in middle-aged women. *Rheumatology* 2007;**46**:861–7. http://dx.doi.org/10.1093/rheumatology/kel434

139. World Health Organization (WHO). *Obesity and Overweight Fact sheet No 311 Updated March 2013*. Geneva: WHO; 2013.

140. Parsons GE, Godfrey H, Jester RF. Living with severe osteoarthritis while awaiting hip and knee joint replacement surgery. *Musculoskeletal Care* 2009;**7**:121–35. http://dx.doi.org/10.1002/msc.145

141. Axford J, Butt A, Heron C, Hammond J, Morgan J, Alavi A, *et al.* Prevalence of anxiety and depression in osteoarthritis: use of the Hospital Anxiety and Depression Scale as a screening tool. *Clin Rheumatol* 2010;**29**:1277–83. http://dx.doi.org/10.1007/s10067-010-1547-7

142. Gleicher Y, Croxford R, Hochman J, Hawker G. A prospective study of mental health care for comorbid depressed mood in older adults with painful osteoarthritis. *BMC Psychiatry* 2011;**11**:147. http://dx.doi.org/10.1186/1471-244X-11-147

143. Vissers MM, Bussmann JB, Verhaar JAN, Busschbach JJV, Bierma-Zeinstra SMA, Reijman M. Psychological factors affecting the outcome of total hip and knee arthroplasty: a systematic review. *Semin Arthritis Rheum* 2012;**41**:576–88. http://dx.doi.org/10.1016/j.semarthrit.2011.07.003

144. Crawford RW, Murray DW. Total hip replacement: indications for surgery and risk factors for failure. *Ann Rheum Dis* 1997;**56**:455–7. http://dx.doi.org/10.1136/ard.56.8.455

145. Scott CE, Bugler KE, Clement ND, MacDonald D, Howie CR, Biant LC. Patient expectations of arthroplasty of the hip and knee. *J Bone Joint Surg Br* 2012;**94**:974–81. http://dx.doi.org/10.1302/0301-620X.94B7.28219

146. Gonzalez Saenz de Tejada M, Escobar A, Herrera C, Garcia L, Aizpuru F, Sarasqueta C. Patient expectations and health-related quality of life outcomes following total joint replacement. *Value Health* 2010;**13**:447–54. http://dx.doi.org/10.1111/j.1524-4733.2009.00685.x

147. Franklin PD, Li W, Ayers DC. Functional outcome after total knee replacement varies with patient attributes. *Clin Orthop Relat Res* 2008;**466**:2597–604. http://dx.doi.org/10.1007/s11999-008-0428-8

148. Baker PN, Deehan DJ, Lees D, Jameson S, Avery PJ, Gregg PJ, *et al.* The effect of surgical factors on early patient-reported outcome measures (PROMS) following total knee replacement. *J Bone Joint Surg Br* 2012;**94 B**:1058–66.

149. Alzahrani K, Gandhi R, Debeer J, Petruccelli D, Mahomed N. Prevalence of clinically significant improvement following total knee replacement. *J Rheumatol* 2011;**38**:753–9. http://dx.doi.org/10.3899/jrheum.100233

150. Lingard EA, Riddle DL. Impact of psychological distress on pain and function following knee arthroplasty. *J Bone Joint Surg Am* 2007;**89**:1161–9. http://dx.doi.org/10.2106/JBJS.F.00914

151. Cushnaghan J, Bennett J, Reading I, Croft P, Byng P, Cox K, *et al.* Long-term outcome following total knee arthroplasty: a controlled longitudinal study. *Ann Rheum Dis* 2009;**68**:642–7. http://dx.doi.org/10.1136/ard.2008.093229

152. Perruccio AV, Power JD, Evans HMK, Mahomed SR, Gandhi R, Mahomed NN, *et al.* Multiple joint involvement in total knee replacement for osteoarthritis: Effects on patient-reported outcomes. *Arthritis Care Res* 2012;**64**:838–46. http://dx.doi.org/10.1002/acr.21629

153. Sullivan M, Tanzer M, Reardon G, Amirault D, Dunbar M, Stanish W. The role of presurgical expectancies in predicting pain and function one year following total knee arthroplasty. *Pain* 2011;**152**:2287–93. http://dx.doi.org/10.1016/j.pain.2011.06.014

154. Naylor JM, Yeo AE, Mittal R, Ko VW, Harris IA. Improvements in knee range and symptomatic and functional behavior after knee arthroplasty based on preoperative restriction in range. *J Arthroplasty* 2012;**27**:1100–5. http://dx.doi.org/10.1016/j.arth.2011.09.023

155. Papakostidou I, Dailiana ZH, Papapolychroniou T, Liaropoulos L, Zintzaras E, Karachalios TS, *et al.* Factors affecting the quality of life after total knee arthroplasties: a prospective study. *BMC Musculoskelet Disord* 2012;**13**:116. http://dx.doi.org/10.1186/1471-2474-13-116

156. Singh JA, Lewallen DG. Medical and psychological comorbidity predicts poor pain outcomes after total knee arthroplasty. *Rheumatology* 2013;**52**:916–23. http://dx.doi.org/10.1093/rheumatology/kes402

157. Heck DA, Robinson RL, Partridge CM, Lubitz RM, Freund DA. Patient outcomes after knee replacement. *Clin Orthop Relat Res* 1998;**356**:93–110. http://dx.doi.org/10.1097/00003086-199811000-00015

158. Merle-Vincent F, Couris CM, Schott AM, Conrozier T, Piperno M, Mathieu P, *et al.* Factors predicting patient satisfaction 2 years after total knee arthroplasty for osteoarthritis. *Joint Bone Spine* 2011;**78**:383–6. http://dx.doi.org/10.1016/j.jbspin.2010.11.013

159. Núñez M, Lozano L, Núñez E, Segur JM, Sastre S, Maculé F, *et al.* Total knee replacement and health-related quality of life: factors influencing long-term outcomes. *Arthritis Rheum* 2009;**61**:1062–9. http://dx.doi.org/10.1002/art.24644

160. Gandhi R, Dhotar H, Razak F, Tso P, Davey JR, Mahomed NN. Predicting the longer term outcomes of total knee arthroplasty. *Knee* 2010;**17**:15–18. http://dx.doi.org/10.1016/j.knee.2009.06.003

161. Deshmukh RG, Hayes JH, Pinder IM. Does body weight influence outcome after total knee arthroplasty? A 1-year analysis. *J Arthroplasty* 2002;**17**:315–19. http://dx.doi.org/10.1054/arth.2002.30776

162. Rajgopal V, Bourne RB, Chesworth BM, MacDonald SJ, McCalden RW, Rorabeck CH. The impact of morbid obesity on patient outcomes after total knee arthroplasty. *J Arthroplasty* 2008;**23**:795–800. http://dx.doi.org/10.1016/j.arth.2007.08.005

163. Ayers DC, Franklin PD, Ploutz-Snyder R, Boisvert CB. Total knee replacement outcome and coexisting physical and emotional illness. *Clin Orthop Relat Res* 2005;**440**:157–61. http://dx.doi.org/10.1097/01.blo.0000185447.43622.93

164. Clement ND, Jenkins PJ, MacDonald D, Nie YX, Patton JT, Breusch SJ, *et al.* Socioeconomic status affects the Oxford knee score and short-form 12 score following total knee replacement. *Bone Joint J* 2013;**95–B**:52–8. http://dx.doi.org/10.1302/0301-620X.95B1.29749

165. Scott CE, Howie CR, MacDonald D, Biant LC. Predicting dissatisfaction following total knee replacement: a prospective study of 1217 patients. *J Bone Joint Surg Br* 2010;**92**:1253–8. http://dx.doi.org/10.1302/0301-620X.92B9.24394

166. Gandhi R, Razak F, Davey JR, Mahomed NN. Metabolic syndrome and the functional outcomes of hip and knee arthroplasty. *J Rheumatol* 2010;**37**:1917–22. http://dx.doi.org/10.3899/jrheum.091242

167. Apold H, Meyer H, Nordsletten L, Furnes O, Baste V, Flugsrud G. Risk factors for knee replacement due to primary osteoarthritis, a population based, prospective cohort study of 315,495 individuals. *BMC Musculoskelet Disord* 2014;**15**:217. http://dx.doi.org/10.1186/1471-2474-15-217

168. Yeung E, Thornton-Bott P, Walter WL. Patient obesity: A growing concern of successful total knee arthroplasty. *Semin Arthroplasty* 2010;**21**:87–91. http://dx.doi.org/10.1053/j.sart.2010.01.001

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

169. Gillespie GN, Porteous AJ. Obesity and knee arthroplasty. *Knee* 2007;**14**:81–6. http://dx.doi.org/10.1016/j.knee.2006.11.004

170. Kerkhoffs GM, Servien E, Dunn W, Dahm D, Bramer JA, Haverkamp D. The influence of obesity on the complication rate and outcome of total knee arthroplasty: a meta-analysis and systematic literature review. *J Bone Joint Surg Am* 2012;**94**:1839–44. http://dx.doi.org/10.2106/JBJS.K.00820

171. Samson AJ, Mercer GE, Campbell DG. Total knee replacement in the morbidly obese: a literature review. *ANZ J Surg* 2010;**80**:595–9. http://dx.doi.org/10.1111/j.1445-2197.2010.05396.x

172. Dowsey MM, Choong PF. Early outcomes and complications following joint arthroplasty in obese patients: a review of the published reports. *ANZ J Surg* 2008;**78**:439–44. http://dx.doi.org/10.1111/j.1445-2197.2008.04554.x

173. McElroy MJ, Pivec R, Issa K, Harwin SF, Mont MA. The effects of obesity and morbid obesity on outcomes in TKA. *J Knee Surg* 2013;**26**:83–8. http://dx.doi.org/10.1055/s-0033-1341407

174. Kirchberger I, Meisinger C, Heier M, Zimmermann AK, Thorand B, Autenrieth CS, *et al.* Patterns of multimorbidity in the aged population. Results from the KORA-Age study. *PLOS ONE* 2012;**7**:e30556. http://dx.doi.org/10.1371/journal.pone.0030556

175. Williams ID, O'Doherty LJ, Mitchell GK, Williams KE. Identifying unmet needs in older patients–nurse-GP collaboration in general practice. *Aust Fam Physician* 2007;**36**:772–6.

176. Kirschner S, Lutzner J, Gunther K-P, Eberlein-Gonska M, Krummenauer F. Adverse events in total knee arthroplasty: Results of a physician independent survey in 260 patients. *Patient Saf Surg* 2010;**4**:12. http://dx.doi.org/10.1186/1754-9493-4-12

177. Bourne R, Chesworth B, Davis A, Mahomed N, Charron K. Patient satisfaction after total knee arthroplasty: Who is satisfied and who is not? *Clin Orthop Relat Res* 2010;**468**:57–63. http://dx.doi.org/10.1007/s11999-009-1119-9

178. Andersson AE, Bergh I, Karlsson J, Nilsson K. Patients' experiences of acquiring a deep surgical site infection: An interview study. *Am J Infect Control* 2010;**38**:711–17. http://dx.doi.org/10.1016/j.ajic.2010.03.017

179. Hunter G, Dandy D. The natural history of the patient with an infected total hip replacement. *J Bone Joint Surg Br* 1977;**59–B**:293–7.

180. Goldhaber SZ, Visani L, De Rosa M. Acute pulmonary embolism: clinical outcomes in the international cooperative pulmonary embolism registry (ICOPER). *Lancet* 1999;**353**:1386–9. http://dx.doi.org/10.1016/S0140-6736(98)07534-5

181. Guanella R, Ducruet T, Johri M, Miron MJ, Roussin A, Desmarais S, *et al.* Economic burden and cost determinants of deep vein thrombosis during 2 years following diagnosis: a prospective evaluation. *J Thrombosis Haemostas* 2011;**9**:2397–405. http://dx.doi.org/10.1111/j.1538-7836.2011.04516.x

182. Khan NA, Quan H, Bugar JM, Lemaire JB, Brant R, Ghali WA. Association of postoperative complications with hospital costs and length of stay in a tertiary care center. *J Gen Intern Med* 2006;**21**:177–80. http://dx.doi.org/10.1007/s11606-006-0254-1

183. Solomon DH, Chibnik LB, Losina E, Huang J, Fossel AH, Husni E, *et al.* Development of a preliminary index that predicts adverse events after total knee replacement. *Arthritis Rheum* 2006;**54**:1536–42. http://dx.doi.org/10.1002/art.21772

184. Cushnaghan J, Coggon D, Reading I, Croft P, Byng P, Cox K, *et al.* Long-term outcome following total hip arthroplasty: a controlled longitudinal study. *Arthritis Rheum* 2007;**57**:1375–80. http://dx.doi.org/10.1002/art.23101

185. Judge A, Javaid MK, Arden NK, Cushnaghan J, Reading I, Croft P, *et al.* Clinical tool to identify patients who are most likely to achieve long-term improvement in physical function after total hip arthroplasty. *Arthritis Care Res* 2012;**64**:881–9. http://dx.doi.org/10.1002/acr.21594

186. Bolognesi MP, Marchant MH, Jr., Viens NA, Cook C, Pietrobon R, Vail TP. The impact of diabetes on perioperative patient outcomes after total hip and total knee arthroplasty in the United States. *J Arthroplasty* 2008;**23**:92–8. http://dx.doi.org/10.1016/j.arth.2008.05.012

187. Chan PKH, Brenkel IJ, Aderinto J. The outcome of total hip arthroplasty in diabetes mellitus. *Br J Diabetes Vasc Dis* 2005;**5**:146–9. http://dx.doi.org/10.1177/14746514050050030601

188. Choong PFM, Dowsey MM, Carr D, Daffy J, Stanley P. Risk factors associated with acute hip prosthetic joint infections and outcome of treatment with a rifampin based regimen. *Acta Orthopaedica* 2007;**78**:755–65. http://dx.doi.org/10.1080/17453670710014527

189. Cordero-Ampuero J, de Dios M. What are the risk factors for infection in hemiarthroplasties and total hip arthroplasties? *Clin Orthop Relat Res* 2010;**468**:3268–77. http://dx.doi.org/10.1007/s11999-010-1411-8

190. Dowsey MM, Choong PFM. Obesity is a major risk factor for prosthetic infection after primary hip arthroplasty. *Clin Orthop Relat Res* 2008;**466**:153–8. http://dx.doi.org/10.1007/s11999-007-0016-3

191. Iorio R, Williams KM, Marcantonio AJ, Specht LM, Tilzey JF, Healy WL. Diabetes mellitus, hemoglobin A1C, and the incidence of total joint arthroplasty infection. *J Arthroplasty* 2012;**27**:726–9.e1. http://dx.doi.org/10.1016/j.arth.2011.09.013

192. Namba RS, Paxton L, Fithian DC, Stone ML. Obesity and perioperative morbidity in total hip and total knee arthroplasty patients. *J Arthroplasty* 2005;**20**:46–50. http://dx.doi.org/10.1016/j.arth.2005.04.023

193. Namba RS, Inacio MCS, Paxton EW. Risk factors associated with surgical site infection in 30,491 primary total hip replacements. *J Bone Joint Surg Br* 2012;**94**:1330–8. http://dx.doi.org/10.1302/0301-620X.94B10.29184

194. Pedersen AB, Mehnert F, Johnsen SP, Sorensen HT. Risk of revision of a total hip replacement in patients with diabetes mellitus: a population-based follow up study. *J Bone Joint Surg Br* 2010;**92**:929–34. http://dx.doi.org/10.1302/0301-620X.92B7.24461

195. Vannini P, Ciavarella A, Olmi R, Flammini M, Moroni A, Galuppi V, *et al.* Diabetes as pro-infective risk factor in total hip replacement. *Acta Diabetologica Latina* 1984;**21**:275–80. http://dx.doi.org/10.1007/BF02642901

196. Bhattacharyya T, Iorio R, Healy WL. Rate of and risk factors for acute inpatient mortality after orthopaedic surgery. *J Bone Joint Surg Am* 2002;**84–A**:562–72.

197. Dy CJ, Wilkinson JD, Tamariz L, Scully SP. Influence of preoperative cardiovascular risk factor clusters on complications of total joint arthroplasty. *Am J Orthoped* 2011;**40**:560–5.

198. Marchant MH, Jr., Viens NA, Cook C, Vail TP, Bolognesi MP. The impact of glycemic control and diabetes mellitus on perioperative outcomes after total joint arthroplasty. *J Bone Joint Surg Am* 2009;**91**:1621–9. http://dx.doi.org/10.2106/JBJS.H.00116

199. Blom A, Pattison G, Whitehouse S, Taylor A, Bannister G. Early death following primary total hip arthroplasty: 1,727 procedures with mechanical thrombo-prophylaxis. *Acta Orthop* 2006;**77**:347–50. http://dx.doi.org/10.1080/17453670610046244

200. Ackland GL, Harris S, Ziabari Y, Grocott M, Mythen M, SOuRCe Investigators. Revised cardiac risk index and postoperative morbidity after elective orthopaedic surgery: a prospective cohort study. *Br J Anaesth* 2010;**105**:744–52. http://dx.doi.org/10.1093/bja/aeq245

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

201. Bozic KJ, Ong K, Lau E, Berry DJ, Vail TP, Kurtz SM, *et al.* Estimating risk in Medicare patients with THA: an electronic risk calculator for periprosthetic joint infection and mortality. *Clin Orthop Relat Res* 2013;**471**:574–83. http://dx.doi.org/10.1007/s11999-012-2605-z

202. Sanders RD, Bottle A, Jameson SS, Mozid A, Aylin P, Edger L, *et al.* Independent preoperative predictors of outcomes in orthopedic and vascular surgery: the influence of time interval between an acute coronary syndrome or stroke and the operation. *Ann Surg* 2012;**255**:901–7. http://dx.doi.org/10.1097/SLA.0b013e31824c438d

203. Singh JA, Lewallen DG. Peptic ulcer disease and heart disease are associated with periprosthetic fractures after total hip replacement. *Acta Orthopaedica* 2012;**83**:353–9. http://dx.doi.org/10.3109/17453674.2012.717844

204. Spahn DR. Anemia and patient blood management in hip and knee surgery: a systematic review of the literature. *Anesthesiology* 2010;**113**:482–95. http://dx.doi.org/10.1097/ALN.0b013e3181e08e97

205. Jämsen E, Puolakka T, Eskelinen A, Jantti P, Kalliovalkama J, Nieminen J, *et al.* Predictors of mortality following primary hip and knee replacement in the aged. A single-center analysis of 1,998 primary hip and knee replacements for primary osteoarthritis. *Acta Orthop* 2013;**84**:44–53. http://dx.doi.org/10.3109/17453674.2012.752691

206. Greenky M, Gandhi K, Pulido L, Restrepo C, Parvizi J. Preoperative anemia in total joint arthroplasty: is it associated with periprosthetic joint infection? *Clin Orthop Relat Res* 2012;**470**:2695–701. http://dx.doi.org/10.1007/s11999-012-2435-z

207. Bozic KJ, Lau E, Kurtz S, Ong K, Rubash H, Vail TP, *et al.* Patient-related risk factors for periprosthetic joint infection and postoperative mortality following total hip arthroplasty in Medicare patients. *J Bone Joint Surg Am* 2012;**94**:794–800. http://dx.doi.org/10.2106/JBJS.K.00072

208. O'Malley NT, Fleming FJ, Gunzler DD, Messing SP, Kates SL. Factors independently associated with complications and length of stay after hip arthroplasty: analysis of the national surgical quality improvement program. *J Arthroplasty* 2012;**27**:1832–7. http://dx.doi.org/10.1016/j.arth.2012.04.025

209. Myers E, O'Grady P, Dolan AM. The influence of preclinical anaemia on outcome following total hip replacement. *Arch Orthop Trauma Surg* 2004;**124**:699–701. http://dx.doi.org/10.1007/s00402-004-0754-6

210. Vanderpump MP, Tunbridge WM, French JM, Appleton D, Bates D, Clark F, *et al.* The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey. *Clin Endocrinol* 1995;**43**:55–68. http://dx.doi.org/10.1111/j.1365-2265.1995.tb01894.x

211. Dowsey MM, Choong PFM. Obese diabetic patients are at substantial risk for deep infection after primary TKA. *Clin Orthop Relat Res* 2009;**467**:1577–81. http://dx.doi.org/10.1007/s11999-008-0551-6

212. Memtsoudis SG, Gonzalez Della Valle A, Besculides MC, Gaber L, Sculco TP. In-hospital complications and mortality of unilateral, bilateral, and revision TKA: based on an estimate of 4,159,661 discharges. *Clin Orthop Relat Res* 2008;**466**:2617–27. http://dx.doi.org/10.1007/s11999-008-0402-5

213. Adams AL, Paxton EW, Wang JQ, Johnson ES, Bayliss EA, Ferrara A, *et al.* Surgical outcomes of total knee replacement according to diabetes status and glycemic control, 2001 to 2009. *J Bone Joint Surg Am* 2013;**95**:481–7. http://dx.doi.org/10.2106/JBJS.L.00109

214. Asensio A, Antolin FJ, Sanchez-Garcia JM, Hidalgo O, Hernandez-Navarrete MJ, Bishopberger C, *et al.* Timing of DVT prophylaxis and risk of postoperative knee prosthesis infection. *Orthopedics* 2010;**33**(11). http://dx.doi.org/10.3928/01477447-20100924-12

215. Chesney D, Sales J, Elton R, Brenkel IJ. Infection after knee arthroplasty a prospective study of 1509 cases. *J Arthroplasty* 2008;**23**:355–9. http://dx.doi.org/10.1016/j.arth.2007.05.052

216. Fan JCH, Hung HH, Fung KY. Infection in primary total knee replacement. *Hong Kong Med J* 2008;**14**:40–5.

217. Galat DD, McGovern SC, Larson DR, Harrington JR, Hanssen AD, Clarke HD, *et al.* Surgical treatment of early wound complications following primary total knee arthroplasty. *J Bone Joint Surg Am* 2009;**91**:48–54. http://dx.doi.org/10.2106/JBJS.G.01371

218. Jämsen E, Nevalainen P, Kalliovalkama J, Moilanen T. Preoperative hyperglycemia predicts infected total knee replacement. *Eur J Intern Med* 2010;**21**:196–201. http://dx.doi.org/10.1016/j.ejim.2010.02.006

219. Meding JB, Reddleman K, Keating ME, Klay A, Ritter MA, Faris PM, *et al.* Total knee replacement in patients with diabetes mellitus. *Clin Orthop Relat Res* 2003:208–16. http://dx.doi.org/10.1097/01.blo.0000093002.90435.56

220. Moon HK, Han CD, Yang IH, Cha BS. Factors affecting outcome after total knee arthroplasty in patients with diabetes mellitus. *Yonsei Med J* 2008;**49**:129–37. http://dx.doi.org/10.3349/ymj.2008.49.1.129

221. Namba RS, Chen Y, Paxton EW, Slipchenko T, Fithian DC. Outcomes of routine use of antibiotic-loaded cement in primary total knee arthroplasty. *J Arthroplasty* 2009;**24**:44–7. http://dx.doi.org/10.1016/j.arth.2009.05.007

222. Gill GS, Mills D, Joshi AB. Mortality following primary total knee arthroplasty. *J Bone Joint Surg Am* 2003;**85–A**:432–5.

223. Bozic KJ, Lau E, Kurtz S, Ong K, Berry DJ. Patient-related risk factors for postoperative mortality and periprosthetic joint infection in medicare patients undergoing TKA. *Clin Orthop Relat Res* 2012;**470**:130–7. http://dx.doi.org/10.1007/s11999-011-2043-3

224. The Royal College of Anaesthetists and The Association of Anaesthetists of Great Britain and Ireland. *You and Your Anaesthetic*. London; The Royal College of Anaesthetists and The Association of Anaesthetists of Great Britain and Ireland; 2008.

225. Fritsch G, Flamm M, Hepner DL, Panisch S, Seer J, Soennichsen A. Abnormal pre-operative tests, pathologic findings of medical history, and their predictive value for perioperative complications. *Acta Anaesthesiol Scand* 2012;**56**:339–50. http://dx.doi.org/10.1111/j.1399-6576.2011.02593.x

226. Bryson GL, Wyand A, Bragg PR. Preoperative testing is inconsistent with published guidelines and rarely changes management. *Can J Anaesth* 2006;**53**:236–41. http://dx.doi.org/10.1007/BF03022208

227. Czoski-Murray C, Lloyd Jones M, McCabe C, Claxton K, Oluboyede Y, Roberts J, *et al.* What is the value of routinely testing full blood count, electrolytes and urea, and pulmonary function tests before elective surgery in patients with no apparent clinical indication and in subgroups of patients with common comorbidities: a systematic review of the clinical and cost-effective literature. *Health Technol Assess* 2012;**16**(50). http://dx.doi.org/10.3310/hta16500

228. INVOLVE. *Briefing Notes for Researchers: Involving the Public in NHS, Public Health and Social Care Research*. Eastleigh: INVOLVE; 2012. URL: www.invo.org.uk/ (accessed 30 June 2015).

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

229. Johnson EC, Horwood J, Gooberman-Hill R. Patients' journeys through total joint replacement: patterns of medication use. *Musculoskeletal Care* 2014;**12**:92–102. http://dx.doi.org/10.1002/msc.1062

230. Johnson EC, Horwood J, Gooberman-Hill R. Conceptualising time before surgery: the experience of patients waiting for hip replacement. *Soc Sci Med* 2014;**116**:126–33. http://dx.doi.org/10.1016/j.socscimed.2014.06.037

231. Hudak PL, Frankel RM, Braddock C 3rd, Nisenbaum R, Luca P, McKeever C, *et al.* Do patients' communication behaviors provide insight into their preferences for participation in decision making? *Med Decis Making* 2008;**28**:385–93. http://dx.doi.org/10.1177/0272989X07312712

232. Harrison A, Appleby J. Reducing waiting times for hospital treatment: lessons from the English NHS. *J Health Serv Res Policy* 2009;**14**:168–73. http://dx.doi.org/10.1258/jhsrp.2008.008118

233. Greener I. Towards a history of choice in UK health policy. *Sociol Health Illn* 2009;**31**:309–24. http://dx.doi.org/10.1111/j.1467-9566.2008.01135.x

234. Fotaki M. Patient choice and equity in the British National Health Service: towards developing an alternative framework. *Sociol Health Illn* 2010;**32**:898–913. http://dx.doi.org/10.1111/j.1467-9566.2010.01254.x

235. Department of Health/Payment by Results team. *Choice Framework*. 2012. URL: www.nhs.uk/choiceintheNHS/Rightsandpledges/NHSConstitution/Documents/2013/choice-framework-2013–14.pdf (accessed 12 November 2013).

236. Davis AM, Agnidis Z, Badley E, Davey JR, Gafni A, Gollish J, *et al.* Waiting for hip revision surgery: the impact on patient disability. *Can J Surg* 2008;**51**:92–6.

237. Ackerman IN, Graves SE, Wicks IP, Bennell KL, Osborne RH, Ackerman IN, *et al.* Severely compromised quality of life in women and those of lower socioeconomic status waiting for joint replacement surgery. *Arthritis Rheum* 2005;**53**:653–8. http://dx.doi.org/10.1002/art.21439

238. Ackerman IN, Bennell KL, Osborne RH, Ackerman IN, Bennell KL, Osborne RH. Decline in Health-Related Quality of Life reported by more than half of those waiting for joint replacement surgery: a prospective cohort study. *BMC Musculoskelet Disord* 2011;**12**:108. http://dx.doi.org/10.1186/1471-2474-12-108

239. Carol Craig, Centre for Confidence and Well-being. *Centre for Confidence and Well-being*. 2014. URL: www.centreforconfidence.co.uk/flourishing-lives.php?p=cGlkPTU3MQ== (accessed 30 June 2015).

240. Merriam–Webster, Incorporated. *Merriam–Webster Dictionary*. URL: www.merriam-webster.com/dictionary/vulnerable (accessed 1 April 2016).

241. Tromp AM, Pluijm SM, Smit JH, Deeg DJ, Bouter LM, Lips P. Fall-risk screening test: a prospective study on predictors for falls in community-dwelling elderly. *J Clin Epidemiol* 2001;**54**:837–44. http://dx.doi.org/10.1016/S0895-4356(01)00349-3

242. Rubenstein LZ. Falls in older people: epidemiology, risk factors and strategies for prevention. *Age Ageing* 2006;**35**:ii37–ii41. http://dx.doi.org/10.1093/ageing/afl084

243. Ziden L, Scherman MH, Wenestam CG. The break remains – elderly people's experiences of a hip fracture 1 year after discharge. *Disabil Rehabil* 2010;**32**:103–13. http://dx.doi.org/10.3109/09638280903009263

244. Grant S, St John W, Patterson E. Recovery from total hip replacement surgery: 'it's not just physical'. *Qual Health Res* 2009;**19**:1612–20. http://dx.doi.org/10.1177/1049732309350683

245. Perry MA, Hudson HS, Meys S, Norrie O, Ralph T, Warner S. Older adults' experiences regarding discharge from hospital following orthopaedic intervention: a metasynthesis. *Disabil Rehabil* 2012;**34**:267–78. http://dx.doi.org/10.3109/09638288.2011.603016

246. Gooberman-Hill R, Ebrahim S. Informal care at times of change in health and mobility: a qualitative study. *Age Ageing* 2006;**35**:261–6. http://dx.doi.org/10.1093/ageing/afj065

247. Sherman AM. Social relations and depressive symptoms in older adults with knee osteoarthritis. *Soc Sci Med* 2003;**56**:247–57. http://dx.doi.org/10.1016/S0277-9536(02)00023-0

248. Evers AW, Kraaimaat FW, Geenen R, Bijlsma JW. Psychosocial predictors of functional change in recently diagnosed rheumatoid arthritis patients. *Behav Res Ther* 1998;**36**:179–93. http://dx.doi.org/10.1016/S0005-7967(98)00019-9

249. Gustafsson BÅ, Heikkilä K, Ekman S-L, Ponzer S. In the hands of formal carers: Older patients' experiences of care across the perioperative period for joint replacement surgery. *Int J Orthop Trauma Nurs* 2010;**14**:96–108. http://dx.doi.org/10.1016/j.ijotn.2010.01.002

250. Perry MA, Hudson S, Ardis K. 'If I didn't have anybody, what would I have done?': Experiences of older adults and their discharge home after lower limb orthopaedic surgery. *J Rehabil Med* 2011;**43**:916–22. http://dx.doi.org/10.2340/16501977-0874

251. Heine J, Koch S, Goldie P. Patients' experiences of readiness for discharge following a total hip replacement. *Aust J Physiother* 2004;**50**:227–33. http://dx.doi.org/10.1016/S0004-9514(14)60112-4

252. Mancuso CA, Jout J, Salvati EA, Sculco TP. Fulfillment of patients' expectations for total hip arthroplasty. *J Bone Joint Surg Am* 2009;**91**:2073–8. http://dx.doi.org/10.2106/JBJS.H.01802

253. Mahomed NN, Liang MH, Cook EF, Daltroy LH, Fortin PR, Fossel AH, *et al.* The importance of patient expectations in predicting functional outcomes after total joint arthroplasty. *J Rhematol* 2002;**29**:1273–9.

254. Noble PC, Conditt MA, Cook KF, Mathis KB. Patient expectations affect satisfaction with total knee arthroplasty. *Clin Orthop Relat Res* 2006;**452**:35–43. http://dx.doi.org/10.1097/01.blo.0000238825.63648.1e

255. Sandelowski M. Qualitative analysis: What it is and how to begin. *Res Nurs Health* 1995;**18**:371–5. http://dx.doi.org/10.1002/nur.4770180411

256. Smith JA. Reflecting on the development of interpretative phenomenological analysis and its contribution to qualitative research in psychology. *Qual Res Psychol* 2004;**1**:39–54.

257. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol* 2006;**3**:77–101. http://dx.doi.org/10.1191/1478088706qp063oa

258. Smith JA, Eatough V. Interpretative Phenomenological Analysis. In Breakwell GM, Hammond S, Fife-Schaw C, Smith JA, editors. *Research Methods in Psychology*. London: Sage; 2006. pp. 322–41.

259. Smith JA, Osborn M. Interpretative Phenomenological Analysis. In Breakwell GM, editor. *Doing Social Psychology Research*. Oxford: The BPS and Blackwell Publishing Ltd; 2004. pp. 229–54. http://dx.doi.org/10.1002/9780470776278.ch10

260. Smith JA, Osborn M. Interpretative Phenomenological Analysis. In Smith JA, editor. *Qualitative Psychology: A Practical Guide to Research Methods*. 2nd edn. London: Sage; 2008. pp. 53–80.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

261. Sturges JE, Hanrahan KJ. Comparing telephone and face-to-face qualitative interviewing: a research note. *Qualitative Research* 2004;**4**:107–18. http://dx.doi.org/10.1177/1468794104041110

262. Wylde V, Blom AW, Bolink S, Brunton L, Dieppe P, Gooberman-Hill R, *et al.* Assessing function in patients undergoing joint replacement: a study protocol for a cohort study. *BMC Musculoskelet Disord* 2012;**13**:220. http://dx.doi.org/10.1186/1471-2474-13-220

263. Wylde V, Lenguerrand E, Brunton L, Dieppe P, Gooberman-Hill R, Mann C, *et al.* Does measuring the range of motion of the hip and knee add to the assessment of disability in people undergoing joint replacement? *Orthop Traumatol Surg Res* 2014;**100**:183–6. http://dx.doi.org/10.1016/j.otsr.2013.09.016

264. Lenguerrand E, Wylde V, Gooberman-Hill R, Sayers A, Brunton L, Beswick AD, *et al.* Trajectories of Pain and Function after Primary Hip and Knee Arthroplasty: The ADAPT Cohort Study. *PLOS ONE* 2016;**11**:e0149306. http://dx.doi.org/10.1371/journal.pone.0149306

265. Bourne RB. Measuring tools for functional outcomes in total knee arthroplasty. *Clin Orthop Relat Res* 2008;**466**:2634–8. http://dx.doi.org/10.1007/s11999-008-0468-0

266. Paterson C, Baarts C, Launso L, Verhoef MJ. Evaluating complex health interventions: a critical analysis of the 'outcomes' concept. *BMC Compl Alternative Med* 2009;**9**:18. http://dx.doi.org/10.1186/1472-6882-9-18

267. Clarke M. Standardising outcomes for clinical trials and systematic reviews. *Trials* 2007;**8**:39. http://dx.doi.org/10.1186/1745-6215-8-39

268. Harris WH. Traumatic arthritis of the hip after dislocation and acetabular fractures: treatment by mold arthroplasty. An end-result study using a new method of result evaluation. *J Bone Joint Surg Am* 1969;**51**:737–55.

269. Hewlett SA. Patients and clinicians have different perspectives on outcomes in arthritis. *J Rheumatol* 2003;**30**:877–9.

270. Gioe TJ, Pomeroy D, Suthers K, Singh JA. Can patients help with long-term total knee arthroplasty surveillance? Comparison of the American Knee Society Score self-report and surgeon assessment. *Rheumatology* 2009;**48**:160–4. http://dx.doi.org/10.1093/rheumatology/ken439

271. Department of Health. *Guidance on the Routine Collection of Patient Reported Outcome Measures (PROMs)*. London: Department of Health; 2009.

272. Nilsdotter AK, Lohmander LS, Klassbo M, Roos EM. Hip disability and osteoarthritis outcome score (HOOS) – validity and responsiveness in total hip replacement. *BMC Musculoskelet Disord* 2003;**4**:10. http://dx.doi.org/10.1186/1471-2474-4-10

273. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS) – development of a self-administered outcome measure. *J Orthop Sports Phys Ther* 1998;**28**:88–96. http://dx.doi.org/10.2519/jospt.1998.28.2.88

274. Dawson J, Fitzpatrick R, Carr A, Murray D. Questionnaire on the perceptions of patients about total hip replacement. *J Bone Joint Surg Br* 1996;**78**:185–90.

275. Nicholas MK. The pain self-efficacy questionnaire: taking pain into account. *Eur J Pain* 2007;**11**:153–63. http://dx.doi.org/10.1016/j.ejpain.2005.12.008

276. Carver CS. You want to measure coping but your protocol's too long: consider the brief COPE. *Int J Behav Med* 1997;**4**:92–100. http://dx.doi.org/10.1207/s15327558ijbm0401_6

277. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res* 1999;**47**:555–67. http://dx.doi.org/10.1016/S0022-3999(99)00057-4

278. Williams A, Kind P. The Present State of Play About QALYs. In Hopkins A, editor. *Measure of the Quality of Life: The Uses To Which They May Be Put.* London: Royal College of Physicians of London; 1992. pp. 21–34.

279. Groll DL, To T, Bombardier C, Wright JG. The development of a comorbidity index with physical function as the outcome. *J Clin Epidemiol* 2005;**58**:595–602. http://dx.doi.org/10.1016/j.jclinepi.2004.10.018

280. Hawker GA, Davis AM, French MR, Cibere J, Jordan JM, March L, *et al.* Development and preliminary psychometric testing of a new OA pain measure – an OARSI/OMERACT initiative. *Osteoarthritis Cart* 2008;**16**:409–14. http://dx.doi.org/10.1016/j.joca.2007.12.015

281. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;**67**:361–70. http://dx.doi.org/10.1111/j.1600-0447.1983.tb09716.x

282. Moss-Morris R, Weinman J, Petrie K, Horne R, Cameron L, Buick D. The revised illness perception questionnaire (IPQ-R). *Psychol & Health* 2002;**17**:1–16. http://dx.doi.org/10.1080/08870440290001494

283. Freynhagen R, Baron R, Gockel U, Tolle TR. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. *Curr Med Res Opin* 2006;**22**:1911–20. http://dx.doi.org/10.1185/030079906X132488

284. Mahomed N, Gandhi R, Daltroy L, Katz JN. The self-administered patient satisfaction scale for primary hip and knee arthroplasty. *Arthritis* 2011;**2011**:591253. http://dx.doi.org/10.1155/2011/591253

285. Pollard B, Dixon D, Dieppe P, Johnston M. Measuring the ICF components of impairment, activity limitation and participation restriction: an item analysis using classical test theory and item response theory. *Health Qual Life Outcomes* 2009;**7**:41. http://dx.doi.org/10.1186/1477-7525-7-41

286. Ware J Jr., Kosinski M, Keller SD. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;**34**:220–33. http://dx.doi.org/10.1097/00005650-199603000-00003

287. Paterson C. Measuring outcomes in primary care: a patient generated measure, MYMOP, compared with the SF-36 health survey. *BMJ* 1996;**312**:1016–20. http://dx.doi.org/10.1136/bmj.312.7037.1016

288. Senden R, Grimm B, Heyligers IC, Savelberg HH, Meijer K. Acceleration-based gait test for healthy subjects: reliability and reference data. *Gait Posture* 2009;**30**:192–6. http://dx.doi.org/10.1016/j.gaitpost.2009.04.008

289. Podsiadlo D, Richardson S. The timed 'Up & Go': a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 1991;**39**:142–8. http://dx.doi.org/10.1111/j.1532-5415.1991.tb01616.x

290. Janssen WG, Bussmann HB, Stam HJ. Determinants of the sit-to-stand movement: a review. *Phys Ther* 2002;**82**:866–79.

291. van den Dikkenberg N, Meijer OG, van der Slikke RM, van Lummel RC, van Dieen JH, Pijls B, *et al.* Measuring functional abilities of patients with knee problems: rationale and construction of the DynaPort knee test. *Knee Surg Sports Traumatol Arthrosc* 2002;**10**:204–12. http://dx.doi.org/10.1007/s00167-002-0279-x

292. Hardcastle P, Nade S. The significance of the Trendelenburg test. *J Bone Joint Surg Br* 1985;**67**:741–6.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

293. Senden R, Grimm B, Meijer K, Savelberg H, Heyligers IC. The importance to including objective functional outcomes in the clinical follow up of total knee arthroplasty patients. *Knee* 2011;**18**:306–11. http://dx.doi.org/10.1016/j.knee.2010.07.008

294. Binkley JM, Stratford PW, Lott SA, Riddle DL. The lower extremity functional scale (LEFS): scale development, measurement properties, and clinical application. North American Orthopaedic Rehabilitation Research Network. *Phys Ther* 1999;**79**:371–83.

295. Amstutz HC, Thomas BJ, Jinnah R, Kim W, Grogan T, Yale C. Treatment of primary osteoarthritis of the hip. A comparison of total joint and surface replacement arthroplasty. *J Bone Joint Surg Am* 1984;**66**:228–41.

296. Powell LE, Myers AM. The activities-specific balance confidence (ABC) scale. *J Gerontol A Biol Sci Med Sci* 1995;**50A**:M28–34. http://dx.doi.org/10.1093/gerona/50A.1.M28

297. Waldrop D, Lightsey OR, Ethington CA, Woemmel CA, Coke AL. Self-efficacy, optimism, health competence, and recovery from orthopedic surgery. *J Couns Psychol* 2001;**48**:233–8. http://dx.doi.org/10.1037/0022-0167.48.2.233

298. Nouri F, Lincoln N. An extended activities of daily living index for stroke patients *Clin Rehabil* 1987;**1**:301–5. http://dx.doi.org/10.1177/026921558700100409

299. Coast J, Peters TJ, Natarajan L, Sproston K, Flynn T. An assessment of the construct validity of the descriptive system for the ICECAP capability measure for older people. *Qual Life Res* 2008;**17**:967–76. http://dx.doi.org/10.1007/s11136-008-9372-z

300. Pollard B, Johnston M, Dieppe P. Exploring the relationships between international classification of functioning, disability and health (ICF) constructs of impairment, activity limitation and participation Restriction in people with osteoarthritis prior to joint replacement. *BMC Musculoskelet Disord* 2011;**12**:97. http://dx.doi.org/10.1186/1471-2474-12-97

301. Kennedy D, Stratford PW, Pagura SM, Walsh M, Woodhouse LJ. Comparison of gender and group differences in self-report and physical performance measures in total hip and knee arthroplasty candidates. *J Arthroplasty* 2002;**17**:70–7. http://dx.doi.org/10.1054/arth.2002.29324

302. Wright AA, Cook CE, Baxter GD, Garcia J, Abbott JH. Relationship between the western Ontario and McMaster Universities osteoarthritis index physical function subscale and physical performance measures in patients with hip osteoarthritis. *Arch Phys Med Rehabil* 2010;**91**:1558–64. http://dx.doi.org/10.1016/j.apmr.2010.07.016

303. National Joint Registry for England and Wales. *National Joint Registry for England and Wales: 8th Annual Report*. Hemel Hempstead: NJR Centre; 2011.

304. Great Britain. *Mental Capacity Act 2005*. London: The Stationary Office; 2005.

305. Bolink SA, van Laarhoven SN, Lipperts M, Heyligers IC, Grimm B. Inertial sensor motion analysis of gait, sit-stand transfers and step-up transfers: differentiating knee patients from healthy controls. *Physiol Meas* 2012;**33**:1947–58. http://dx.doi.org/10.1088/0967-3334/33/11/1947

306. Roos E, Toksvig-Larsen S. Knee injury and osteoarthritis outcome score (KOOS) – validation and comparison to the WOMAC in total knee replacement. *Health Qual Life Outcomes* 2003;**1**:17. http://dx.doi.org/10.1186/1477-7525-1-17

307. Hunt SM, McEwen J. The development of a subjective health indicator. *Sociol Health Illn* 1980;**2**:231–46. http://dx.doi.org/10.1111/1467-9566.ep11340686

308. Ornetti P, Maillefert JF, Laroche D, Morisset C, Dougados M, Gossec L. Gait analysis as a quantifiable outcome measure in hip or knee osteoarthritis: a systematic review. *Joint Bone Spine* 2010;**77**:421–5. http://dx.doi.org/10.1016/j.jbspin.2009.12.009

309. Reininga IH, Stevens M, Wagenmakers R, Boerboom AL, Groothoff JW, Bulstra SK, *et al.* Compensatory trunk movements in patients with hip osteoarthritis: accuracy and reproducibility of a body-fixed sensor-based assessment. *Am J Phys Med Rehabil* 2011;**90**:681–7. http://dx.doi.org/10.1097/PHM.0b013e31820f955e

310. van den Akker-Scheek I, Zijlstra W, Groothoff JW, Bulstra SK, Stevens M. Physical functioning before and after total hip arthroplasty: perception and performance. *Phys Ther* 2008;**88**:712–19. http://dx.doi.org/10.2522/ptj.20060301

311. Stratford PW, Kennedy DM. Performance measures were necessary to obtain a complete picture of osteoarthritic patients. *J Clin Epidemiol* 2006;**59**:160–7. http://dx.doi.org/10.1016/j.jclinepi.2005.07.012

312. Gandhi R, Tsvetkov D, Davey JR, Syed KA, Mahomed NN. Relationship between self-reported and performance-based tests in a hip and knee joint replacement population. *Clin Rheumatol* 2009;**28**:253–7. http://dx.doi.org/10.1007/s10067-008-1021-y

313. Boardman DL, Dorey F, Thomas BJ, Lieberman JR. The accuracy of assessing total hip arthroplasty outcomes: a prospective correlation study of walking ability and 2 validated measurement devices. *J Arthroplasty* 2000;**15**:200–4. http://dx.doi.org/10.1016/S0883-5403(00)90242-0

314. Kennedy DM, Stratford PW, Wessel J, Gollish JD, Penney D. Assessing stability and change of four performance measures: a longitudinal study evaluating outcome following total hip and knee arthroplasty. *BMC Musculoskelet Disord* 2005;**6**:3. http://dx.doi.org/10.1186/1471-2474-6-3

315. Stevens-Lapsley JE, Schenkman ML, Dayton MR. Comparison of self-reported knee injury and osteoarthritis outcome score to performance measures in patients after total knee arthroplasty. *PM&R* 2011;**3**:541–9. http://dx.doi.org/10.1016/j.pmrj.2011.03.002

316. Stratford PW, Kennedy DM, Riddle DL. New study design evaluated the validity of measures to assess change after hip or knee arthroplasty. *J Clin Epidemiol* 2009;**62**:347–52. http://dx.doi.org/10.1016/j.jclinepi.2008.06.008

317. Mizner RL, Petterson SC, Clements KE, Zeni JA Jr, Irrgang JJ, Snyder-Mackler L. Measuring functional improvement after total knee arthroplasty requires both performance-based and patient-report assessments: a longitudinal analysis of outcomes. *J Arthroplasty* 2011;**26**:728–37. http://dx.doi.org/10.1016/j.arth.2010.06.004

318. Terwee CB, van der Slikke RM, van Lummel RC, Benink RJ, Meijers WG, de Vet HC. Self-reported physical functioning was more influenced by pain than performance-based physical functioning in knee-osteoarthritis patients. *J Clin Epidemiol* 2006;**59**:724–31. http://dx.doi.org/10.1016/j.jclinepi.2005.11.019

319. Bream E, Black N. What is the relationship between patients' and clinicians' reports of the outcomes of elective surgery? *J Health Serv Res Policy* 2009;**14**:174–82. http://dx.doi.org/10.1258/jhsrp.2009.008115

320. Kauppila AM, Kyllonen E, Mikkonen P, Ohtonen P, Laine V, Siira P, *et al.* Disability in end-stage knee osteoarthritis. *Disabil Rehabil* 2009;**31**:370–80. http://dx.doi.org/10.1080/09638280801976159

321. Lin YC, Davey RC, Cochrane T. Tests for physical function of the elderly with knee and hip osteoarthritis. *Scand J Med Sci Sports* 2001;**11**:280–6. http://dx.doi.org/10.1034/j.1600-0838.2001.110505.x

322. Swinkels A, Allain TJ. Physical performance tests, self-reported outcomes, and accidental falls before and after total knee arthroplasty: An exploratory study. *Physiother Theory Pract* 2013;**26**:432–42. http://dx.doi.org/10.3109/09593985.2012.755590

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

323. Unnanuntana A, Mait JE, Shaffer AD, Lane JM, Mancuso CA. Performance-based tests and self-reported questionnaires provide distinct information for the preoperative evaluation of total hip arthroplasty patients. *J Arthroplasty* 2012;**27**:770–5e1.

324. McGrory BJ, Freiberg AA, Shinar AA, Harris WH. Correlation of measured range of hip motion following total hip arthroplasty and responses to a questionnaire. *J Arthroplasty* 1996;**11**:565–71. http://dx.doi.org/10.1016/S0883-5403(96)80111-2

325. Ghanem E, Pawasarat I, Lindsay A, May L, Azzam K, Joshi A, *et al.* Limitations of the knee society score in evaluating outcomes following revision total knee arthroplasty. *J Bone Joint Surg Am* 2010;**92**:2445–51. http://dx.doi.org/10.2106/JBJS.I.00252

326. Lingard EA, Katz JN, Wright RJ, Wright EA, Sledge CB. Validity and responsiveness of the knee society clinical rating system in comparison with the SF-36 and WOMAC. *J Bone Joint Surg Am* 2001;**83–A**:1856–64.

327. Jacobs CA, Christensen CP. Correlations between knee society function scores and functional force measures. *Clin Orthop Relat Res* 2009;**467**:2414–19. http://dx.doi.org/10.1007/s11999-009-0811-0

328. Shields RK, Enloe LJ, Evans RE, Smith KB, Steckel SD. Reliability, validity, and responsiveness of functional tests in patients with total joint replacement. *Phys Ther* 1995;**75**:169–76.

329. Steultjens MP, Dekker J, van Baar ME, Oostendorp RA, Bijlsma JW. Range of joint motion and disability in patients with osteoarthritis of the knee or hip. *Rheumatology* 2000;**39**:955–61. http://dx.doi.org/10.1093/rheumatology/39.9.955

330. Cress ME, Schechtman KB, Mulrow CD, Fiatarone MA, Gerety MB, Buchner DM. Relationship between physical performance and self-perceived physical function. *J Am Geriatr Soc* 1995;**43**:93–101. http://dx.doi.org/10.1111/j.1532-5415.1995.tb06372.x

331. Dowd JB, Todd M. Does self-reported health bias the measurement of health inequalities in U.S. adults? Evidence using anchoring vignettes from the health and retirement study. *J Gerontol B Psychol Sci Soc Sci* 2011;**66**:478–89. http://dx.doi.org/10.1093/geronb/gbr050

332. Louie GH, Ward MM. Association of measured physical performance and demographic and health characteristics with self-reported physical function: implications for the interpretation of self-reported limitations. *Health Qual Life Outcomes* 2010;**8**:84. http://dx.doi.org/10.1186/1477-7525-8-84

333. Wright AA, Hegedus EJ, Baxter GD, Abbott JH. Measurement of function in hip osteoarthritis: developing a standardized approach for physical performance measures. *Physiother Theory Pract* 2011;**27**:253–62. http://dx.doi.org/10.3109/09593985.2010.491150

334. Gajdosik RL, Bohannon RW. Clinical measurement of range of motion. Review of goniometry emphasizing reliability and validity. *Phys Ther* 1987;**67**:1867–72.

335. Williams SL, Haskard KB, DiMatteo MR. The therapeutic effects of the physician-older patient relationship: effective communication with vulnerable older patients. *Clin Interv Aging* 2007;**2**:453–67.

336. Jordan KP, Wilkie R, Muller S, Myers H, Nicholls E, Arthritis Res Campaign Natl P. Measurement of change in function and disability in osteoarthritis: current approaches and future challenges. *Curr Opin Rheumatol* 2009;**21**:525–30. http://dx.doi.org/10.1097/BOR.0b013e32832e45fc

337. Clark DO. Age, socioeconomic status, and exercise self-efficacy. *Gerontologist* 1996;**36**:157–64. http://dx.doi.org/10.1093/geront/36.2.157

338. Miner AL, Lingard EA, Wright EA, Sledge CB, Katz JN. Knee range of motion after total knee arthroplasty: how important is this as an outcome measure? *J Arthroplasty* 2003;**18**:286–94. http://dx.doi.org/10.1054/arth.2003.50046

339. Rabe-Hesketh S, Skrondal A. *Multilevel and Longitudinal Modeling Using Stata Volume II: Categorical Responses, Counts, and Survival*. 3rd edn. College Station, TX: Stata Press; 2012.

340. Ethgen O, Bruyere O, Richy F, Dardennes C, Reginster JY. Health-related quality of life in total hip and total knee arthroplasty: a qualitative and systematic review of the literature. *J Bone Joint Surg Am* 2004;**86–A**:963–74.

341. Halket A, Stratford PW, Kennedy DM, Woodhouse LJ. Using hierarchical linear modeling to explore predictors of pain after total hip and knee arthroplasty as a consequence of osteoarthritis. *J Arthroplasty* 2010;**25**:254–62. http://dx.doi.org/10.1016/j.arth.2009.01.007

342. Kennedy DM, Stratford PW, Hanna SE, Wessel J, Gollish JD. Modeling early recovery of physical function following hip and knee arthroplasty. *BMC Musculoskelet Disord* 2006;**7**:100. http://dx.doi.org/10.1186/1471-2474-7-100

343. Escobar A, Quintana JM, Bilbao A, Arostegui I, Lafuente I, Vidaurreta I. Responsiveness and clinically important differences for the WOMAC and SF-36 after total knee replacement. *Osteoarthritis Cart* 2007;**15**:273–80. http://dx.doi.org/10.1016/j.joca.2006.09.001

344. Quintana JM, Escobar A, Bilbao A, Arostegui I, Lafuente I, Vidaurreta I. Responsiveness and clinically important differences for the WOMAC and SF-36 after hip joint replacement. *Osteoarthritis Cart* 2005;**13**:1076–83. http://dx.doi.org/10.1016/j.joca.2005.06.012

345. Davis AM, Perruccio AV, Ibrahim S, Hogg-Johnson S, Wong R, Streiner DL, *et al.* The trajectory of recovery and the inter-relationships of symptoms, activity and participation in the first year following total hip and knee replacement. *Osteoarthritis Cart* 2011;**19**:1413–21. http://dx.doi.org/10.1016/j.joca.2011.08.007

346. Fitzgerald JD, Orav EJ, Lee TH, Marcantonio ER, Poss R, Goldman L, *et al.* Patient quality of life during the 12 months following joint replacement surgery. *Arthritis Rheum* 2004;**51**:100–9. http://dx.doi.org/10.1002/art.20090

347. Heiberg KE, Ekeland A, Bruun-Olsen V, Mengshoel AM. Recovery and prediction of physical functioning outcomes during the first year after total hip arthroplasty. *Arch Phys Med Rehabil* 2013;**94**:1352–9. http://dx.doi.org/10.1016/j.apmr.2013.01.017

348. Kennedy DM, Stratford PW, Riddle DL, Hanna SE, Gollish JD. Assessing recovery and establishing prognosis following total knee arthroplasty. *Phys Ther* 2008;**88**:22–32. http://dx.doi.org/10.2522/ptj.20070051

349. Kennedy DM, Stratford PW, Robarts S, Gollish JD. Using outcome measure results to facilitate clinical decisions the first year after total hip arthroplasty. *J Orthop Sports Phys Ther* 2011;**41**:232–9. http://dx.doi.org/10.2519/jospt.2011.3516

350. Naylor JM, Harmer AR, Heard RC, Harris IA. Patterns of recovery following knee and hip replacement in an Australian cohort. *Aust Health Rev* 2009;**33**:124–35. http://dx.doi.org/10.1071/AH090124

351. Baker P, Cowling P, Kurtz S, Jameson S, Gregg P, Deehan D. Reason for revision influences early patient outcomes after aseptic knee revision. *Clin Orthop Relat Res* 2012;**470**:2244–52. http://dx.doi.org/10.1007/s11999-012-2278-7

352. Field RE, Cronin MD, Singh PJ. The Oxford hip scores for primary and revision hip replacement. *J Bone Joint Surg Br* 2005;**87**:618–22. http://dx.doi.org/10.1302/0301-620X.87B5.15390

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

353. Stratford PW, Kennedy DM. Does parallel item content on WOMAC's pain and function subscales limit its ability to detect change in functional status? *BMC Musculoskelet Disord* 2004;**5**:17. http://dx.doi.org/10.1186/1471-2474-5-17

354. Ekstrom H, Dahlin-Ivanoff S, Elmstahl S. Effects of walking speed and results of timed get-up-and-go tests on quality of life and social participation in elderly individuals with a history of osteoporosis-related fractures. *J Aging Health* 2011;**23**:1379–99. http://dx.doi.org/10.1177/0898264311418504

355. Desrosiers J, Noreau L, Rochette A, Bourbonnais D, Bravo G, Bourget A. Predictors of long-term participation after stroke. *Disabil Rehabil* 2006;**28**:221–30. http://dx.doi.org/10.1080/09638280500158372

356. Hamzat TK, Kobiri A. Effects of walking with a cane on balance and social participation among community-dwelling post-stroke individuals. *Eur J Phys Rehabil Med* 2008;**44**:121–6.

357. Fujita K, Takahashi H, Miura C, Ohkubo T, Sato Y, Ugajin T, *et al.* Walking and mortality in Japan: the Miyagi cohort study. *J Epidemiol* 2004;**14**(Suppl. 1):S26–32. http://dx.doi.org/10.2188/jea.14.S26

358. Kujala UM, Kaprio J, Sarna S, Koskenvuo M. Relationship of leisure-time physical activity and mortality: the Finnish twin cohort. *JAMA* 1998;**279**:440–4. http://dx.doi.org/10.1001/jama.279.6.440

359. LaCroix AZ, Leveille SG, Hecht JA, Grothaus LC, Wagner EH. Does walking decrease the risk of cardiovascular disease hospitalizations and death in older adults? *J Am Geriatr Soc* 1996;**44**:113–20. http://dx.doi.org/10.1111/j.1532-5415.1996.tb02425.x

360. Lee IM, Rexrode KM, Cook NR, Manson JE, Buring JE. Physical activity and coronary heart disease in women: is 'no pain, no gain' passe? *JAMA* 2001;**285**:1447–54. http://dx.doi.org/10.1001/jama.285.11.1447

361. Morioka S. [A cohort study on the relationship between lifestyles and total mortality.] *Nihon Koshu Eisei Zasshi* 1996;**43**:469–78.

362. Seki N. [Relationships between walking hours, sleeping hours, meaningfulness of life (ikigai) and mortality in the elderly: prospective cohort study.] *Nihon Eiseigaku Zasshi* 2001;**56**:535–40. http://dx.doi.org/10.1265/jjh.56.535

363. Horwood J, Johnson E, Gooberman-Hill R. Understanding involvement in surgical orthopaedic randomized controlled trials: a qualitative study of patient and health professional views and experiences. *Int J Orthop Trauma Nurs* 2016;**20**:3–12. http://dx.doi.org/10.1016/j.ijotn.2015.05.002

364. Marques E, Blom AW, Lenguerrand E, Wylde V, Noble SM. Local anaesthetic wound infiltration in addition to standard anaesthetic regimen in total hip and knee replacement: long-term cost-effectiveness analyses alongside the APEX randomised controlled trials. *BMC Medicine* 2015;**15**:151. http://dx.doi.org/10.1186/s12916-015-0389-1

365. Wylde V, Gooberman-Hill R, Horwood J, Beswick A, Noble S, Brookes S, *et al.* The effect of local anaesthetic wound infiltration on chronic pain after lower limb joint replacement: a protocol for a double-blind randomised controlled trial. *BMC Musculoskelet Disord* 2011;**12**:53. http://dx.doi.org/10.1186/1471-2474-12-53

366. Marques E, Jones H, Elvers K, Pyke M, Blom A, Beswick A. Local anaesthetic infiltration for peri-operative pain control in total hip and knee replacement: systematic review and meta-analyses of short- and long-term effectiveness. *BMC Musculoskelet Disord* 2014;**15**:220. http://dx.doi.org/10.1186/1471-2474-15-220

367. Wylde V, Lenguerrand E, Gooberman-Hill R, Beswick AD, Marques E, Noble S, *et al.* Effect of local anaesthetic infiltration on chronic postsurgical pain after total hip and knee replacement: the APEX randomised controlled trials. *Pain* 2015;**156**:1161–70.

368. Mann C, Delgado D, Horwood J. Evaluation of internal peer-review to train nurses recruiting to a randomized controlled trial – Internal Peer-review for Recruitment Training in Trials (InterPReTiT). *J Adv Nurs* 2014;**70**:777–90. http://dx.doi.org/10.1111/jan.12254

369. Caffo O, Amichetti M, Ferro A, Lucenti A, Valduga F, Galligioni E. Pain and quality of life after surgery for breast cancer. *Breast Cancer Res Treat* 2003;**80**:39–48. http://dx.doi.org/10.1023/A:1024435101619

370. Poobalan AS, Bruce J, King PM, Chambers WA, Krukowski ZH, Smith WC. Chronic pain and quality of life following open inguinal hernia repair. *Br J Surg* 2001;**88**:1122–6. http://dx.doi.org/10.1046/j.0007-1323.2001.01828.x

371. Perttunen K, Tasmuth T, Kalso E. Chronic pain after thoracic surgery: a follow-up study. *Acta Anaesthesiol Scand* 1999;**43**:563–7. http://dx.doi.org/10.1034/j.1399-6576.1999.430513.x

372. Jin F, Chung F. Multimodal analgesia for postoperative pain control. *J Clin Anesth* 2001;**13**:524–39. http://dx.doi.org/10.1016/S0952-8180(01)00320-8

373. Liu SS, Richman JM, Thirlby RC, Wu CL. Efficacy of continuous wound catheters delivering local anesthetic for postoperative analgesia: A quantitative and qualitative systematic review of randomized controlled trials. *J Am Coll Surg* 2006;**203**:914–32. http://dx.doi.org/10.1016/j.jamcollsurg.2006.08.007

374. Bianconi M, Ferraro L, Traina GC, Zanoli G, Antonelli T, Guberti A, *et al.* Pharmacokinetics and efficacy of ropivacaine continuous wound instillation after joint replacement surgery. *Br J Anaesth* 2003;**91**:830–5. http://dx.doi.org/10.1093/bja/aeg277

375. Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, *et al.* Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ* 2011;**343**:d4002. http://dx.doi.org/10.1136/bmj.d4002

376. Kerr DR, Kohan L. Local infiltration analgesia: a technique for the control of acute postoperative pain following knee and hip surgery: a case study of 325 patients. *Acta Orthop* 2008;**79**:174–83. http://dx.doi.org/10.1080/17453670710014950

377. Walter SD, Yao X. Effect sizes can be calculated for studies reporting ranges for outcome variables in systematic reviews. *J Clin Epidemiol* 2007;**60**:849–52. http://dx.doi.org/10.1016/j.jclinepi.2006.11.003

378. Hedges LV, Olkin I. *Statistical Methods for Meta-analysis*. San Diego: Academic Press; 1985.

379. Scholten RJPM, de Beurs E, Bouter LM. From effect size into number needed to treat. *Lancet* 1999;**354**:598. http://dx.doi.org/10.1016/S0140-6736(05)77952-6

380. Toftdahl K, Nikolajsen L, Haraldsted V, Madsen F, Tonnesen EK, Soballe K. Comparison of peri- and intraarticular analgesia with femoral nerve block after total knee arthroplasty: a randomized clinical trial. *Acta Orthop* 2007;**78**:172–9. http://dx.doi.org/10.1080/17453670710013645

381. Thorsell M, Holst P, Hyldahl HC, Weidenhielm L. Pain control after total knee arthroplasty: a prospective study comparing local infiltration anesthesia and epidural anesthesia. *Orthopedics* 2010;**33**:75–80. http://dx.doi.org/10.3928/01477447-20100104-13

382. Higgins JP, White IR, Anzures-Cabrera J. Meta-analysis of skewed data: combining results reported on log-transformed or raw scales. *Stat Med* 2008;**27**:6072–92. http://dx.doi.org/10.1002/sim.3427

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

383. Bradburn MJ, Deeks JJ, Berlin JA, Russell Localio A. Much ado about nothing: a comparison of the performance of meta-analytical methods with rare events. *Stat Med* 2007;**26**:53–77. http://dx.doi.org/10.1002/sim.2528

384. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;**21**:1539–58. http://dx.doi.org/10.1002/sim.1186

385. Andersen KV, Pfeiffer-Jensen M, Haraldsted V, Soballe K, Andersen KV, Pfeiffer-Jensen M, *et al.* Reduced hospital stay and narcotic consumption, and improved mobilization with local and intraarticular infiltration after hip arthroplasty: a randomized clinical trial of an intraarticular technique versus epidural infusion in 80 patients. *Acta Orthop* 2007;**78**:180–6. http://dx.doi.org/10.1080/17453670710013654

386. Parvataneni HK, Shah VP, Howard H, Cole N, Ranawat AS, Ranawat CS. Controlling pain after total hip and knee arthroplasty using a multimodal protocol with local periarticular injections. A prospective randomized study. *J Arthroplasty* 2007;**22**:33–8. http://dx.doi.org/10.1016/j.arth.2007.03.034

387. Aguirre J, Baulig B, Dora C, Ekatodramis G, Votta-Velis G, Ruland P, *et al.* Continuous epicapsular ropivacaine 0.3% infusion after minimally invasive hip arthroplasty: a prospective, randomized, double-blinded, placebo-controlled study comparing continuous wound infusion with morphine patient-controlled analgesia. *Anesth Analg* 2012;**114**:456–61. http://dx.doi.org/10.1213/ANE.0b013e318239dc64

388. Andersen LJ, Poulsen T, Krogh B, Nielsen T, Andersen LJ, Poulsen T, *et al.* Postoperative analgesia in total hip arthroplasty: a randomized double-blinded, placebo-controlled study on peroperative and postoperative ropivacaine, ketorolac, and adrenaline wound infiltration. *Acta Orthop* 2007;**78**:187–92. http://dx.doi.org/10.1080/17453670710013663

389. Busch CA, Whitehouse MR, Shore BJ, MacDonald SJ, McCalden RW, Bourne RB. The efficacy of periarticular multimodal drug infiltration in total hip arthroplasty. *Clin Orthop Relat Res* 2010;**468**:2152–9. http://dx.doi.org/10.1007/s11999-009-1198-7

390. Dobie I, Bennett D, Spence DJ, Murray JM, Beverland DE. Periarticular local anesthesia does not improve pain or mobility after THA. *Clin Orthop Relat Res* 2012;**470**:1958–65. http://dx.doi.org/10.1007/s11999-012-2241-7

391. Lee K-J, Min B-W, Bae K-C, Cho C-H, Kwon D-H. Efficacy of multimodal pain control protocol in the setting of total hip arthroplasty. *Clin Orthop Surg* 2009;**1**:155–60. http://dx.doi.org/10.4055/cios.2009.1.3.155

392. Liu W, Cong R, Li X, Wu Y, Wu H. Reduced opioid consumption and improved early rehabilitation with local and intraarticular cocktail analgesic injection in total hip arthroplasty: a randomized controlled clinical trial. *Pain Med* 2011;**12**:387–93. http://dx.doi.org/10.1111/j.1526-4637.2010.01043.x

393. Lu ZD, Li P. Analgesic effect of periarticular Ropivacaine infiltration and cyclooxygenase-2 inhibitor following total hip arthroplasty. *J Clin Rehabil Tissue Engineering Res* 2010;**14**:7991–4.

394. Lunn TH, Husted H, Solgaard S, Kristensen BB, Otte KS, Kjersgaard AG, *et al.* Intraoperative local infiltration analgesia for early analgesia after total hip arthroplasty: a randomized, double-blind, placebo-controlled trial. *Reg Anesth Pain Med* 2011;**36**:424–9. http://dx.doi.org/10.1097/AAP.0b013e3182186866

395. Murphy TP, Byrne DP, Curtin P, Baker JF, Mulhall KJ. Can a periarticular levobupivacaine injection reduce postoperative opiate consumption during primary hip arthroplasty? *Clin Orthop Relat Res* 2012;**470**:1151–7. http://dx.doi.org/10.1007/s11999-011-2108-3

396. Rikalainen-Salmi R, Forster JG, Makela K, Virolainen P, Leino KA, Pitkanen MT, *et al.* Local infiltration analgesia with levobupivacaine compared with intrathecal morphine in total hip arthroplasty patients. *Acta Anaesthesiol Scand* 2012;**56**:695–705. http://dx.doi.org/10.1111/j.1399-6576.2012.02667.x

397. Affas F, Nygårds E-B, Stiller C-O, Wretenberg P, Olofsson C. Pain control after total knee arthroplasty: a randomized trial comparing local infiltration anesthesia and continuous femoral block. *Acta Orthop* 2011;**82**:441–7. http://dx.doi.org/10.3109/17453674.2011.581264

398. Andersen KV, Bak M, Christensen BV, Harazuk J, Pedersen NA, Soballe K. A randomized, controlled trial comparing local infiltration analgesia with epidural infusion for total knee arthroplasty. *Acta Orthop* 2010;**81**:606–10. http://dx.doi.org/10.3109/17453674.2010.519165

399. Busch CA, Shore BJ, Bhandari R, Ganapathy S, MacDonald SJ, Bourne RB, *et al.* Efficacy of periarticular multimodal drug injection in total knee arthroplasty. A randomized trial. *J Bone Joint Surg Am* 2006;**88**:959–63. http://dx.doi.org/10.2106/JBJS.E.00344

400. Carli F, Clemente A, Asenjo JF, Kim DJ, Mistraletti G, Gomarasca M, *et al.* Analgesia and functional outcome after total knee arthroplasty: periarticular infiltration vs continuous femoral nerve block. *Br J Anaesth* 2010;**105**:185–95. http://dx.doi.org/10.1093/bja/aeq112

401. Chen Y, Zhang Y, Zhu YL, Fu P. Efficacy and safety of an intra-operative intra-articular magnesium/ropivacaine injection for pain control following total knee arthroplasty. *J Int Med Res* 2012;**40**:2032–40. http://dx.doi.org/10.1177/030006051204000548

402. Essving P, Axelsson K, Kjellberg J, Wallgren O, Gupta A, Lundin A. Reduced morphine consumption and pain intensity with local infiltration analgesia (LIA) following total knee arthroplasty: a randomized double-blind study involving 48 patients. *Acta Orthop* 2010;**81**:354–60. http://dx.doi.org/10.3109/17453674.2010.487241

403. Essving P, Axelsson K, Aberg E, Spannar H, Gupta A, Lundin A. Local infiltration analgesia versus intrathecal morphine for postoperative pain management after total knee arthroplasty: a randomized controlled trial. *Anesth Analg* 2011;**113**:926–33. http://dx.doi.org/10.1213/ANE.0b013e3182288deb

404. Fu P, Wu Y, Wu H, Li X, Qian Q, Zhu Y. Efficacy of intra-articular cocktail analgesic injection in total knee arthroplasty – a randomized controlled trial. *Knee* 2009;**16**:280–4. http://dx.doi.org/10.1016/j.knee.2008.12.012

405. Fu PL, Xiao J, Zhu YL, Wu HS, Li XH, Wu YL, *et al.* Efficacy of a multimodal analgesia protocol in total knee arthroplasty: a randomized, controlled trial. *J Int Med Res* 2010;**38**:1404–12. http://dx.doi.org/10.1177/147323001003800422

406. Han CD, Lee DH, Yang IH. Intra-synovial ropivacaine and morphine for pain relief after total knee arthroplasty: a prospective, randomized, double blind study. *Yonsei Med J* 2007;**48**:295–300. http://dx.doi.org/10.3349/ymj.2007.48.2.295

407. Koh IJ, Kang YG, Chang CB, Do SH, Seong SC, Kim TK. Does periarticular injection have additional pain relieving effects during contemporary multimodal pain control protocols for TKA?: A randomised, controlled study. *Knee* 2012;**19**:253–9. http://dx.doi.org/10.1016/j.knee.2011.03.007

408. Krenzel BA, Cook C, Martin GN, Vail TP, Attarian DE, Bolognesi MP. Posterior capsular injections of ropivacaine during total knee arthroplasty: a randomized, double-blind, placebo-controlled study. *J Arthroplasty* 2009;**24**:138–43. http://dx.doi.org/10.1016/j.arth.2009.03.014

409. Mahadevan D, Walter RP, Minto G, Gale TC, McAllen CJ, Oldman M. Combined femoral and sciatic nerve block vs combined femoral and periarticular infiltration in total knee arthroplasty. A randomized controlled trial. *J Arthroplasty* 2012;**27**:1806–11. http://dx.doi.org/10.1016/j.arth.2012.05.018

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

410. Meftah M, Wong AC, Nawabi DH, Yun RJ, Ranawat AS, Ranawat CS. Pain management after total knee arthroplasty using a multimodal approach. *Orthopedics* 2012;**35**:e660–4. http://dx.doi.org/10.3928/01477447-20120426-19

411. Ng FY, Ng JKF, Chiu KY, Yan CH, Chan CW. Multimodal periarticular injection vs continuous femoral nerve block after total knee arthroplasty. A prospective, crossover, randomized clinical trial. *J Arthroplasty* 2012;**27**:1234–8. http://dx.doi.org/10.1016/j.arth.2011.12.021

412. Spreng UJ, Dahl V, Hjall A, Fagerland MW, Ræder J. High-volume local infiltration analgesia combined with intravenous or local ketorolac+morphine compared with epidural analgesia after total knee arthroplasty. *Br J Anaesth* 2010;**105**:675–82. http://dx.doi.org/10.1093/bja/aeq232

413. Vendittoli PA, Makinen P, Drolet P, Lavigne M, Fallaha M, Guertin MC, *et al.* A multimodal analgesia protocol for total knee arthroplasty. A randomized, controlled study. *J Bone Joint Surg Am* 2006;**88**:282–9. http://dx.doi.org/10.2106/JBJS.E.00173

414. Zhang J, Jiang Y, Shao JJ, Shen H, Wang Q, Zhang XL. Effect of periarticular multimodal drug injection on pain after total knee arthroplasty. *Chinese J Clin Rehabil* 2007;**11**:8678–82.

415. Auroy Y, Benhamou D, Bargues L, Ecoffey C, Falissard B, Mercier FJ, *et al.* Major complications of regional anesthesia in France: the SOS Regional Anesthesia Hotline Service. *Anesthesiology* 2002;**97**:1274–80. http://dx.doi.org/10.1097/00000542-200211000-00034

416. Sharma S, Iorio R, Specht L, Davies-Lepie S, Healy W. Complications of femoral nerve block for total knee arthroplasty. *Clin Orthop Relat Res* 2010;**468**:135–40. http://dx.doi.org/10.1007/s11999-009-1025-1

417. Tang R, Evans H, Chaput A, Kim C, Tang R, Evans H, *et al.* Multimodal analgesia for hip arthroplasty. *Orthop Clin North Am* 2009;**40**:377–87. http://dx.doi.org/10.1016/j.ocl.2009.04.001

418. Perkins FM, Kehlet H. Chronic pain as an outcome of surgery. A review of predictive factors. *Anesthesiology* 2000;**93**:1123–33. http://dx.doi.org/10.1097/00000542-200010000-00038

419. Macrae WA. Chronic post-surgical pain: 10 years on. *Br J Anaesth* 2008;**101**:77–86. http://dx.doi.org/10.1093/bja/aen099

420. Gupta A. Wound infiltration with local anaesthetics in ambulatory surgery. *Curr Opin Anaesthesiol* 2010;**23**:708–13. http://dx.doi.org/10.1097/ACO.0b013e32833f0dd7

421. Gibbs DM, Green TP, Esler CN. The local infiltration of analgesia following total knee replacement: a review of current literature. *J Bone Joint Surg Br* 2012;**94**:1154–9. http://dx.doi.org/10.1302/0301-620X.94B9.28611

422. Neugebauer EA, Wilkinson RC, Kehlet H, Schug SA. PROSPECT: a practical method for formulating evidence-based expert recommendations for the management of postoperative pain. *Surg Endosc* 2007;**21**:1047–53. http://dx.doi.org/10.1007/s00464-006-9186-4

423. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis* 1957;**16**:494–502. http://dx.doi.org/10.1136/ard.16.4.494

424. Tubach F, Ravaud P, Baron G, Falissard B, Logeart I, Bellamy N, *et al.* Evaluation of clinically relevant changes in patient reported outcomes in knee and hip osteoarthritis: the minimal clinically important improvement. *Ann Rheum Dis* 2005;**64**:29–33. http://dx.doi.org/10.1136/ard.2004.022905

425. Ehrich EW, Davies GM, Watson DJ, Bolognese JA, Seidenberg BC, Bellamy N. Minimal perceptible clinical improvement with the Western Ontario and McMaster Universities osteoarthritis index questionnaire and global assessments in patients with osteoarthritis. *J Rheumatol* 2000;**27**:2635–41.

426. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med* 2011;**30**:377–99. http://dx.doi.org/10.1002/sim.4067

427. Hardin J, Hilbe J. *Generalized Linear Models and Extensions*. Second edn. College Station, TX: Stata Press; 2007.

428. Zou G. A modified poisson regression approach to prospective studies with binary data. *Am J Epidemiol* 2004;**159**:702–6. http://dx.doi.org/10.1093/aje/kwh090

429. Zou G, Donner A. Extension of the modified Poisson regression model to prospective studies with correlated binary data. *Stat Methods Med Res* 2013;**22**:661–70. http://dx.doi.org/10.1177/0962280211427759

430. Garellick G, Karrholm J, Rogmark C, Rolfson O, Herberts P. *Swedish Hip Arthroplasty Register Annual Report*. Göteborg: Centre of Registers Region Västra Götaland; 2011.

431. O'Connor AB, Dworkin RH. Treatment of neuropathic pain: an overview of recent guidelines. *Am J Med* 2009;**122**:S22–32. http://dx.doi.org/10.1016/j.amjmed.2009.04.007

432. Marques E, Johnson EC, Gooberman-Hill R, Blom AW, Noble S. Using resource use logs to reduce the amount of missing data in economic evaluations alongside trials. *Value Health* 2013;**16**:195–201. http://dx.doi.org/10.1016/j.jval.2012.09.008

433. Noble S. *APEX – Hip Replacement Participant Resource Use Log: 0 to 3 Months*. DIRUM; 2012. URL: www.dirum.org/instruments/details/54 (accessed 21 July 2016).

434. Noble S. *APEX – 3-Month postoperative Hip Questionnaire*. DIRUM; 2012. URL: www.dirum.org/instruments/details/55 (accessed 21 July 2016).

435. Payment by Results team. *Reference Costs 2011–2012*. London: Department of Health. URL: www.gov.uk/government/uploads/system/uploads/attachment_data/file/213060/2011-12-reference-costs-publication.pdf (accessed 21 July 2016).

436. Curtis L. *Unit Costs of Health and Social Care 2013*. Canterbury: University of Kent; 2014.

437. EuroQol Group. EuroQol – a new facility for the measurement of health-related quality of life. *Health Policy* 1990;**16**:199–208. http://dx.doi.org/10.1016/0168-8510(90)90421-9

438. Patrick DL, Starks HE, Cain KC, Uhlmann RF, Pearlman RA. Measuring preferences for health states worse than death. *Med Decis Making* 1994;**14**:9–18. http://dx.doi.org/10.1177/0272989X9401400102

439. Dolan P, Gudex C, Kind P, Williams A. *A Social Tariff for EuroQol: Results From a UK General Population Survey*. Working Papers, vol. 138. York: University of York, Centre for Health Economics; 1995.

440. Edwards RT, Hounsome B, Russell D, Russell I, Williams N. *QALY calculation alongside randomised controlled trials: from the torch to the traffic light*. Paris: paper presented at first Franco-British Meeting in Health Economics CES/HESG; 2004.

441. Curtis L. *Unit Costs of Health and Social Care*. Canterbury: University of Kent; 2012.

442. White H. A heteroskedasticity-consistent covariance matrix estimator and a direct test for heteroskedasticity. *Econometrica* 1980;**48**:817–38. http://dx.doi.org/10.2307/1912934

443. Manca A, Hawkins N, Sculpher MJ. Estimating mean QALYs in trial-based cost-effectiveness analysis: the importance of controlling for baseline utility. *Health Econ* 2005;**14**:487–96. http://dx.doi.org/10.1002/hec.944

444. Royston P. Multiple imputation of missing values: update. *Stata J* 2005;**5**:188–201.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

445. Ritchie J, Spencer L. Qualitative Data Analysis for Applied Policy Research. In Bryman A, Burgess RG, editors. *Analyzing Qualitative Data.* London: Routledge; 1994. pp. 173–94. http://dx.doi.org/10.4324/9780203413081_chapter_9

446. Watson JM, Torgerson DJ. Increasing recruitment to randomised trials: a review of randomised controlled trials. *BMC Med Res Methodol* 2006;**6**:34. http://dx.doi.org/10.1186/1471-2288-6-34

447. Wade J, Donovan JL, Lane JA, Neal DE, Hamdy FC. It's not just what you say, it's also how you say it: opening the 'black box' of informed consent appointments in randomised controlled trials. *Soc Sci Med* 2009;**68**:2018–28. http://dx.doi.org/10.1016/j.socscimed.2009.02.023

448. Robinson EJ, Kerr CE, Stevens AJ, Lilford RJ, Braunholtz DA, Edwards SJ, *et al.* Lay public's understanding of equipoise and randomisation in randomised controlled trials. *Health Technol Assess* 2005;**9**(8). http://dx.doi.org/10.3310/hta9080

449. Lane JA, Wade J, Down L, Bonnington S, Holding PN, Lennon T, *et al.* A peer review intervention for monitoring and evaluating sites (PRIME) that improved randomized controlled trial conduct and performance. *J Clin Epidemiol* 2011;**64**:628–36. http://dx.doi.org/10.1016/j.jclinepi.2010.10.003

450. de Salis I, Tomlin Z, Toerien M, Donovan J. Using qualitative research methods to improve recruitment to randomized controlled trials: the Quartet study. *J Health Serv Res Policy* 2008;**13**(Suppl. 3):92–6. http://dx.doi.org/10.1258/jhsrp.2008.008028

451. Fletcher B, Gheorghe A, Moore D, Wilson S, Damery S. Improving the recruitment activity of clinicians in randomised controlled trials: a systematic review. *BMJ Open* 2012;**2**:e000496. http://dx.doi.org/10.1136/bmjopen-2011-000496

452. Rout A, Roberts P. Peer review in nursing and midwifery: a literature review. *J Clin Nurs* 2008;**17**:427–42.

453. Cameron N, McMillan R. Enhancing communication skills by peer review of consultation videos. *Education for Primary Care* 2006;**17**:40–8. http://dx.doi.org/10.1080/1475990X.2006.11493509

454. Paramasivan S, Huddart R, Hall E, Lewis R, Birtle A, Donovan JL. Key issues in recruitment to randomised controlled trials with very different interventions: a qualitative investigation of recruitment to the SPARE trial (CRUK/07/011). *Trials* 2011;**12**:78. http://dx.doi.org/10.1186/1745-6215-12-78

455. Weaver T, Renton A, Tyrer P, Ritchie J. Combining qualitative studies with randomised controlled trials is often useful. *BMJ* 1996;**313**:629. http://dx.doi.org/10.1136/bmj.313.7057.629

456. Donovan J, Little P, Mills N, Smith M, Brindle L, Jacoby A, *et al.* Quality improvement report. Improving design and conduct of randomised trials by embedding them in qualitative research: ProtecT (prostate testing for cancer and treatment) study. *BMJ* 2002;**325**:766–70. http://dx.doi.org/10.1136/bmj.325.7367.766

457. Lewin S, Glenton C, Oxman AD. Use of qualitative methods alongside randomised controlled trials of complex healthcare interventions: methodological study. *BMJ* 2009;**339**:b3496. http://dx.doi.org/10.1136/bmj.b3496

458. Bhandari M, Devereaux PJ, Swiontkowski MF, Tornetta P 3rd, Obremskey W, Koval KJ, *et al.* Internal fixation compared with arthroplasty for displaced fractures of the femoral neck. A meta-analysis. *J Bone Joint Surg Am* 2003;**85–A**:1673–81.

459. Garrett WE Jr., Swiontkowski MF, Weinstein JN, Callaghan J, Rosier RN, Berry DJ, *et al.* American board of orthopaedic surgery practice of the orthopaedic surgeon: part-II, certification examination case mix. *J Bone Joint Surg Am* 2006;**88**:660–7. http://dx.doi.org/10.2106/JBJS.E.01208

460. Swiontkowski MF, Agel J. Lessons learned from benchmark orthopaedic trials. *J Bone Joint Surg Am* 2012;**94**(Suppl. 1):11–4. http://dx.doi.org/10.2106/JBJS.K.01622

461. Sikweyiya Y, Jewkes R. Potential motivations for and perceived risks in research participation: ethics in health research. *Qual Health Res* 2013;**23**:999–1009. http://dx.doi.org/10.1177/1049732313490076

462. Gooberman-Hill R, Heathcote C, Reid CM, Horwood J, Beswick AD, Williams S, *et al.* Professional experience guides opioid prescribing for chronic joint pain in primary care. *Fam Pract* 2011;**28**:102–9. http://dx.doi.org/10.1093/fampra/cmq083

463. National Institute for Health and Care Excellence (NICE). *The Care and Management of Osteoarthritis in Adults*. London: NICE; 2008.

464. Joelsson M, Olsson LE, Jakobsson E. Patients' experience of pain and pain relief following hip replacement surgery. *J Clin Nurs* 2010;**19**:2832–8. http://dx.doi.org/10.1111/j.1365-2702.2010.03215.x

465. Niemi-Murola L, Poyhia R, Onkinen K, Rhen B, Makela A, Niemi TT. Patient satisfaction with postoperative pain management–effect of preoperative factors. *Pain Manag Nurs* 2007;**8**:122–9. http://dx.doi.org/10.1016/j.pmn.2007.05.003

466. Boyatzis R. *Transforming Qualitative Information: Thematic Analysis and Code Development*. Thousand Oaks, CA: Sage; 1998.

467. Charmaz K. *Constructing Grounded Theory: A Practical Guide Through Qualitative Analysis*. London: Sage; 2006.

468. Jerosch-Herold C, Shepstone L, Vaughan S, Barrett B, Larson D, Chojnowski A. A questionnaire-based survey of participants' decisions regarding recruitment and retention in a randomised controlled trial – lessons learnt from the SCoRD trial. *Contemp Clin Trials* 2011;**32**:363–8. http://dx.doi.org/10.1016/j.cct.2011.01.014

469. Hallowell N, Cooke S, Crawford G, Lucassen A, Parker M, Snowdon C. An investigation of patients' motivations for their participation in genetics-related research. *J Med Ethics* 2010;**36**:37–45. http://dx.doi.org/10.1136/jme.2009.029264

470. Locock L, Smith L. Personal benefit, or benefiting others? Deciding whether to take part in clinical trials. *Clin Trials* 2011;**8**:85–93. http://dx.doi.org/10.1177/1740774510392257

471. McCann S, Campbell M, Entwistle V. Reasons for participating in randomised controlled trials: conditional altruism and considerations for self. *Trials* 2010;**11**:31. http://dx.doi.org/10.1186/1745-6215-11-31

472. Wylde V, Sayers A, Lenguerrand E, Gooberman-Hill R, Pyke M, Beswick AD, *et al.* Preoperative widespread pain sensitization and chronic pain after hip and knee replacement: a cohort analysis. *Pain* 2015;**156**:47–54. http://dx.doi.org/10.1016/j.pain.0000000000000002

473. Sayers A, Wylde V, Lenguerrand E, Beswick AD, Gooberman-Hill R, Pyke M, *et al.* Rest pain and movement-evoked pain as unique constructs in hip and knee replacements. *Arthritis Care Res* 2016;**68**:237–45. http://dx.doi.org/10.1002/acr.22656

474. Bedson J, Croft P. The discordance between clinical and radiographic knee osteoarthritis: A systematic search and summary of the literature. *BMC Musculoskelet Disord* 2008;**9**:116. http://dx.doi.org/10.1186/1471-2474-9-116

475. Hannan MT, Felson DT, Pincus T. Analysis of the discordance between radiographic changes and knee pain in osteoarthritis of the knee. *J Rheumatol* 2000;**27**:1513–7.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

476. Valdes AM, Doherty SA, Zhang W, Muir KR, Maciewicz RA, Doherty M. Inverse relationship between preoperative radiographic severity and postoperative pain in patients with osteoarthritis who have undergone total joint arthroplasty. *Semin Arthritis Rheum* 2012;**41**:568–75. http://dx.doi.org/10.1016/j.semarthrit.2011.07.002

477. Dowsey MM, Nikpour M, Dieppe P, Choong PF. Associations between pre-operative radiographic changes and outcomes after total knee joint replacement for osteoarthritis. *Osteoarthritis Cart* 2012;**20**:1095–102. http://dx.doi.org/10.1016/j.joca.2012.05.015

478. Altman RD, Gold GE. Atlas of individual radiographic features in osteoarthritis, revised. *Osteoarthritis Cart* 2007;**15**(Suppl. A):A1–56.

479. Dieppe P, Judge A, Williams S, Ikwueke I, Guenther K-P, Floeren M, *et al.* Variations in the pre-operative status of patients coming to primary hip replacement for osteoarthritis in European orthopaedic centres. *BMC Musculoskelet Disord* 2009;**10**:19. http://dx.doi.org/10.1186/1471-2474-10-19

480. Australian Institute of Health and Welfare. *Australian Hospital Statistics 2012–13. Elective Surgery Waiting Times*. Canberra, ACT: Australian Institute of Health and Welfare; 2013.

481. Gooberman-Hill R, Sansom A, Sanders C, Dieppe P, Horwood J, Learmonth I, *et al.* Unstated factors in orthopaedic decision-making: a qualitative study. *BMC Musculoskelet Disord* 2010;**11**:213. http://dx.doi.org/10.1186/1471-2474-11-213

482. Srikandarajah S, Gilron I. Systematic review of movement-evoked pain versus pain at rest in postsurgical clinical trials and meta-analyses: a fundamental distinction requiring standardized measurement. *Pain* 2011;**152**:1734–9. http://dx.doi.org/10.1016/j.pain.2011.02.008

483. StataCorp. *Stata 13 Structural Equation Modeling Reference Manual*. College Station: TX: Stata Press; 2013.

484. Wylde V, Palmer S, Learmonth ID, Dieppe P. The association between pre-operative pain sensitisation and chronic pain after knee replacement: an exploratory study. *Osteoarthritis Cart* 2013;**21**:1253–6. http://dx.doi.org/10.1016/j.joca.2013.05.008

485. Suokas AK, Walsh DA, McWilliams DF, Condon L, Moreton B, Wylde V, *et al.* Quantitative sensory testing in painful osteoarthritis: a systematic review and meta-analysis. *Osteoarthritis Cart* 2012;**20**:1075–85. http://dx.doi.org/10.1016/j.joca.2012.06.009

486. Leckie G, Charlton C. runmlwin: a Program to Run the MLwiN Multilevel Modeling Software from within Stata. *J Stat Softw* 2013;**52**:1–40.

487. Berge DJ, Dolin SJ, Williams AC, Harman R. Pre-operative and postoperative effect of a pain management programme prior to total hip replacement: a randomized controlled trial. *Pain* 2004;**110**:33–9. http://dx.doi.org/10.1016/j.pain.2004.03.002

488. Bitterli R, Sieben JM, Hartmann M, de Bruin ED. Pre-operative, sensory–motor training for patients undergoing total hip replacement: a randomised controlled trial. *Phys Med Rehab Kuror* 2009;**19**:193–201. http://dx.doi.org/10.1055/s-0029-1220725

489. Butler GS, Hurley CA, Buchanan KL, Smith-VanHorne J. Prehospital education: effectiveness with total hip replacement surgery patients. *Patient Educ Couns* 1996;**29**:189–97. http://dx.doi.org/10.1016/0738-3991(96)00883-X

490. Clode-Baker EG, Draper E, Raymond N, Haslam C, Gregg P. Preparing patients for total hip replacement. A randomized controlled trial of a preoperative educational intervention. *J Health Psychol* 1997;**2**:107–14. http://dx.doi.org/10.1177/135910539700200111

491. Cooil J, Bithell C. Pre-operative education for patients undergoing total hip replacement: a comparison of two methods. *Physiother Theory Pract* 1997;**13**:163–73. http://dx.doi.org/10.3109/09593989709036459

492. Doering S, Katzlberger F, Rumpold G, Roessler S, Hofstoetter B, Schatz DS, *et al.* Videotape preparation of patients before hip replacement surgery reduces stress. *Psychosom Med* 2000;**62**:365–73. http://dx.doi.org/10.1097/00006842-200005000-00010

493. Ferrara PE, Rabini A, Aprile I, Maggi L, Piazzini DB, Logroscino G, *et al.* Effect of pre-operative physiotherapy in patients with end-stage osteoarthritis undergoing hip arthroplasty. *Clin Rehabil* 2008;**22**:977–86. http://dx.doi.org/10.1177/0269215508094714

494. Gilbey HJ, Ackland TR, Wang AW, Morton AR, Trouchet T, Tapper J. Exercise improves early functional recovery after total hip arthroplasty. *Clin Orthop Relat Res* 2003:193–200. http://dx.doi.org/10.1097/00003086-200303000-00025

495. Giraudet-Le Quintrec J-S, Coste J, Vastel L, Pacault V, Jeanne L, Lamas J-P, *et al.* Positive effect of patient education for hip surgery: a randomized trial. *Clin Orthop Relat Res* 2003:112–20. http://dx.doi.org/10.1097/01.blo.0000079268.91782.bc

496. Gocen Z, Sen A, Unver B, Karatosun V, Gunal I. The effect of preoperative physiotherapy and education on the outcome of total hip replacement: a prospective randomized controlled trial. *Clin Rehabil* 2004;**18**:353–8. http://dx.doi.org/10.1191/0269215504cr758oa

497. Hoogeboom TJ, Dronkers JJ, van den Ende CHM, Oosting E, van Meeteren NLU. Preoperative therapeutic exercise in frail elderly scheduled for total hip replacement: a randomized pilot trial. *Clin Rehabil* 2010;**24**:901–10. http://dx.doi.org/10.1177/0269215510371427

498. Johansson K, Salantera S, Katajisto J. Empowering orthopaedic patients through preadmission education: results from a clinical study. *Patient Educ Couns* 2007;**66**:84–91. http://dx.doi.org/10.1016/j.pec.2006.10.011

499. Lilja Y, Rydn S, Fridlund B. Effects of extended preoperative information on perioperative stress: an anaesthetic nurse intervention for patients with breast cancer and total hip replacement. *Intensive Crit Care Nurs* 1998;**14**:276–82. http://dx.doi.org/10.1016/S0964-3397(98)80688-5

500. Mancuso CA, Graziano S, Briskie LM, Peterson MGE, Pellicci PM, Salvati EA, *et al.* Randomized trials to modify patients' preoperative expectations of hip and knee arthroplasties. *Clin Orthop Relat Res* 2008;**466**:424–31. http://dx.doi.org/10.1007/s11999-007-0052-z

501. McGregor AH, Rylands H, Owen A, Dore CJ, Hughes SPF. Does preoperative hip rehabilitation advice improve recovery and patient satisfaction? *J Arthroplasty* 2004;**19**:464–8. http://dx.doi.org/10.1016/j.arth.2003.12.074

502. Oosting E, Jans MP, Dronkers JJ, Naber RH, Dronkers-Landman CM, Appelman-de Vries SM, *et al.* Preoperative home-based physical therapy versus usual care to improve functional health of frail older adults scheduled for elective total hip arthroplasty: a pilot randomized controlled trial. *Arch Phys Med Rehabil* 2012;**93**:610–6. http://dx.doi.org/10.1016/j.apmr.2011.11.006

503. Rooks DS, Huang J, Bierbaum BE, Bolus SA, Rubano J, Connolly CE, *et al.* Effect of preoperative exercise on measures of functional status in men and women undergoing total hip and knee arthroplasty. *Arthritis Rheum* 2006;**55**:700–8. http://dx.doi.org/10.1002/art.22223

504. Sandell C-L. A multidisciplinary assessment and intervention for patients awaiting total hip replacement to improve their quality of life. *J Orthop Nurs* 2008;**12**:26–34. http://dx.doi.org/10.1016/j.joon.2007.11.002

505. Santavirta N, Lillqvist G, Sarvimaki A, Honkanen V, Konttinen YT, Santavirta S. Teaching of patients undergoing total hip replacement surgery. *Int J Nurs Stud* 1994;**31**:135–42. http://dx.doi.org/10.1016/0020-7489(94)90040-X

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

506. Vukomanovic A, Popovic Z, Durovic A, Krstic L. The effects of short-term preoperative physical therapy and education on early functional recovery of patients younger than 70 undergoing total hip arthroplasty. *Vojnosanit Pregl* 2008;**65**:291–7. http://dx.doi.org/10.2298/VSP0804291V

507. Wijgman AJ, Dekkers GH, Waltje E, Krekels T, Arens HJ. No positive effect of preoperative exercise therapy and teaching in patients to be subjected to hip arthroplasty. *Ned Tijdschr Genees* 1994;**138**:949–52.

508. Wong J, Wong S. A randomized controlled trial of a new approach to preoperative teaching and patient compliance. *Int J Nurs Stud* 1985;**22**:105–15. http://dx.doi.org/10.1016/0020-7489(85)90021-5

509. Aoki O, Tsumura N, Kimura A, Okuyama S, Takikawa S, Hirata S. Home stretching exercise is effective for improving knee range of motion and gait in patients with knee osteoarthritis. *J Phys Ther Sci* 2009;**21**:113–19. http://dx.doi.org/10.1589/jpts.21.113

510. Beaupre LA, Lier D, Davies DM, Johnston DBC. The effect of a preoperative exercise and education program on functional recovery, health related quality of life, and health service utilization following primary total knee arthroplasty. *J Rheumatol* 2004;**31**:1166–73.

511. Börjesson M, Robertson E, Weidenhielm L, Mattsson E, Olsson E. Physiotherapy in knee osteoarthrosis: effect on pain and walking. *Physiother Res Int* 1996;**1**:89–97. http://dx.doi.org/10.1002/pri.6120010205

512. Brown K, Topp R, Brosky JA, Lajoie AS, Brown K, Topp R, *et al.* Prehabilitation and quality of life three months after total knee arthroplasty: a pilot study. *Perceptual & Motor Skills* 2012;**115**:765–74. http://dx.doi.org/10.2466/15.06.10.PMS.115.6.765-774

513. D'Lima DD, Colwell CW Jr., Morris BA, Hardwick ME, Kozin F. The effect of preoperative exercise on total knee replacement outcomes. *Clin Orthop Relat Res* 1996:174–82. http://dx.doi.org/10.1097/00003086-199605000-00020

514. Evgeniadis G, Beneka A, Malliou P, Mavromoustakos S, Godolias G. Effects of pre- or postoperative therapeutic exercise on the quality of life, before and after total knee arthroplasty for osteoarthritis. *J Back Musculoskelet* 2008;**21**:161–9.

515. Gstoettner M, Raschner C, Dirnberger E, Leimser H, Krismer M. Preoperative proprioceptive training in patients with total knee arthroplasty. *Knee* 2011;**18**:265–70. http://dx.doi.org/10.1016/j.knee.2010.05.012

516. Heikkinen K, Helena LK, Taina N, Anne K, Sanna S. A comparison of two educational interventions for the cognitive empowerment of ambulatory orthopaedic surgery patients. *Patient Educ Couns* 2008;**73**:272–9. http://dx.doi.org/10.1016/j.pec.2008.06.015

517. Huang SW, Chen PH, Chou YH. Effects of a preoperative simplified home rehabilitation education program on length of stay of total knee arthroplasty patients. *Orthop Traumatol Surg Res* 2012;**98**:259–64. http://dx.doi.org/10.1016/j.otsr.2011.12.004

518. McDonald DD, Molony SL. Postoperative pain communication skills for older adults. *West J Nurs Res* 2004;**26**:836–52; discussion 53–9. http://dx.doi.org/10.1177/0193945904269292

519. McKay C, Prapavessis H, Doherty T. The effect of a prehabilitation exercise program on quadriceps strength for patients undergoing total knee arthroplasty: a randomized controlled pilot study. *PM&R* 2012;**4**:647–56. http://dx.doi.org/10.1016/j.pmrj.2012.04.012

520. Mitchell C, Walker J, Walters S, Morgan AB, Binns T, Mathers N. Costs and effectiveness of pre- and postoperative home physiotherapy for total knee replacement: randomized controlled trial. *J Eval Clin Pract* 2005;**11**:283–92. http://dx.doi.org/10.1111/j.1365-2753.2005.00535.x

521. Nuñez M, Nuñez E, Segur JM, Macule F, Quinto L, Hernandez MV, *et al.* The effect of an educational program to improve health-related quality of life in patients with osteoarthritis on waiting list for total knee replacement: a randomized study. *Osteoarthritis Cart* 2006;**14**:279–85. http://dx.doi.org/10.1016/j.joca.2005.10.002

522. Sjoling M, Nordahl G, Olofsson N, Asplund K. The impact of preoperative information on state anxiety, postoperative pain and satisfaction with pain management. *Patient Educ Couns* 2003;**51**:169–76. http://dx.doi.org/10.1016/S0738-3991(02)00191-X

523. Swank AM, Kachelman JB, Bibeau W, Quesada PM, Nyland J, Malkani A, *et al.* Prehabilitation before total knee arthroplasty increases strength and function in older adults with severe osteoarthritis. *J Strength Cond Res* 2011;**25**:318–25. http://dx.doi.org/10.1519/JSC.0b013e318202e431

524. Weidenhielm L, Mattsson E, Brostrom LA, Wersall-Robertsson E. Effect of preoperative physiotherapy in unicompartmental prosthetic knee replacement. *Scand J Rehabil Med* 1993;**25**:33–9.

525. Williamson L, Wyatt MR, Yein K, Melton JT. Severe knee osteoarthritis: a randomized controlled trial of acupuncture, physiotherapy (supervised exercise) and standard management for patients awaiting knee replacement. *Rheumatology* 2007;**46**:1445–9. http://dx.doi.org/10.1093/rheumatology/kem119

526. Bondy LR, Sims N, Schroeder DR, Offord KP, Narr BJ. The effect of anesthetic patient education on preoperative patient anxiety. *Reg Anesth Pain Med* 1999;**24**:158–64. http://dx.doi.org/10.1016/s1098-7339(99)90078-0

527. Crotty M, Prendergast J, Baftersby MW, Rowett D, Graves SE, Leach G, *et al.* Self-management and peer support among people with arthritis on a hospital joint replacement waiting list: a randomised controlled trial. *Osteoarthritis Cart* 2009;**17**:1428–33. http://dx.doi.org/10.1016/j.joca.2009.05.010

528. Crowe J, Henderson J. Pre-arthroplasty rehabilitation is effective in reducing hospital stay. *Can J Occup Ther* 2003;**70**:88–96. http://dx.doi.org/10.1177/000841740307000204

529. Cuñádo Barrio A, Legarre Gil MJ, Ruiz Castón J, Silveira de la Torre JS, Caballero Martínez L, García López F. The effect of a structured, individualized 'nursing visit' on the anxiety of surgical patients. A randomized clinical study. *Enfermería Clínica* 1999;**9**:98–104.

530. Daltroy LH, Morlino CI, Eaton HM, Poss R, Liang MH. Preoperative education for total hip and knee replacement patients. *Arthritis Care Res* 1998;**11**:469–78. http://dx.doi.org/10.1002/art.1790110607

531. Lewis C, Gunta K, Wong D. Patient knowledge, behaviour, and satisfaction with the use of a preoperative DVD. *Orthop Nurs* 2002;**21**:41–3, 5–9.

532. Liu W, Lu M. Empowerment model of preoperative education for orthopaedic patients. *Chin J Clin Rehab* 2004;**8**:840–1.

533. McDonald DD, Freeland M, Thomas G, Moore J. Testing a preoperative pain management intervention for elders. *Res Nurs Health* 2001;**24**:402–9. http://dx.doi.org/10.1002/nur.1040

534. Pellino T, Tluczek A, Collins M, Trimborn S, Norwick H, Engelke ZK, *et al.* Increasing self-efficacy through empowerment: preoperative education for orthopaedic patients. *Orthop Nurs* 1998;**17**:48–51, 54–9. http://dx.doi.org/10.1097/00006416-199807000-00009

535. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

536. Wylde V, Marques E, Artz N, Blom A, Gooberman-Hill R. Effectiveness and cost-effectiveness of a group-based pain self-management intervention for patients undergoing total hip replacement: feasibility study for a randomized controlled trial. *Trials* 2014;**15**:176. http://dx.doi.org/10.1186/1745-6215-15-176

537. Buszewicz M, Rait G, Griffin M, Nazareth I, Patel A, Atkinson A, *et al.* Self management of arthritis in primary care: randomised controlled trial. *BMJ* 2006;**333**:879. http://dx.doi.org/10.1136/bmj.38965.375718.80

538. Ackerman IN, Buchbinder R, Osborne RH. Factors limiting participation in arthritis self-management programmes: an exploration of barriers and patient preferences within a randomized controlled trial. *Rheumatology* 2013;**52**:472–9. http://dx.doi.org/10.1093/rheumatology/kes295

539. Ackerman IN, Buchbinder R, Osborne RH. Challenges in evaluating an Arthritis Self-Management Program for people with hip and knee osteoarthritis in real-world clinical settings. *J Rheumatol* 2012;**39**:1047–55. http://dx.doi.org/10.3899/jrheum.111358

540. Newman S, Steed L, Mulligan K. Self-management interventions for chronic illness. *Lancet* 2004;**364**:1523–37. http://dx.doi.org/10.1016/S0140-6736(04)17277-2

541. Bruce B, Lorig K, Laurent D. Participation in patient self-management programs. *Arthritis Rheum* 2007;**57**:851–4. http://dx.doi.org/10.1002/art.22776

542. Lancaster GA, Dodd S, Williamson PR. Design and analysis of pilot studies: recommendations for good practice. *J Eval Clin Pract* 2004;**10**:307–12. http://dx.doi.org/10.1111/j..2002.384.doc.x

543. McMurran M, Cox WM, Whitham D, Hedges L. The addition of a goal-based motivational interview to treatment as usual to enhance engagement and reduce dropouts in a personality disorder treatment service: results of a feasibility study for a randomized controlled trial. *Trials* 2013;**14**:50. http://dx.doi.org/10.1186/1745-6215-14-50

544. Farrin A, Russell I, Torgerson D, Underwood M. Differential recruitment in a cluster randomized trial in primary care: the experience of the UK back pain, exercise, active management and manipulation (UK BEAM) feasibility study. *Clin Trials* 2005;**2**:119–24. http://dx.doi.org/10.1191/1740774505cn073oa

545. Eldridge SM, Ashby D, Feder GS, Rudnicka AR, Ukoumunne OC. Lessons for cluster randomized trials in the twenty-first century: a systematic review of trials in primary care. *Clin Trials* 2004;**1**:80–90. http://dx.doi.org/10.1191/1740774504cn006rr

546. Lancaster GA, Campbell MJ, Eldridge S, Farrin A, Marchant M, Muller S, *et al.* Trials in primary care: statistical issues in the design, conduct and evaluation of complex interventions. *Stat Methods Med Res* 2010;**19**:349–77. http://dx.doi.org/10.1177/0962280209359883

547. Cramer H, Salisbury C, Conrad J, Eldred J, Araya R. Group cognitive behavioural therapy for women with depression: pilot and feasibility study for a randomised controlled trial using mixed methods. *BMC Psychiatry* 2011;**11**:82. http://dx.doi.org/10.1186/1471-244X-11-82

548. McCracken LM, Sato A, Wainwright D, House W, Taylor GJ. A feasibility study of brief group-based acceptance and commitment therapy for chronic pain in general practice: recruitment, attendance, and patient views. *Prim Health Care Res Dev* 2013;**15**:312–23. http://dx.doi.org/10.1017/S1463423613000273

549. Poston L, Briley AL, Barr S, Bell R, Croker H, Coxon K, *et al.* Developing a complex intervention for diet and activity behaviour change in obese pregnant women (the UPBEAT trial); assessment of behavioural change and process evaluation in a pilot randomised controlled trial. *BMC Pregnancy Childbirth* 2013;**13**:148. http://dx.doi.org/10.1186/1471-2393-13-148

550. Gooberman-Hill R, Burston A. *Improving Musculoskeletal Research in North Bristol Through Public Participation*. 6th June 2013.

551. Evans S, Royston P, Day S. *Minim: Allocation by Minimisation in Clinical Trials*. 2004. URL: www-users.york.ac.uk/~mb55/guide/minim.htm (accessed 21 July 2016).

552. Gondwe R, Andrea-Jones S, Cowlard J, Taylor M, Yaylor A, Undy B. Evaluate the effectiveness of a new self-management programme for patients with chronic pain. *Ann Rheum Dis* 2008;**67**(Suppl. II):678.

553. Billingham SA, Whitehead AL, Julious SA. An audit of sample sizes for pilot and feasibility trials being undertaken in the United Kingdom registered in the United Kingdom Clinical Research Network database. *BMC Med Res Methodol* 2013;**13**:104. http://dx.doi.org/10.1186/1471-2288-13-104

554. Shanyinde M, Pickering RM, Weatherall M. Questions asked and answered in pilot and feasibility randomized controlled trials. *BMC Med Res Methodol* 2011;**11**:117. http://dx.doi.org/10.1186/1471-2288-11-117

555. Ross S, Grant A, Counsell C, Gillespie W, Russell I, Prescott R. Barriers to participation in randomised controlled trials: a systematic review. *J Clin Epidemiol* 1999;**52**:1143–56. http://dx.doi.org/10.1016/S0895-4356(99)00141-9

556. Lansdown H, Howard K, Brealey S, MacPherson H. Acupuncture for pain and osteoarthritis of the knee: a pilot study for an open parallel-arm randomised controlled trial. *BMC Musculoskelet Disord* 2009;**10**:130. http://dx.doi.org/10.1186/1471-2474-10-130

557. Stafford L, Foley E, Judd F, Gibson P, Kiropoulos L, Couper J. Mindfulness-based cognitive group therapy for women with breast and gynecologic cancer: a pilot study to determine effectiveness and feasibility. *Support Care Cancer* 2013;**21**:3009–19. http://dx.doi.org/10.1007/s00520-013-1880-x

558. Treweek S, Lockhart P, Pitkethly M, Cook JA, Kjeldstrom M, Johansen M, *et al.* Methods to improve recruitment to randomised controlled trials: Cochrane systematic review and meta-analysis. *BMJ Open* 2013;**3**:e002360. http://dx.doi.org/10.1136/bmjopen-2012-002360

559. Klitzman R. How IRBs view and make decisions about coercion and undue influence. *J Med Ethics* 2013;**39**:224–9. http://dx.doi.org/10.1136/medethics-2011-100439

560. Chambers SK, Foley E, Galt E, Ferguson M, Clutton S. Mindfulness groups for men with advanced prostate cancer: a pilot study to assess feasibility and effectiveness and the role of peer support. *Support Care Cancer* 2012;**20**:1183–92. http://dx.doi.org/10.1007/s00520-011-1195-8

561. Wang OJ, Krumholz HM. Clinical trial participation: are we studying the patients we are trying to treat? *Eur J Heart Fail* 2009;**11**:1021–2. http://dx.doi.org/10.1093/eurjhf/hfp137

562. Jepson P, Sands G, Beswick AD, Davis ET, Blom AW, Sackley CM. A feasibility randomised controlled trial of pre-operative occupational therapy to optimise recovery for patients undergoing primary total hip replacement for osteoarthritis (PROOF-THR). *Clin Rehabil* 2015;**30**:156–66. http://dx.doi.org/10.1177/0269215515576811

563. National Audit Office. *Hip Replacements: An Update*. London: National Audit Office; 2003.

564. NHS Choices. *Hip Replacement – Recovery*. 2014. URL: www.nhs.uk/Conditions/Hip-replacement/Pages/Recovery.aspx (accessed 7 April 2014).

565. Westby MD, Kennedy D, Jones D, Jones A, Doyle-Waters MM, Backman C. Post-acute physiotherapy for primary total knee arthroplasty. *Cochrane Database Syst Rev* 2008;**2**:CD007099. http://dx.doi.org/10.1002/14651858.cd007099

566. Orpen N, Harris J. Patients' perceptions of preoperative home-based occupational therapy and/or physiotherapy interventions prior to total hip replacement. *Brit J Occup Ther* 2010;**73**:461–9. http://dx.doi.org/10.4276/030802210X12865330218267

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

567. Munin MC, Rudy TE, Glynn NW, Crossett LS, Rubash HE. Early inpatient rehabilitation after elective hip and knee arthroplasty. *JAMA* 1998;**279**:847–52. http://dx.doi.org/10.1001/jama.279.11.847

568. Siggeirsdottir K, Olafsson O, Jonsson H, Iwarsson S, Gudnason V, Jonsson BY. Short hospital stay augmented with education and home-based rehabilitation improves function and quality of life after hip replacement: randomized study of 50 patients with 6 months of follow-up. *Acta Orthop* 2005;**76**:555–62. http://dx.doi.org/10.1080/17453670510041565

569. Weaver FM, Hughes SL, Almagor O, Wixson R, Manheim L, Fulton B, *et al.* Comparison of two home care protocols for total joint replacement. *J Am Geriatr Soc* 2003;**51**:523–8. http://dx.doi.org/10.1046/j.1532-5415.2003.51162.x

570. Jolles BM, Bogoch ER. Posterior versus lateral surgical approach for total hip arthroplasty in adults with osteoarthritis. *Cochrane Database Syst Rev* 2006;**3**:CD003828. http://dx.doi.org/10.1002/14651858.cd003828.pub3

571. Mahoney CR, Pellicci PM. Complications in primary total hip arthroplasty: avoidance and management of dislocations. *Instr Course Lect* 2003;**52**:247–55.

572. Lucas B. Total hip and total knee replacement: postoperative nursing management. *Br J Nurs* 2008;**17**:1410–14. http://dx.doi.org/10.12968/bjon.2008.17.22.31866

573. Peak EL, Parvizi J, Ciminiello M, Purtill JJ, Sharkey PF, Hozack WJ, *et al.* The role of patient restrictions in reducing the prevalence of early dislocation following total hip arthroplasty. A randomized, prospective study. *J Bone Joint Surg Am* 2005;**87**:247–53. http://dx.doi.org/10.2106/JBJS.C.01513

574. Restrepo C, Mortazavi SM, Brothers J, Parvizi J, Rothman RH. Hip dislocation: are hip precautions necessary in anterior approaches? *Clin Orthop Relat Res* 2011;**469**:417–22. http://dx.doi.org/10.1007/s11999-010-1668-y

575. Clemson L, Roland M, Cumming R. Occupational therapy assessment of potential hazards in the homes of elderly people: an inter-rater reliability study. *Aust Occup Therap J* 1992;**39**:23–6. http://dx.doi.org/10.1111/j.1440-1630.1992.tb01753.x

576. Murray DW, Fitzpatrick R, Rogers K, Pandit H, Beard DJ, Carr AJ, *et al.* The use of the Oxford hip and knee scores. *J Bone Joint Surg Br* 2007;**89**:1010–14. http://dx.doi.org/10.1302/0301-620X.89B8.19424

577. Beecham JK, Knapp MRJ. Costing Psychiatric Interventions. In Thornicroft G, Brewin C, Wing JK, editors. *Measuring Mental Health Needs*. London: Gaskell; 1992. pp. 163–83.

578. Beecham J. Collecting and Estimating Costs. In Knapp M, editor. *The Economics of Mental Health Care.* Aldershot: Arena; 1995. pp. 157–74.

579. Jan MH, Hung JY, Lin JC, Wang SF, Liu TK, Tang PF. Effects of a home program on strength, walking speed, and function after total hip replacement. *Arch Phys Med Rehabil* 2004;**85**:1943–51. http://dx.doi.org/10.1016/j.apmr.2004.02.011

580. Larsen K, Sørensen OG, Hansen TB, Thomsen PB, Søballe K. Accelerated perioperative care and rehabilitation intervention for hip and knee replacement is effective: a randomized clinical trial involving 87 patients with 3 months of follow-up. *Acta Orthop* 2008;**79**:149–59. http://dx.doi.org/10.1080/17453670710014923

581. Davis LL, Broome ME, Cox RP. Maximizing retention in community-based clinical trials. *J Nurs Scholarsh* 2002;**34**:47–53. http://dx.doi.org/10.1111/j.1547-5069.2002.00047.x

582. Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomised controlled trials. *BMJ* 1999;**319**:670–4. http://dx.doi.org/10.1136/bmj.319.7211.670

583. Wood AM, White IR, Thompson SG. Are missing outcome data adequately handled? A review of published randomized controlled trials in major medical journals. *Clin Trials* 2004;**1**:368–76. http://dx.doi.org/10.1191/1740774504cn032oa

584. Edwards P, Roberts I, Clarke M, DiGuiseppi C, Pratap S, Wentz R, *et al.* Increasing response rates to postal questionnaires: systematic review. *BMJ* 2002;**324**:1183. http://dx.doi.org/10.1136/bmj.324.7347.1183

585. Artz N, Elvers KT, Lowe CM, Sackley C, Jepson P, Beswick AD. Effectiveness of physiotherapy exercise following total knee replacement: systematic review and meta-analysis. *BMC Musculoskelet Disord* 2015;**16**:15. http://dx.doi.org/10.1186/s12891-015-0469-6

586. Artz N, Dixon S, Wylde V, Marques E, Beswick AD, Lenguerrand E, *et al.* Comparison of group-based outpatient physiotherapy with usual care after total knee replacement: a feasibility study for a randomized controlled trial. *Clin Rehabil* 2016;**10**:epub ahead of print 11 April. http://dx.doi.org/10.1177/0269215516642503

587. British Orthopaedic Association, British Association for Surgery of the Knee. *Knee Replacement: A Guide to Good Practice*. London; British Orthopaedic Association; 1999.

588. Frost H, Lamb SE, Robertson S. A randomized controlled trial of exercise to improve mobility and function after elective knee arthroplasty. Feasibility, results and methodological difficulties. *Clin Rehabil* 2002;**16**:200–9. http://dx.doi.org/10.1191/0269215502cr483oa

589. Fung V, Ho A, Shaffer J, Chung E, Gomez M. Use of Nintendo Wii Fit in the rehabilitation of outpatients following total knee replacement: a preliminary randomised controlled trial. *Physiotherapy* 2012;**98**:183–8. http://dx.doi.org/10.1016/j.physio.2012.04.001

590. Harmer AR, Naylor JM, Crosbie J, Russell T. Land-based versus water-based rehabilitation following total knee replacement: a randomized, single-blind trial. *Arthritis Rheum* 2009;**61**:184–91. http://dx.doi.org/10.1002/art.24420

591. Kauppila AM, Kyllonen E, Ohtonen P, Hamalainen M, Mikkonen P, Laine V, *et al.* Multidisciplinary rehabilitation after primary total knee arthroplasty: a randomized controlled study of its effects on functional capacity and quality of life. *Clin Rehabil* 2010;**24**:398–411. http://dx.doi.org/10.1177/0269215509346089

592. Kramer JF, Speechley M, Bourne R, Rorabeck C, Vaz M. Comparison of clinic- and home-based rehabilitation programs after total knee arthroplasty. *Clin Orthop Relat Res* 2003;**410**:225–34 http://dx.doi.org/10.1097/01.blo.0000063600.67412.11

593. Liebs TR, Herzberg W, Ruther W, Haasters J, Russlies M, Hassenpflug J. Ergometer cycling after hip or knee replacement surgery: a randomized controlled trial. *J Bone Joint Surg Am* 2010;**92**:814–22. http://dx.doi.org/10.2106/JBJS.H.01359

594. Madsen M, Larsen K, Madsen IK, Soe H, Hansen TB. Late group-based rehabilitation has no advantages compared with supervised home-exercises after total knee arthroplasty. *Dan Med J* 2013;**60**:A4607.

595. Minns Lowe CJ, Barker KL, Holder R, Sackley CM. Comparison of postdischarge physiotherapy versus usual care following primary total knee arthroplasty for osteoarthritis: an exploratory pilot randomized clinical trial. *Clin Rehabil* 2012;**26**:629–41. http://dx.doi.org/10.1177/0269215511427749

596. Mockford BJ, Thompson NW, Humphreys P, Beverland DE. Does a standard outpatient physiotherapy regime improve the range of knee motion after primary total knee arthroplasty? *J Arthroplasty* 2008;**23**:1110–14. http://dx.doi.org/10.1016/j.arth.2007.08.023

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

597. Moffet H, Collet J-P, Shapiro SH, Paradis G, Marquis F, Roy L. Effectiveness of intensive rehabilitation on functional ability and quality of life after first total knee arthroplasty: a single-blind randomized controlled trial. *Arch Phys Med Rehabil* 2004;**85**:546–56. http://dx.doi.org/10.1016/j.apmr.2003.08.080

598. Monticone M, Ferrante S, Rocca B, Salvaderi S, Fiorentini R, Restelli M, *et al.* Home-based functional exercises aimed at managing kinesiophobia contribute to improving disability and quality of life of patients undergoing total knee arthroplasty: a randomized controlled trial. *Arch Phys Med Rehabil* 2013;**94**:231–9. http://dx.doi.org/10.1016/j.apmr.2012.10.003

599. Piqueras M, Marco E, Coll M, Escalada F, Ballester A, Cinca C, *et al.* Effectiveness of an interactive virtual telerehabilitation system in patients after total knee arthoplasty: a randomized controlled trial. *J Rehabil Med* 2013;**45**:392–6. http://dx.doi.org/10.2340/16501977-1119

600. Piva SR, Gil AB, Almeida GJM, DiGioia AM, III, Levison TJ, Fitzgerald GK. A balance exercise program appears to improve function for patients with total knee arthroplasty: a randomized clinical trial. *Phys Ther* 2010;**90**:880–94. http://dx.doi.org/10.2522/ptj.20090150

601. Rajan RA, Pack Y, Jackson H, Gillies C, Asirvatham R. No need for outpatient physiotherapy following total knee arthroplasty: a randomized trial of 120 patients. *Acta Orthop Scand* 2004;**75**:71–3. http://dx.doi.org/10.1080/00016470410001708140

602. Tousignant M, Moffet H, Boissy P, Corriveau H, Cabana F, Marquis F. A randomized controlled trial of home telerehabilitation for post-knee arthroplasty. *J Telemed Telecare* 2011;**17**:195–8. http://dx.doi.org/10.1258/jtt.2010.100602

603. Barron CJ, Klaber Moffett JA, Potter M. Patient expectations of physiotherapy: Definitions, concepts, and theories. *Physiother Theory Pract* 2007;**23**:37–46. http://dx.doi.org/10.1080/09593980601147843

604. Westby MD, Brittain A, Backman CL. Expert consensus on best practices for post-acute rehabilitation after total hip and knee arthroplasty: a Canada and United States Delphi study. *Arthritis Care Res* 2014;**66**:411–23. http://dx.doi.org/10.1002/acr.22164

605. Muniesa JM, Marco E, Tejero M, Boza R, Duarte E, Escalada F, *et al.* Analysis of the expectations of elderly patients before undergoing total knee replacement. *Arch Gerontol Geriatr* 2010;**51**:e83–7. http://dx.doi.org/10.1016/j.archger.2010.01.003

606. Mancuso CA, Sculco TP, Wickiewicz TL, Jones EC, Robbins L, Warren RF, *et al.* Patients' expectations of knee surgery. *J Bone Joint Surg Am* 2001;**83**:1005–12.

607. Tew M, Forster IW, Wallace WA. Effect of total knee arthroplasty on maximal flexion. *Clin Orthop Relat Res* 1989:168–74. http://dx.doi.org/10.1097/00003086-198910000-00027

608. Park KK, Chang CB, Kang YG, Seong SC, Kim TK. Correlation of maximum flexion with clinical outcome after total knee replacement in Asian patients. *J Bone Joint Surg Br* 2007;**89**:604–8. http://dx.doi.org/10.1302/0301-620X.89B5.18117

609. Parent E, Moffet H. Comparative responsiveness of locomotor tests and questionnaires used to follow early recovery after total knee arthroplasty. *Arch Phys Med Rehabil* 2002;**83**:70–80. http://dx.doi.org/10.1053/apmr.2002.27337

610. Lindemann U, Becker C, Unnewehr I, Muche R, Aminin K, Dejnabadi H, *et al.* Gait analysis and WOMAC are complementary in assessing functional outcome in total hip replacement. *Clin Rehabil* 2006;**20**:413–20. http://dx.doi.org/10.1191/0269215506cr958oa

611. Alviar MJ, Olver J, Brand C, Hale T, Khan F. Do patient-reported outcome measures used in assessing outcomes in rehabilitation after hip and knee arthroplasty capture issues relevant to patients? Results of a systematic review and ICF linking process. *J Rehabil Med* 2011;**43**:374–81. http://dx.doi.org/10.2340/16501977-0801

612. McLean SM, Burton M, Bradley L, Littlewood C. Interventions for enhancing adherence with physiotherapy: A systematic review. *Manual Ther* 2010;**15**:514–21. http://dx.doi.org/10.1016/j.math.2010.05.012

613. Beswick A, Rees K, Griebsch I, Taylor F, Burke M, West R, *et al.* Provision, uptake and cost of cardiac rehabilitation programmes: improving services to under-represented groups. *Health Technol Assess* 2004;**8**(41). http://dx.doi.org/10.3310/hta8410

614. National Joint Registry for England and Wales. *National Joint Registry for England and Wales: 7th Annual Report*. Hemel Hempstead: National Joint Registry Centre; 2010.

615. Judge A, Chard J, Learmonth I, Dieppe P. The effects of surgical volumes and training centre status on outcomes following total joint replacement: analysis of the Hospital Episode Statistics for England. *J Public Health* 2006;**28**:116–24. http://dx.doi.org/10.1093/pubmed/fdl003

616. Hunt GR, Crealey G, Murthy BVS, Hall GM, Constantine P, O'Brien S, *et al.* The consequences of early discharge after hip arthroplasty for patient outcomes and health care costs: comparison of three centres with differing durations of stay. *Clin Rehabil* 2009;**23**:1067–77. http://dx.doi.org/10.1177/0269215509339000

617. Salmon P, Hall GM, Peerbhoy D, Shenkin A, Parker C. Recovery from hip and knee arthroplasty: Patients' perspective on pain, function, quality of life, and well-being up to 6 months postoperatively. *Arch Phys Med Rehabil* 2001;**82**:360–6. http://dx.doi.org/10.1053/apmr.2001.21522

618. de Beer J, Petruccelli D, Adili A, Piccirillo L, Wismer D, Winemaker M. Patient perspective survey of total hip vs total knee arthroplasty surgery. *J Arthroplasty* 2012;**27**:865–9.e5. http://dx.doi.org/10.1016/j.arth.2011.12.031

619. Lingard EA, Berven S, Katz JN, Kinemax Outcomes G. Management and care of patients undergoing total knee arthroplasty: variations across different health care settings. *Arthritis Care Res* 2000;**13**:129–36. http://dx.doi.org/10.1002/1529-0131(200006)13:3%3C129::AID-ANR1%3E3.0.CO;2-6

620. Naylor J, Harmer A, Fransen M, Crosbie J, Innes L. Status of physiotherapy rehabilitation after total knee replacement in Australia. *Physiother Res Int* 2006;**11**:35–47. http://dx.doi.org/10.1002/pri.40

621. Hurley MV, Walsh N, Bhavnani V, Britten N, Stevenson F. Health beliefs before and after participation on an exercised-based rehabilitation programme for chronic knee pain: doing is believing. *BMC Musculoskelet Disord* 2010;**11**:31. http://dx.doi.org/10.1186/1471-2474-11-31

622. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, *et al.* OARSI recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009. *Osteoarthritis Cart* 2010;**18**:476–99. http://dx.doi.org/10.1016/j.joca.2010.01.013

623. Weiss JM, Noble PC, Conditt MA, Kohl HW, Roberts S, Cook KF, *et al.* What functional activities are important to patients with knee replacements? *Clin Orthop Relat Res* 2002:172–88. http://dx.doi.org/10.1097/00003086-200211000-00030

624. Noble PC, Gordon MJ, Weiss JM, Reddix RN, Conditt MA, Mathis KB. Does total knee replacement restore normal knee function? *Clin Orthop Relat Res* 2005:157–65. http://dx.doi.org/10.1097/01.blo.0000150130.03519.fb

625. Hurley MV, Walsh NE, Mitchell HL, Pimm TJ, Williamson E, Jones RH, *et al.* Economic evaluation of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain. *Arthritis Rheum* 2007;**57**:1220–9. http://dx.doi.org/10.1002/art.23011

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

626. Westby M, Backman C. Patient and health professional views on rehabilitation practices and outcomes following total hip and knee arthroplasty for osteoarthritis: a focus group study. *BMC Health Serv Res* 2010;**10**:119. http://dx.doi.org/10.1186/1472-6963-10-119

627. Orbell S, Johnston M, Rowley D, Davey P, Espley A. Self-efficacy and goal importance in the prediction of physical disability in people following hospitalization: a prospective study. *Br J Health Psychol* 2001;**6**:25–40. http://dx.doi.org/10.1348/135910701169034

628. Naylor JM, Mittal R, Carroll K, Harris IA. Introductory insights into patient preferences for outpatient rehabilitation after knee replacement: implications for practice and future research. *J Eval Clin Pract* 2012;**18**:586–92. http://dx.doi.org/10.1111/j.1365-2753.2010.01619.x

629. Rogers KD, Blyth FM, March LM, Jorm L. A nested case–control analysis of self-reported physical functioning after total knee replacement surgery in the 45 and Up Study Cohort. *BMJ Open* 2013;**3**:e002291. http://dx.doi.org/10.1136/bmjopen-2012-002291

630. Wright JG, Santaguida PL, Young N, Hawker GA, Schemitsch E, Owen JL. Patient preferences before and after total knee arthroplasty. *J Clin Epidemiol* 2010;**63**:774–82. http://dx.doi.org/10.1016/j.jclinepi.2009.08.022

631. Young NL, Cheah D, Waddell JP, Wright JG. Patient characteristics that affect the outcome of total hip arthroplasty: a review. *Can J Surg* 1998;**41**:188–95.

632. Minns Lowe CJ, Davies L, Sackley CM, Barker KL. Effectiveness of land-based physiotherapy exercise following hospital discharge following hip arthroplasty for osteoarthritis: an updated systematic review. *Physiotherapy* 2015;**101**:252–65. http://dx.doi.org/10.1016/j.physio.2014.12.003

633. Wylde V, Artz N, Marques E, Lenguerrand E, Dixon S, Beswick AD, *et al.* Effectiveness and cost-effectiveness of outpatient physiotherapy after knee replacement for osteoarthritis: study protocol for a randomised controlled trial. *Trials* 2016;**17**:289. http://dx.doi.org/10.1186/s13063-016-1418-x

634. Beswick AD, Rees K, Dieppe P, Ayis S, Gooberman-Hill R, Horwood J, *et al.* Complex interventions to improve physical function and maintain independent living in elderly people: a systematic review and meta-analysis. *Lancet* 2008;**371**:725–35. http://dx.doi.org/10.1016/S0140-6736(08)60342-6

635. Jepson P, Beswick A, Smith TO, Sands G, Drummond A, Davis ET, *et al.* Assistive devices, hip precautions, environmental modifications and training to prevent dislocation and improve function after hip arthroplasty. *Cochrane Database Syst Rev* 2013:**11**:CD010815. http://dx.doi.org/10.1002/14651858.cd010815

636. Gooberman-Hill R, Burston A, Clark E, Johnson E, Nolan S, Wells V, *et al.* Involving patients in research: considering good practice. *Musculoskeletal Care* 2013;**11**:187–90.

637. Marques E, Noble S, Blom AW, Hollingworth W. Disclosing total waiting times for joint replacement: evidence from the English NHS using linked HES data. *Health Econ* 2014;**23**:806–20. http://dx.doi.org/10.1002/hec.2954

638. Wylde V, Jeffery A, Dieppe P, Gooberman-Hill R. The assessment of persistent pain after joint replacement. *Osteoarthritis Cart* 2012;**20**:102–5. http://dx.doi.org/10.1016/j.joca.2011.11.011

639. Brunton LR, Wylde V, Dieppe PA. Assessing the health status of people with arthritis: example of osteoarthritis of the knee. *Rheumatology* 2012;**51**:1143–4. http://dx.doi.org/10.1093/rheumatology/ker301

Appendix 1 PRISMA checklist

Relating to *Chapters 6, 8, 10* and *11*

Section/topic	Number	Checklist item	Reported in section
Title			
Title	1	Identify the report as a systematic review, meta-analysis, or both	Yes
Abstract			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number	Abstracts reflect overall report including systematic reviews
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known	All yes
Objectives	4	Provide an explicit statement of questions being addressed with reference to PICOS	All yes
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g. web address), and, if available, provide registration information including registration number	Reviews commenced before registration became widely adopted excepting Review 11a which is registered as a Cochrane review
Eligibility criteria	6	Specify study characteristics (e.g. PICOS, length of follow-up) and report characteristics (e.g. years considered, language, publication status) used as criteria for eligibility, giving rationale	All yes
Information sources	7	Describe all information sources (e.g. databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched	All yes
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated	*Appendix 3*
Study selection	9	State the process for selecting studies (i.e. screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis)	All yes
Data collection process	10	Describe method of data extraction from reports (e.g. piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators	All yes
Data items	11	List and define all variables for which data were sought (e.g. PICOS, funding sources) and any assumptions and simplifications made	All yes
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis	All yes

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Section/topic	Number	Checklist item	Reported in section
Summary measures	13	State the principal summary measures (e.g. risk ratio, difference in means)	All yes
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g. I^2) for each meta-analysis	All yes
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g. publication bias, selective reporting within studies)	All yes
Additional analyses	16	Describe methods of additional analyses (e.g. sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified	All yes
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram	All yes
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g. study size, PICOS, follow-up period) and provide the citations	All yes
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12)	All yes
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and CIs, ideally with a forest plot	Where appropriate
Synthesis of results	21	Present results of each meta-analysis done, including CIs and measures of consistency	All yes
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15)	All yes
Additional analysis	23	Give results of additional analyses, if done [e.g. sensitivity or subgroup analyses, meta-regression (see Item 16)]	Where appropriate
Discussion			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g. health-care providers, users, and policy-makers)	All yes
Limitations	25	Discuss limitations at study and outcome level (e.g. risk of bias), and at review-level (e.g. incomplete retrieval of identified research, reporting bias)	All yes
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research	All yes
Funding			
Funding	27	Describe sources of funding for the systematic review and other support (e.g. supply of data); role of funders for the systematic review	As for the whole report

Appendix 2 MOOSE checklist

Relating to *Chapter 2*

Recommendation	Reported
Reporting of background should include	
Problem definition	All yes
Hypothesis statement	Aim described for all
Description of study outcome(s)	All yes
Type of exposure or intervention used	All yes
Type of study designs used	All yes
Study population	All yes
Reporting of search strategy should include	
Qualifications of searchers (e.g. librarians and investigators)	In the context of the overall programme
Search strategy, including time period included in the synthesis and keywords	*Appendix 3*
Effort to include all available studies, including contact with authors	Where appropriate. We did not request new analyses of longitudinal studies
Databases and registries searched	All yes
Search software used, name and version, including special features used (e.g. explosion)	All yes
Use of hand searching (e.g. reference lists of obtained articles)	All yes
List of citations located and those excluded, including justification	Reasons for exclusion summarised in Review flow diagrams. Details of individual reasons for study exclusion available from report authors
Method of addressing articles published in languages other than English	Described in each review methods section
Method of handling abstracts and unpublished studies	Generally excluded
Description of any contact with authors	Authors of studies with appropriate data but with specific missing information were contacted by e-mail
Reporting of methods should include	
Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	All yes
Rationale for the selection and coding of data (e.g. sound clinical principles or convenience)	Where appropriate
Documentation of how data were classified and coded (e.g. multiple raters, blinding, and interrater reliability)	Where appropriate
Assessment of confounding (e.g. comparability of cases and controls in studies where appropriate)	Not relevant
Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	Cohort generalisability

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Recommendation	Reported
Assessment of heterogeneity	In relation to methods of assessment
Description of statistical methods (eg, complete description of fixed or random-effects models, justification of whether the chosen models account for predictors of study results, dose–response models, or cumulative meta-analysis) in sufficient detail to be replicated	Where applicable described in methods sections
Provision of appropriate tables and graphics	All yes
Reporting of results should include	
Graphic summarising individual study estimates and overall estimate	Where applicable included in results sections
Table giving descriptive information for each study included	All yes
Results of sensitivity testing (eg, subgroup analysis)	In narrative reviews considering different measures
Indication of statistical uncertainty of findings	All yes
Reporting of discussion should include	
Quantitative assessment of bias (e.g. publication bias)	Risk of bias limited by strict inclusion criteria
Justification for exclusion (e.g. exclusion of non–English-language citations)	As feasible in individual reviews
Assessment of quality of included studies	If appropriate, good-quality studies identified according to inclusion criteria
Reporting of conclusions should include	
Consideration of alternative explanations for observed results	All yes
Generalisation of the conclusions (i.e. appropriate for the data presented and within the domain of the literature review)	All yes
Guidelines for future research	All yes
Disclosure of funding source	As for overall programme

Appendix 3 Systematic review search strategies as applied in MEDLINE via Ovid SP

Total hip or total knee replacement terms

1. Arthroplasty, Replacement, Knee/ or Arthroplasty, Replacement, Hip/
2. exp Arthroplasty, Replacement, Hip/ or exp Hip Prosthesis/ or hip replacement.mp.
3. exp Arthroplasty, Replacement, Knee/ or exp Knee Prosthesis/ or knee replacement.mp.
4. hip prosthesis.mp. or exp Hip Prosthesis/
5. knee prosthesis.mp. or exp Knee Prosthesis/
6. total hip.tw.
7. total knee.tw.
8. hip implant.mp.
9. knee implant.mp.
10. (knee$ adj5 (arthroplast$ or replacement$ or implant$ or prothes$)).mp.
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10

Osteoarthritis

1. osteoarthriti$.mp. or Osteoarthritis, Hip/ or Osteoarthritis/ or Osteoarthritis, Knee/

Epidemiological study design

1. survey.mp. or exp Data Collection/
2. randomized controlled trial.mp. or exp Randomized Controlled Trials/
3. prospective study.mp. or exp Prospective Studies/
4. observational study.mp.
5. Comparative Study/
6. exp EPIDEMIOLOGY/ or epidemiology.mp.
7. longitudinal study.mp. or exp Longitudinal Studies/
8. case control study.mp. or exp Case-Control Studies/
9. evaluation study.mp. or exp Evaluation Studies/
10. follow up study.mp. or exp Follow-Up Studies/
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or10

Key patient-reported pain outcome measures

1. WOMAC.mp.
2. western ontario.mp.
3. american knee.mp.
4. aks.mp.
5. arthritis impact.mp.
6. oxford hip.mp.
7. oxford knee.mp.
8. hoos.mp.
9. koos.mp.
10. lequesne.mp.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

11. self appraisal.mp.
12. vas.mp.
13. visual analogue.mp.
14. osteoarthritis outcome score.mp.
15. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14

Chronic pain

1. exp Pain/ or exp Complex Regional Pain Syndromes/ or exp Pain Clinics/ or exp Pain, Postoperative/ or exp Pain, Intractable/ or exp Pain Measurement/ or exp Patellofemoral Pain Syndrome/ or exp Pain, Referred/ or pain.mp. or exp Pain Threshold/ or exp Pain Perception/
2. (pain adj5 (chronic or persistent or long-term)).mp.
3. analgesi$.mp.
4. ache$.mp.
5. discomfort$.mp.
6. outcome$.mp.
7. neuropath$.mp.
8. 1 or 2 or 3 or 4 or 5 or 6 or 7

Patient-reported outcome measures (hip, knee, osteoarthritis, generic)

1. Arthritis Impact Measurement Scale.tw.
2. "Quality of Life"/ or Sickness Impact Profile/ or Assessment of Quality of Life.mp.
3. Osteoarthritis Treatment Satisfaction Questionnaire.tw.
4. Euroqol.tw.
5. eq5d.mp.
6. eq-5d.mp.
7. (Hip and knee questionnaire).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]
8. Health Status Questionnaire.mp.
9. (Knee Injury and Osteoarthritis Outcome Score).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]
10. McMaster Toronto Arthritis Patient Preference Disability Questionnaire.mp.
11. McGill Pain.mp.
12. Patient-based Measure of the Severity of Osteoarthritis of the Knee.mp.
13. Nottingham health profile.mp.
14. Oxford knee score.mp.
15. Osteoarthritis Pain Assessment.mp.
16. Rand 36-Item.mp.
17. sf12.tw.
18. sf-12.tw.
19. MOS short.tw.
20. sf36.tw.
21. sf-36.tw.
22. Arthoplasty Outcome Evaluation Questionnaire.tw.
23. Visual analog.tw.
24. World Health Organization Quality of Life assessment instrument.tw.
25. (Western Ontario and McMaster Universities Arthritis Index).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

26. Hip disability.mp. and Osteoarthritis Outcome Score.tw. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]
27. International Knee Documentation Committee Subjective Knee Form.tw.
28. bristol knee score.mp.
29. Short Musculoskeletal Function Assessment.tw.
30. Lequesne.mp.
31. New zealand score.mp.
32. modems.tw.
33. mood adjective.tw.
34. MACL.tw.
35. arthritis impact.tw.
36. KOOS.tw.
37. HOOS.tw.
38. osteoarthitis outcome score.tw.
39. mactar.tw.
40. NHP.tw.
41. Nottingham health.tw.
42. OHS.tw.
43. OKS.tw.
44. Oxford hip score.tw.
45. short form.tw.
46. vas.tw.
47. womac.mp.
48. western ontario.tw.
49. IKD.tw.
50. International knee.tw.
51. smfa.tw.
52. short musculoskeletal.tw.
53. satisfaction.tw.
54. function score.tw.
55. (activit$ adj8 daily living).tw.
56. ADL.tw.
57. QOL.tw.
58. likert.tw.
59. depression.tw.
60. anxiety.tw.
61. PROM.tw.
62. patient reported.tw.
63. visual analog$.tw.
64. expectation.mp. or EXPECTATION/
65. satisfaction.mp. or SATISFACTION/ or PATIENT SATISFACTION/
66. depressive symptoms.tw.
67. POSTOPERATIVE PAIN/
68. POSTOPERATIVE COMPLICATION/
69. psychological distress.tw.
70. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Pre-surgical exercise and education

1. exp preoperative care/
2. preoperative period.mp. or Preoperative Period/
3. pre-surg$.tw.
4. presurg$.tw.
5. before surg$.tw.
6. pre-operat$.tw.
7. preoperat$.tw.
8. 1 or 2 or 3 or 4 or 5 or 6 or 7

Anaesthsia and analgesia in joint replacement

1. Anesthetics, Local/ or local anaesthetic.mp.
2. Anesthetics, Local/ or Anesthesia, Local/ or Local anaesthesia.mp.
3. Anesthetics/ or Anesthesia/ or anaesthesia.mp. or Anesthetics, Local/ or Anesthesia, Local/
4. anesthesia.mp.
5. anaesthetic.mp.
6. amides.mp. or Amides/
7. ("Huneke neural therapy" or " Neural therapy of Huneke" or benzocaine or bensokain or " Aminobenzoic Acid" or " Aminobenzoate" or bupivacain* or buvacaina or sensorcaine or marcain* or svedocain* or levobupivacaine or carticain* or articain* or dibucaine or cinchocaine or Cincain or Nupercain* or Sovcaine or etidocaine or duranest or " W19053" or " W 19053" or " W-19053" or Lidocaine or Lignocaine or Octocaine or Xylesthesin or Xylocaine or Dalcaine or Xylocitin or Xyloneural or Mepivacain* or Carbocaine or Polocaine or isocaine or isogaine or Scandicain* or prilocaine or Propitocaine or Tetracaine or Tetrakain or Amethocaine or Dicaine or Pantocaine or Pontocaine or Trimecaine or Mesocaine or ropivacaine).mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
8. 1 or 2 or 3 or 4 or 5 or 6 or 7

Perioperative wound infiltration

1. (incision or port* or (surg* and wound)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
2. acetabular.mp.
3. infiltration.mp.
4. wound infiltration.mp.
5. wound catheter.mp.
6. peri-articular.mp.
7. periarticular.mp.
8. intraarticular.mp.
9. intra-articular.mp.
10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9

Randomised controlled trial

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized.ab.
4. placebo.ab.
5. randomly.ab.
6. trial.ab.
7. groups.ab.
8. (animals not (humans and animals)).sh.
9. 1 or 2 or 3 or 4 or 5 or 6 or 7
10. 9 not 8

Randomised controlled trial terms for physiotherapy systematic review

1. Randomized Controlled Trials as Topic/
2. randomized controlled trial/
3. random allocation/
4. double blind method/
5. single blind method/
6. clinical trial/
7. clinical trial, phase i.pt.
8. clinical trial, phase ii.pt.
9. clinical trial, phase iii.pt.
10. clinical trial, phase iv.pt.
11. randomized controlled trial.pt.
12. multicenter study.pt.
13. clinical trial.pt.
14. exp clinical trials as topic/
15. (clinical adj trial$).tw.
16. ((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.
17. Placebos/
18. placebo$.tw.
19. randomly allocated.tw.
20. (allocated adj2 random$).tw.
21. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20

Occupational therapy

1. occupational therapy.sh.
2. self help devices.sh.
3. splints.sh.
4. (occupational adj1 therap$).ti,ab.
5. splint$.ti,ab.
6. ((assist$ or help$) adj5 (device$ or technolog$)).ti,ab.
7. ((sel$ or home$) adj5 (care$ or manage$)).ti,ab.
8. ((environment$ or home$ or domestic$ or house$) adj5 adapt$).ti,ab.
9. ((daily or domestic$ or house$ or home$) adj5 (activit$ or task$ or skill$ or chore$)).ti,ab.
10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Physiotherapy

1. physical therapy techniques/ or cryotherapy/ or electric stimulation therapy/ or transcutaneous electric nerve stimulation/ or hydrotherapy/
2. exercise movement techniques/ or exercise/ or exercise therapy/ or walking/
3. rehabilitation/ or "activities of daily living"/ or early ambulation/
4. Postoperative Care/
5. Ambulatory Care/
6. Rehabilitation Centers/
7. Home Care Services/
8. (physiotherap$ or physio therap$ or pt).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
9. therap$.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
10. rehab$.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10

Appendix 4 Systematic review of long-term pain after hip or knee replacement: study characteristics

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Author; country; date of baseline	Population; study design; losses to follow-up	Study type; mean age (SD) (years); % female; indication	Pain outcome measure	Number of patients with:		
				Favourable outcome	Uncertain outcome	Unfavourable outcome
THR						
Nikolajson and colleagues 2006;[51] Denmark; 2003	1231 consecutive patients in a national joint registry with 94% of hip replacements recorded. 93.6% response rate to postal questionnaire; 5.9% lost to follow-up	Registry; 71.6 (SD 8.7); % female not reported; 100% degenerative hip arthritis, operation through a posterolateral surgical approach	Authors' own scale of presence of hip pain and impact on daily life; self-completed; 12- to 18-month follow-up	754 (hip pain not present)	4 died, 117 lost to follow-up, 62 bilateral or further operation, 167 hip pain present with no/mild impact on daily life	127 (pain with moderate, severe or very severe impact on daily life)
Jones and colleagues 2000;[58] Canada; 1995–7	242 consecutive patients listed for and received joint replacement in health region; 5.8% lost to follow-up or died (estimated as not reported for hip and knee separately)	Multiple centres; 68.2 (SD 11.1); 60%; 94% osteoarthritis	WOMAC pain; self-completed; losses to follow-up estimated proportionately as not reported for hip and knee separately; 6-month follow-up	208 (no pain/mild pain defined as more than a 10-point gain on the 100 point WOMAC pain dimension)	14 lost to follow-up (estimated)	20 (moderate/severe pain defined as a gain of less than 10 points on the 100-point WOMAC pain dimension)
Quintana and colleagues 2006;[102] Spain; 1999–2000	784 consecutive patients willing to participate and with complete pre-surgical data scheduled to undergo THR in seven teaching hospitals. 82.4% response; prospective; 25.5% lost to follow-up	Multiple centres; 69.2 (SD 9.2); 48.3%; 94% osteoarthritis	WOMAC pain; self-completed (postal); 6-month follow-up	456 (patients reporting improvement in pain greater than minimal clinical important difference 24.55/100)	200 lost to follow-up	128 (patients reporting no improvement in pain greater than minimal clinical important difference 24.55/100)
Nilsdotter and colleagues 2003;[103] Sweden; 1995–8	219 consecutive patients with 2 surgical methods at single department of orthopaedics. For proportion with pain at follow-up $n = 92$; 5.9% lost to follow-up	Single centre; 71 (range 50–92); 55%; 100% osteoarthritis	WOMAC pain; self-completed; favourable/unfavourable estimates based on extrapolation of partial follow-up; mean 43-month follow-up	153 (pain improved by more than 10/100 units reflecting detectable clinical improvement)	8 died, 13 lost to follow-up	45 (pain improved by $< 10/100$ units reflecting no detectable clinical improvement)

Author; country; date of baseline	Population; study design; losses to follow-up	Study type; mean age (SD) (years); % female; indication	Pain outcome measure	Number of patients with:		
				Favourable outcome	Uncertain outcome	Unfavourable outcome
Singh and Lewallen 2010;[104] USA; 1993–2005	9154 consecutive patients from joint registry sent postal questionnaire or completed at outpatient clinic or telephone; mean age of patients followed up 65.0 years (SD 13); 37.7% lost to follow-up	Single centre; 65.0 (SD 13.3); 51%; 87% osteoarthritis	Single question: how much pain do you have in your operated hip? None, mild, moderate or severe; 24-month follow-up (also 60-month with greater losses to follow-up)	5272 (none or mild pain)	3447 lost to follow-up	435 (moderate or severe pain)
Wylde and colleagues 2011;[49] UK; 2004–6	1401 consecutive patients on an orthopaedic centre database with postal follow-up; 47.6% lost to follow-up	Single centre; median 73 (range 65–78); 63%; majority osteoarthritis	WOMAC pain; median 41-month follow-up (range 35–48 months)	818 (no pain for the past 3 months or mild persistent pain in replaced hip)	71 died, 1 revision, 667 lost to follow-up	114 (moderate or severe persistent pain for 3 months in replaced hip, WOMAC 0–75/100)
TKR						
Baker and colleagues 2007;[105] UK; 2003	9417 questionnaire follow-up of random sample of patients in joint registry; 14.9% lost to follow-up	Registry; 70.7 (range 25–98); 57% (estimate); 96% osteoarthritis	OKS pain dimension; self-completed postal questionnaire; 12-month follow-up or latest available	6427 (did not report persistent knee pain)	1407 lost to follow-up or died	1583 (reported persistent knee pain)
Jones and colleagues 2000;[58] Canada; 1995–7	$n = 292$, approximately 81% of consecutive patients listed for and who subsequently received joint replacement in health region; 5.8% lost to follow-up or died (estimated as not reported for hip and knee separately)	Multiple centres; 69.2 (SD 9.2); 59%; 94% osteoarthritis	WOMAC pain; self completed; losses to follow-up estimated proportionately as not reported for hip and knee separately; 6-month follow-up	222 (no pain/mild pain defined as more than a 10-point gain on the WOMAC pain dimension)	16 lost to follow-up or died (estimated)	54 (moderate/severe pain defined as a gain of < 10 points on the WOMAC pain dimension)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Author; country; date of baseline	Population; study design; losses to follow-up	Study type; mean age (SD) (years); % female; indication	Pain outcome measure	Number of patients with:		
				Favourable outcome	Uncertain outcome	Unfavourable outcome
Quintana and colleagues 2006;[102] Spain; 1999–2000	792 consecutive patients scheduled to undergo TKR in seven teaching hospitals willing to participate and with complete pre-surgical data (83.4% response); 24.1% lost to follow-up	Multiple centres; 71.9; 73%; 100% osteoarthritis	WOMAC pain; self-completed; 6-month follow-up	402 (patients reporting improvement in pain greater than minimal clinical important difference 22.6/100)	191 lost to follow-up	199 (patients reporting no improvement in pain greater than minimal clinical important difference 22.6/100)
Núñez and colleagues 2007;[47] Spain; 2000–1	88 consecutive patients at a single tertiary care centre 8.0% lost to follow-up	Multiple centres; 74.8 (SD 5.6); 81%; 100% osteoarthritis	WOMAC pain; self-completed; 36-month follow-up	60 (improvement in postoperative pain scores)	1 died, 7 lost to follow-up, 13 contralateral or other surgery	7 (no improvement in postoperative pain scores)
Stephens and colleagues 2002;[106] USA; date not specified	68 patients referred for and received knee replacement aged ≥ 50 years; 7.4% lost to follow-up	Single centre; 67.4 (SD 8.1) followed up; 54% followed up; 100% osteoarthritis	WOMAC pain; self-completed (postal); 6-month follow-up	52 (decrease in pain)	5 lost to follow-up	11 (no change or increase in pain)
Lundblad and colleagues 2008;[107] Sweden; date not specified	69 patients scheduled for knee replacement; 10.1% lost to follow-up (including deaths)	Single centre; 68 (range 40–80); 50.7%; 100% osteoarthritis	VAS pain; self-completed postal; 18-month follow-up	21 (no pain at rest or with movement)	7 lost to follow-up or died, 26 pain with movement	15 (pain at rest and movement)
Nilsdotter and colleagues 2009;[108] Sweden; 1999–2001	102 responders to postal survey on waiting list for knee replacement; 12.7% lost to follow-up	Single centre; 71 (SD 8); 61.8%; 100% osteoarthritis	KOOS pain compared with pre-operatively; self-completed postal; 60-month follow-up	47 (much less or less pain than pre-operatively)	9 died, 13 lost to follow-up, 6 operated bilaterally	27 (similar or more pain than pre-operatively)
Vuorenmaa and colleagues 2008;[109] Finland; date not specified	51 patients referred for knee replacement; 11.8% lost to follow-up	Single centre; 70 (SD 5); 86%; 100% osteoarthritis	VAS pain; self-completed; pain calculated from 20% followed up had moderate or severe pain (defined as score of > 30 on a 100-mm pain VAS); 3-month follow-up	34 (none or mild pain)	1 died, 6 lost to follow-up, 1 infection	9 (moderate or severe pain)

Author; country; date of baseline	Population; study design; losses to follow-up	Study type; mean age (SD) (years); % female; indication	Pain outcome measure	Number of patients with:		
				Favourable outcome	Uncertain outcome	Unfavourable outcome
Czurda and colleagues 2010;[110] Austria; 2003–5	411 consecutive patients with computer assisted or conventional surgery with at least 18 months follow-up; 13.4% lost to follow-up	Single centre; 75–76 (range 45–96); 76%; 100% osteoarthritis	WOMAC pain; telephone interview; mean 26-month follow-up (range 18–42 months)	273 (no report of painful knees – no moderate or worse response in any WOMAC pain dimension)	2 died, 55 lost to follow-up, 24 infection, trauma, reoperation, poor general condition	57 (painful knees – moderate or worse response in any WOMAC pain dimension)
Wylde and colleagues 2011;[49] UK; 2004–6	1394 consecutive patients on an orthopaedic centre database; 45.3% lost to follow-up	Single centre; median 73 (range 28–96); 59%; Majority osteoarthritis	WOMAC pain; self-completed postal questionnaire; median 28-month follow-up (range 14–43)	433 (no pain for the past 3 months or mild persistent pain in replaced hip)	62 died, 4 revision, 696 lost to follow-up	199 (moderate or severe persistent pain for 3 months in replaced hip, WOMAC 0–75/100)
Brander and colleagues 2003;[50] USA 1998–2000	116 consecutive patients (1 surgeon); 0% lost to follow-up	Single surgeon; 66 (SD 10.5); 55.2%; 94% osteoarthritis	VAS pain; self-completed questionnaire; 12-month follow-up	98 (no significant pain, VAS score of ≤ 40)	1 died, 2 revision or dislocation	15 (significant pain, VAS score of > 40)

Studies ordered within hip and knee replacement groups by decreasing representativeness (multiple compared with single centre) and by increasing losses to follow-up.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 5 Systematic review of pre-operative predictors of patient-centred outcomes after total hip replacement: study characteristics

Study; country; dates	Number of patients; follow-up	Statistical analysis and variables in analysis	Predictor	Outcome measures
Registry				
Rolfson and colleagues 2009;[125] Sweden; 2002–5	$n = 6$, 158 (approximately 92% of eligible); 12 months, estimated 8% not followed up	ANCOVA with EQ-5D anxiety and depression, age, sex, comorbidities, VAS pain, EQ-5D	Mental health	VAS pain, satisfaction, EQ-5D domains
Multiple centres				
Hajat and colleagues 2002;[126] UK; 1996–7	$n = 3600$ (4657 eligible); 12 months, 22.7% not followed up	Multiple regression analysis with OHS, waiting time, comorbidities, age, sex, housing, surgical factors	Physical function	OHS
Jones and colleagues 2012;[127] Canada; 1995–7	$n =$ approximately 167 (231 eligible); 3 years, 28% not followed up	Linear mixed model with BMI (< 25, 25–29.9, 30–34.9, ≥ 35 kg/m^2), age, sex, diabetes and cardiac disease	BMI	WOMAC
Judge and colleagues 2011;[31] Europe; dates not specified	$n = 845$ (1327 eligible); 12-month follow-up, 36.3% with no baseline or follow-up data	Ordered logistic regression modelling with WOMAC score, EQ-5D, age, sex, BMI, education, living arrangements, ambulatory status, comorbidities and radiographic status	Physical function	WOMAC
Judge and colleagues 2013;[128] UK; 1999–2002	$n = 1375$ patients with 1431 THR at baseline; 60 months, 20% lost to 1-year follow-up, 30% lost to 5-year follow-up	Repeated measures linear regression with BMI as a continuous variable, age, sex, primary diagnosis, occupation, specific comorbidities, SF-36, OHS, ROM, surgical variables	BMI, mental health physical function	OHS
Stevens and colleagues 2012;[129] Netherlands; 2005–7	$n = 653$ (848 eligible); 12 months, 23% lost to follow-up	Linear regression (structural equation model) with BMI (< 25, 25–30, > 30 kg/m^2), age, sex, comorbidities and complications	BMI	WOMAC, SF-36
Single centre				
Anakwe and colleagues 2011;[130] UK; 2003–8	Osteoarthritis estimated 98%; $n = 850$ (907 eligible); 12 months, 6.3% not followed up	Multivariate binary logistic regression with SF-12 mental health component, diabetes, hypertension, history of depression, age, sex, SF-12 physical components, OHS, musculoskeletal comorbidities	Mental health, physical function	Satisfaction
Clement and colleagues 2011;[131] UK; 2006–8	Osteoarthritis; $n = 1312$ patients with 1359 THR followed up; 12 months, no loss to follow-up information	Ordinal logistic regression with SF-12 mental health, age, deprivation, Charlson comorbidities including depression, OHS, length of stay and SF-12 physical health	Mental health, physical function	OHS

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Study; country; dates	Number of patients; follow-up	Statistical analysis and variables in analysis	Predictor	Outcome measures
Davis and colleagues 2011;[132] UK; 1998–2005	$n = 1095$ (1617 at baseline); 60 months, 32% not followed up	Multiple regression linear analysis with BMI (< 25, 25–29.9, 30–34.9, ≥ 35 kg/m^2), age, sex, pre-operative HHS, SF-36, comorbidities, consultant	BMI	SF-36
Gandhi and colleagues 2010;[133] Canada; 1998–2005	$n = 636$ with pre- and postoperative data; 12 months and up to 72 months (mean 39 months), loss to follow-up not described	Multivariable longitudinal regression with BMI as a continuous variable, age, sex, comorbidities, WOMAC, SF-36	BMI, mental health	WOMAC, SF-36 physical function
Garbuz and colleagues 2006;[134] also Xu and colleagues 2005;[136] Canada; 2001–3	$n = 147$ (total 201 eligible); 12 months, 27% lost to follow-up	Log-linear regression with WOMAC pain, age, sex and comorbidities	Pain, physical function	WOMAC pain
Moran and colleagues 2005;[135] UK; 1998–2000	$n = 687$ (800 eligible); minimum 18 months, 14% lost to follow-up	Multiple linear regression analysis with BMI as a continuous variable, sex, comorbidities, OHS, SF-36	BMI	SF-36
Nilsdotter and colleagues 2003;[103] Sweden; 1995–8	$n = 198$ (total 219 recruited); 12 month and at mean 43-month follow-up, 6% lost to follow-up	Stepwise multivariate logistic regression with BMI as a continuous variable, age, sex, comorbidity, WOMAC, SF-36 (including mental health), employment, marital status, contralateral osteoarthritis, need of walking assistance, walking distance, analgesic use, regional or widespread pain	BMI, mental health, pain	WOMAC function
Singh and Lewallen 2010;[104] USA; 1993–2005	$n = 5707$ (9154 at baseline); 24 months (and longer), 38% of patients not followed up at 2 years	Multivariable-adjusted logistic regression analyses with BMI (< 25, 25–29.9, 30–34.9, 35–39.9, ≥ 40 kg/m^2), age, sex, Deyo-Charlson, ASA, depression, anxiety, operative diagnosis, distance from centre and implant design	BMI, mental health	Pain (5-item response scale)

ANCOVA, analysis of covariance; ASA, American Society of Anesthesiologists.

Appendix 6 Systematic review of pre-operative predictors of patient-centred outcomes after total knee replacement: study characteristics

Study; country; dates	Number of patients; follow-up	Statistical analysis and variables in analysis		Outcome measures
Registry				
Baker and colleagues 2012;[148] UK; 2008–11	$n = 22,691$ (40,925 eligible); minimum 6-month follow-up, 44.6% not followed up	Stepwise multiple regression analysis with EQ-5D depression and anxiety, age, OKS, EQ-5D, comorbidities, disability, general health, ASA grade, and surgical and hospital variables	Mental health	OKS, EQ-5D
Franklin and colleagues 2008;[147] USA; 2000–5	$n = 8050$ (17,270 eligible); follow-up at 12 months, 53.4% not followed up	Multivariate mixture models with BMI analysed as < 30, 30–40, > 40 kg/m^2, sex, age, SF-12 MCS and PCS, osteoarthritis diagnosis and poor quadriceps strength	BMI, mental health	SF-12 PCS
Multiple centres				
Alzahrani and colleagues 2011;[149] Canada; 1998–2007	$n = 3,177$; follow-up at 12 months, losses to follow-up not described	Multivariable logistic regression modelling with BMI analysed as a continuous variable, age, sex and comorbidities	BMI	OKS (2720 patients), total WOMAC (457 patients)
Cushnaghan and colleagues 2009;[151] UK; 1995–7	$n = 259$ (657 eligible but not all had TKR); mean follow-up of 6 years, approximately 60.6% not followed up	Linear regression with BMI analysed as < 25, 25 to < 30, ≥ 30 kg/m^2, age, sex, SF-36 PCS, smoking habits, comorbidities, Kellgren and Lawrence grade, previous knee injury, other painful joints and Heberden's nodes	BMI	SF-36 PCS
Heck and colleagues 1998;[157] USA; 1992–3	$n = 268$ (291 eligible); 24-month follow-up, 7.9% not followed up	Stepwise logistic regression model with SF-36 mental health, age, ethnicity, sex, poverty, patient health status, WOMAC scales, SF-36, knee ROM, comorbidities, surgical factors and joint problems in the other knee	Mental health, pain, physical function	SF-36 physical component
Jones and colleagues 2012;[127] Canada; 1995–7	$n =$ approximately 209 (289 eligible); follow-up at 3 years, approximately 27.7% not followed up	Linear mixed modelling with BMI analysed as binary variable (30–34.9 and ≥ 35 kg/m^2), age, sex and comorbidities	BMI	WOMAC
Lingard and colleagues 2004;[46] UK, USA, Australia; 1997–8	$n = 741$ at 1 year, 678 at 2 years (860 eligible); follow-up at 12 and 24 months, 13.8% and 21.2% lost to follow-up at 12 and 24 months	Hierarchical model with BMI analysed as a continuous variable, age, sex, PROMs score, mental health, knee flexion, working status, education, income, comorbidities and country	BMI, pain, physical function	WOMAC pain and function, SF-36 PCS

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Study; country; dates	Number of patients; follow-up	Statistical analysis and variables in analysis		Outcome measures
Lingard and colleagues 2007;[150] also Lingard and colleagues 2004;[46] UK, USA, Australia; 1997–8	$n = 682$ (974 eligible); follow-up at 12 and 24 months, 30.0% not followed up at 2 years	General linear model with SF-36 mental distress, age, sex, and comorbidities	Mental health	WOMAC pain and function scores
Merle-Vincent and colleagues 2011;[158] France; dates not specified	$n = 264$ (299 eligible); 24-month follow-up, 13.3% not followed up	Multivariate logistic regression with feelings of depression, age, sex, BMI, Lequesne index and joint space narrowing	Mental health	Satisfaction
Naylor and colleagues 2012;[154] Australia; 2008–9	$n = 146$ (191 eligible); follow-up at 12 months, 23.6% not followed up	Mixed model with BMI analysed as continuous variable, age and sex as covariates. Performed separately for pre-operative flexion and extension variables	BMI	OKS
Papakostidou and colleagues 2012;[155] Greece; dates not specified	$n = 204$ (224 eligible); follow-up at 12 months, 9.8% not followed up	General linear model multivariable analysis with BMI analysed as binary variable (under and over 30 kg/m^2), sex, education, social support, age, place of residence, baseline status of knee	BMI, mental health, pain	WOMAC
Perruccio and colleagues 2012;[152] Canada; 2006–8	$n = 435$ (494 eligible); mean follow-up at 12.5 months, 11.9% not followed up	Linear regression with BMI analysed as 25–29 kg/m^2 (overweight) and > 30 kg/m^2 (obese), age, sex, education, comorbidity count, other painful joints and pain/function	BMI	WOMAC
Singh and Lewallen 2013;[156] USA; 1993–2005	$n = 7139$ (approximately 10,980 eligible); follow-up at 2 and 5 years, 35% and 43% lost to follow-up, respectively	Multivariable adjusted model with age, sex, BMI, ASA class, distance from medical centre, operative diagnosis, implant fixation (cement status), six Deyo-Charlson comorbidity categories, anxiety and depression	Mental health	Pain severity questionnaire
Sullivan and colleagues 2011;[153] Canada; dates not specified	$n = 120$ (number eligible not specified); follow-up at 12 months, loss to follow-up not described	Multiple regression with BMI analysed as continuous variable, pain, function, age, sex, comorbidities, surgery duration, surgeon, pain catastrophising, pain-related fear of movement and depression	BMI, pain	WOMAC function and pain

Study; country; dates	Number of patients; follow-up	Statistical analysis and variables in analysis		Outcome measures
Single centre				
Ayers and colleagues 2005;[163] USA; dates not specified	$n = 165$ (number eligible not specified); 12 months, loss to follow-up not described	Blocked multiple regression analysis with SF-36 mental health, age, sex, comorbidities, SF-36 physical component and WOMAC physical function	Mental health, physical function	WOMAC physical function, SF-36 physical component
Brander and colleagues 2003;[50] USA; 1998–2000	$n = 116$ consecutive patients with 149 TKRs (no information on eligibility); follow-up at 12 months, no information on losses to follow-up	Multiple regression analysis with anxiety (STAI) and depression (Beck Depression Inventory), age, sex, BMI, physiologic, psychometric and heightened pain	Mental health	Pain VAS and McGill questionnaire-SF scores
Clement and colleagues 2013;[164] UK; 2007–9	$n = 966$ (number eligible not specified); 12-month follow-up, losses to follow-up not described	Multivariate linear and bivariate regression analyses with SF-36 mental health component, age, sex, comorbidities, socioeconomic deprivation, OKS and SF-12 physical component	Mental health, physical function	OKS, satisfaction
Deshmukh and colleagues 2002;[161] UK; 1992–5	$n = 139$ (180 eligible); follow-up at 12 months, 22.8% not followed up	Hierarchical multiple regression analysis with BMI analysed as continuous variable, age, sex, side of arthritis, comorbidities, NHP and AKSS scores	BMI	NHP
Gandhi and colleagues 2010;[160] Gandhi and colleagues 2010;[166] Canada; 1998–2005	$n = 551$ (number eligible not specified); mean follow-up 3 years, loss to follow-up not described	Multivariable longitudinal regression model with BMI analysed as continuous variable, age, sex, ethnicity, education, comorbidities and SF-36 mental health	BMI, mental health	Total WOMAC score, SF-36 Role Physical, SF-36 Physical Function
Núñez; and colleagues 2009;[159] Spain; 2000	$n = 112$ (146 eligible); follow-up at 7 years, 23.3% not followed up	Explanatory multiple linear regression models with BMI analysed as a binary variable (< 35 and ≥ 35 kg/m^2), age, sex, comorbidities, sociodemographic and clinical characteristics, intraoperative variables, inpatient variables, postoperative clinical variables and pre-operative WOMAC scores	BMI	WOMAC function and pain
Rajgopal and colleagues 2008;[162] Canada; 1987–2004	$n = 550$ (number eligible not specified); follow-up at 1 year, loss to follow-up not described	Linear regression model with BMI analysed as binary variable (< 40 or ≥ 40 kg/m^2), age, sex, mental health, prior contralateral TKR, WOMAC score and presence of comorbidity affecting gait	BMI	WOMAC
Scott and colleagues 2010;[165] UK; 2006–8	$n = 1141$ (1290 eligible); 12 months, 13.1% not followed up	Multiple ordinal logistic regression with depression, SF-12 MCS, age, sex, SF-12 PCS, OKS and comorbidities	Mental health, pain, physical function	Satisfaction

ASA, American Society of Anesthesiologists; MCS, mental component score.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 7 Systematic review of comorbid conditions and long-term patient-centred outcomes after total hip replacement: study characteristics

Study; country; dates	Number of patients; follow-up	Statistical analysis and variables in analysis	Comorbidity	Outcome measures
Multiple centres				
Cushnaghan and colleagues 2007;[184] Judge and colleagues 2012;[185] UK; 1993–5; two health districts	Osteoarthritis; $n = 249$ (643 eligible); mean follow-up approximately 96 months, 49.9% not followed up	Logistic regression modelling; diabetes, hypertension, thyroid disease, age, sex, BMI, smoking habit, previous knee injury, Heberden's nodes, number of painful joints and radiographic grade	Hypertension	SF-36 PCS
Jones and colleagues 2012;[127] Canada; 1995–7	$n =$ approximately 167 (231 eligible); 3 years, 28% not followed up	Linear mixed modelling; comorbidity including diabetes and cardiac disease, age, sex, BMI, education, principal diagnosis, living arrangements, type of living accommodation, previous joint surgery, ambulatory status and number of comorbid conditions	Diabetes, cardiovascular disease	WOMAC function and pain
Judge and colleagues 2012;[185] Cushnaghan and colleagues 2007;[184] UK; 1993–5	Osteoarthritis; $n = 249$ (643 eligible); mean follow-up approximately 96 months, 49.9% not followed up	Logistic regression modelling; diabetes, hypertension, thyroid disease, age, sex, BMI, smoking habit, previous knee injury, Heberden's nodes, number of painful joints and radiographic grade	Diabetes, thyroid disease	SF-36
Single centre				
Anakwe and colleagues 2011;[130] UK; 2003–8	Osteoarthritis estimated 98%; $n = 850$ (907 eligible); 12 months, 6.3% not followed up	Multivariate binary logistic regression; diabetes, hypertension, history of depression, age, sex, SF-12 physical and mental components, OHS and musculoskeletal comorbidities	Diabetes, hypertension	Satisfaction
Gandhi and colleagues 2010;[166] Canada; 1998–2006	Osteoarthritis; $n = 707$ (approximately 850 eligible); 12 months, 16.7% not followed up	Linear regression; number of metabolic syndrome factors (BMI of > 30 kg/m^2, diabetes, hypertension and hypercholesterolaemia), age, sex, BMI, WOMAC and Cumulative Illness Rating Scale	Diabetes, hypertension	WOMAC

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 8 Systematic review of comorbid conditions and long-term patient-centred outcomes after total knee replacement: study characteristics

Study; country; dates	Number of patients; follow-up	Statistical analysis and variables in analysis	Comorbidity	Outcome measures
Multiple centres				
Cushnaghan and colleagues 2009;[151] UK; 1995–7	*n* = 259 (657 eligible but not all had TKR); mean follow-up of 6 years, approximately 60.6% not followed up	Linear regression; diabetes, hypertension, thyroid disease, age, sex, BMI, smoking habit, previous knee injury, Heberden's nodes, number of painful joints, and radiographic grade	Diabetes, hypertension, thyroid disease	SF-36 physical function
Jones and colleagues 2012;[127] Canada; 1995–7	*n* = approximately 209 (289 eligible); follow-up at 3 years, approximately 27.7% not followed up	Linear mixed modelling; comorbidity including cardiac disease and diabetes, age, sex, BMI, education, principal diagnosis, living arrangements, type of living accommodation, previous joint surgery, ambulatory status and number of comorbid conditions	Diabetes, cardiovascular disease	WOMAC
Single centre				
Ayers and colleagues 2005;[163] USA; not specified	*n* = 165 (number eligible not specified); 12 months, loss to follow-up not described	Blocked multiple regression analyses with cardiovascular disease, pulmonary disease, lower extremity (non-arthritis), rheumatoid, endocrine disease, age, sex, SF-36 physical and mental health, components and WOMAC physical component	Diabetes, cardiovascular disease	WOMAC function, SF-36 physical component
Clement and colleagues 2013;[164] UK; 2007–9	*n* = 966 (number eligible not specified); 12-month follow-up, losses to follow-up not described	Multivariate linear and bivariate regression analyses with SF-36 mental health component, age, sex, comorbidities, socioeconomic deprivation, OKS and SF-12 physical component	Diabetes, cardiovascular disease, hypertension, anaemia	OKS Satisfaction
Gandhi and colleagues 2010;[166] Canada; 1998–2006	*n* = 889 (approximately 1067 eligible); 12 months, 16.7% not followed up	Linear regression; number of metabolic syndrome risk factors (BMI of > 30 kg/m^2; diabetes, hypertension and hypercholesterolaemia), age, sex, BMI, WOMAC and Cumulative Illness Rating Scale	Diabetes, hypertension	WOMAC
Scott and colleagues 2010;[165] UK; 2006–8	*n* = 1141 (1,290 eligible); 12 months, 13.1% not followed up	Multiple ordinal logistic regression; heart disease, hypertension, lung disease, vascular disease, neurological problems, diabetes, stomach ulcer kidney disease, liver disease, anaemia and depression	Diabetes, cardiovascular disease, hypertension	Satisfaction

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 9 Local anaesthetic infiltration in total knee and hip replacement: Cochrane risk-of-bias table

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel	Blinding of outcome assessment (detection bias)	Incomplete outcome data addressed (attrition bias)	Lack of selective reporting (reporting bias)	Lack of other sources of bias	Power calculation reported	Our evaluation
THR									
Andersen KV and colleagues 2007[385]	✓	✓	✗	✗	✓	✓	✓	✓	Unclear: no reason to assume bias
Lee and colleagues 2009[391]	~	~	✗	✗	✓	✓	✓	✗	Unclear: no reason to assume bias
Lu and Li 2010[393]	~	~	~	~	~	~	~	✗	Unclear: no reason to assume bias
Aguirre and colleagues 2012[387]	~	~	✓	✓	✓	✓	✓	✓	Low risk of bias
Andersen LJ and colleagues 2007[388]	✓	✓	✓	✓	✓	✓	~	✓	Low risk of bias
Bianconi and colleagues 2003[374]	✓	✓	✗	✓	✓	✓	✓	✓	Low risk of bias
Busch and colleagues 2010[389]	✓	~	✗	✓	✓	✓	✓	✓	Low risk of bias
Dobie and colleagues 2012[390]	✓	✓	✗	✓	✓	✓	✓	✓	Low risk of bias
Liu and colleagues 2011[392]	✓	✓	✓	✓	✓	✓	✓	✓	Low risk of bias
Lunn and colleagues 2011[394]	✓	✓	✓	✓	~	✓	✓	✓	Low risk of bias (except pain during activity with 18 patients unable to complete test)
Murphy and colleagues 2012[395]	~	✓	✗	✓	✓	✓	✓	✓	Low risk of bias
Parvataneni and colleagues 2007[386]	~	~	✗	✓	✓	✓	✓	✓	Low risk of bias
Rikalainen-Salmi and colleagues 2012[396]	✓	✓	✗	✓	✓	✓	✓	✓	Low risk of bias

Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel	Blinding of outcome assessment (detection bias)	Incomplete outcome data addressed (attrition bias)	Lack of selective reporting (reporting bias)	Lack of other sources of bias	Power calculation reported	Our evaluation
TKR									
Affas and colleagues 2011[397]	✓	✓	✗	✗	✓	✓	✓	✓	Unclear: no reason to assume bias
Andersen KV and colleagues 2010[398]	✓	✓	✗	✗	✓	✓	~	✓	Unclear: no reason to assume bias (small difference in reasons for losses to follow-up)
Meftah and colleagues 2012[410]	~	~	✗	~	✓	✓	✓	✗	Unclear: no reason to assume bias
Toftdahl and colleagues 2007[380]	~	✓	✗	✗	✓	✓	✓	✓	Unclear: no reason to assume bias
Zhang and colleagues 2007[414]	~	~	✗	~	✓	✓	✓	✓	Unclear: no reason to assume bias
Busch and colleagues 2006[399]	✓	~	✗	✓	✓	✓	✓	✗	Low risk of bias
Carli and colleagues 2010[400]	✓	✓	✓	✓	✓	✓	✓	✓	Low risk of bias
Chen and colleagues 2012[401]	✓	✓	✓	✓	✓	✓	✓	✓	Low risk of bias
Essving and colleagues 2010[402]	✓	~	✗	✓	✓	✓	✓	✓	Low risk of bias
Essving and colleagues 2011[403]	✓	✓	✗	✓	✓	✓	~	✓	Low risk of bias
Fu and colleagues 2009[404]	✓	✓	✓	✓	✓	✓	✓	✓	Low risk of bias
Fu and colleagues 2010[405]	✓	✓	✓	✓	✓	✓	✓	✗	Low risk of bias

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel	Blinding of outcome assessment (detection bias)	Incomplete outcome data addressed (attrition bias)	Lack of selective reporting (reporting bias)	Lack of other sources of bias	Power calculation reported	Our evaluation
Han and colleagues 2007[406]	✓	~	~	✓	✓	✓	✓	✗	Low risk of bias
Han and colleagues 2007[406]	✓	~	~	✓	✓	✓	✓	✗	Low risk of bias
Koh and colleagues 2012[407]	✓	✓	✗	✓	✓	✓	✓	✓	Low risk of bias
Krenzel and colleagues 2009[408]	~	~	✓	✓	✓	✓	✓	✓	Low risk of bias
Mahadevan and colleagues 2012[409]	✓	✓	✗	✓	✓	✓	✓	✓	Low risk of bias
Ng and colleagues 2012[411]	✓	~	✓	✓	✓	✓	✓	✓	Low risk of bias
Parvataneni and colleagues 2007[386]	~	~	✗	✓	✓	✓	✓	✓	Low risk of bias
Spreng and colleagues (no i.v. injection) 2010[412]	✓	✓	✗	✓	✓	✓	✓	✓	Low risk of bias
Spreng and colleagues (with i.v. injection) 2010[412]	✓	✓	✗	✓	✓	✓	✓	✓	Low risk of bias
Vendittoli and colleagues 2006[413]	✓	~	✗	✓	✓	✓	✓	✓	Low risk of bias
Thorsell and colleagues 2010[381]	~	~	✗	~	✗	✓	✓	✗	Possible bias (large uneven losses to follow-up; allocation to groups on basis of date of birth)

✓ low risk of bias, ✗ risk of bias; ~ no reason to assume bias.

Appendix 10 CONSORT 2010 checklist of information for APEX randomised controlled trial

Section/topic	Item	Checklist item	Reported
Title and abstract			
	1a	Identification as a randomised trial in the title	Yes
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	Yes
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	Yes
	2b	Specific objectives or hypotheses	Yes
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Yes
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	Yes
	4b	Settings and locations where the data were collected	Yes
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Yes
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Yes
	6b	Any changes to trial outcomes after the trial commenced, with reasons	Statistical analysis as described
Sample size	7a	How sample size was determined	Yes
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			Yes
Sequence generation	8a	Method used to generate the random allocation sequence	Yes
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Yes
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Yes
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Yes
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Yes
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	Yes
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	Yes

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Section/topic	Item	Checklist item	Reported
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Yes
	13b	For each group, losses and exclusions after randomisation, together with reasons	Yes
Recruitment	14a	Dates defining the periods of recruitment and follow-up	Yes
	14b	Why the trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Yes
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Yes
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% CI)	Yes
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	N/A
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Yes
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	Yes
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	Yes
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Yes
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	Yes
Other information			
Registration	23	Registration number and name of trial registry	Yes
Protocol	24	Where the full trial protocol can be accessed, if available	Yes
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Yes

N/A, not applicable.

Appendix 11 Pain on admission to the recovery ward, on discharge from the recovery ward and during the day of surgery for the APEX THR and TKR trial

	Hips			Knees		
Pain outcome	Intervention, ($N = 163$), *n* (%)	Standard care, ($N = 159$), *n* (%)	*p*-values[a,b]	Intervention, ($N = 157$), *n* (%)	Standard care, ($N = 159$), *n* (%)	*p*-values[a,b]
Pain on admission to the recovery ward			0.169			0.062
No pain	115 (70.6)	111 (69.8)		108 (68.8)	86 (54.1)	
Mild pain	9 (5.5)	3 (1.9)		7 (4.5)	11 (6.9)	
Moderate pain	4 (2.5)	10 (6.3)		8 (5.1)	16 (10.1)	
Severe pain	4 (2.5)	2 (1.3)		12 (7.6)	18 (11.3)	
Missing	31 (19)	33 (20.8)		22 (14)	28 (17.6)	
Pain on discharge from the recovery ward			0.759			0.097
No pain	92 (56.4)	87 (54.7)		93 (59.2)	78 (49.1)	
Mild pain	29 (17.8)	25 (15.7)		34 (21.7)	31 (19.5)	
Moderate pain	4 (2.5)	6 (3.8)		6 (3.8)	13 (8.2)	
Severe pain	0 (0)	0 (0)		1 (0.6)	5 (3.1)	
Missing	38 (23.3)	41 (25.8)		23 (14.6)	32 (20.1)	
Pain during day of surgery			0.515			0.325
No pain	26 (16)	28 (17.6)		37 (23.6)	30 (18.9)	
Mild pain	65 (39.9)	51 (32.1)		41 (26.1)	36 (22.6)	
Moderate pain	44 (27)	43 (27)		44 (28)	61 (38.4)	
Severe pain	8 (4.9)	11 (6.9)		14 (8.9)	16 (10.1)	
Missing	20 (12.3)	26 (16.4)		21 (13.4)	16 (10.1)	

a Between-arms comparisons were only conducted in the complete cases.
b Chi-squared test or Fisher-exact test.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 12 Length of stay for the APEX THR and TKR trial

	Hips			Knees		
Length of hospital stay	Intervention, ($n = 163$)	Standard care, ($n = 159$)	p-value1,2[a,b]	Intervention, ($n = 157$)	Standard care, ($n = 159$)	p-value1,2[a,b]
Median days (25th, 75th)	4 (4, 5)	5 (4, 6)	0.2476	4 (4, 6)	5 (4, 6)	0.5864
Missing, *n* (%)	10 (6.1)	8 (5.0)		14 (8.9)	12 (7.6)	

a Between-arms comparisons were only conducted in the complete cases.
b Wilcoxon–Mann–Whitney test.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 13 Postoperative inpatient pain scores for the APEX THR and TKR trial

Postoperative day	Pain outcome	Hips		Knees	
		Intervention, ($n = 163$)	Standard care, ($n = 159$)	Intervention, ($n = 157$)	Standard care, ($n = 159$)
Pain at night					
Day 1	Median (IQR[a])	35 (50)	36 (45)	48 (55)	42 (55)
	Missing number (%)	17 (10.4)	12 (7.5)	28 (17.8)	18 (11.3)
Day 2	Median (IQR[a])	12 (22)	23 (33)	45 (55)	39 (49)
	Missing number (%)	18 (11.0)	13 (8.2)	23 (14.7)	15 (9.4)
Day 3	Median (IQR[a])	8 (20)	11 (28)	24 (37)	32 (47)
	Missing number (%)[b]	22 (14.2)	17 (11.1)	29 (18.8)	25 (16.0)
Pain at rest					
Day 1	Median (IQR[a])	23 (28)	26 (30)	37 (34)	44 (32)
	Missing number (%)	16 (9.8)	10 (6.3)	26 (16.7)	17 (10.7)
Day 2	Median (IQR[a])	12 (26)	16 (24)	35 (53)	35 (37)
	Missing number (%)	17 (10.4)	13 (8.2)	22 (14.0)	15 (9.4)
Day 3	Median (IQR[a])	7 (18)	13 (18)	21 (28)	21 (36)
	Missing number (%)[b]	23 (14.8)	17 (11.1)	29 (18.8)	25 (16.0)
Pain on movement					
Day 1	Median (IQR[a])	52 (34)	56 (37)	58 (37)	62 (26)
	Missing number (%)	16 (9.8)	10 (6.3)	26 (16.6)	17 (10.7)
Day 2	Median (IQR[a])	39 (41)	42 (40)	56 (37)	57 (36)
	Missing number (%)	18 (11.0)	13 (8.2)	22 (14.0)	15 (9.4)
Day 3	Median (IQR[a])	28 (44)	32 (37)	42 (39)	46 (40)
	Missing number (%)[b]	23 (14.8)	17 (11.1)	29 (18.8)	25 (16.0)

a The IQR is the difference between the 25th and 75th quintiles.
b Percentage derived from the patients still hospitalised. In the THR trial, eight patients (4.9%) had been discharged in the intervention group and six (3.8%) in the standard care group. In the TKR trial, three patients (1.9%) had been discharged in the intervention group and three (1.9%) in the standard care group.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 14 Drugs and side effects during recovery for the APEX THR and TKR trial

Drugs and side effects		Hips			Knees		
		Intervention, ($n = 163$)	Standard care, ($n = 159$)	p-value[a,b]	Intervention, ($n = 157$)	Standard care, ($n = 159$)	p-value[a,b]
Drugs							
Drugs administered	Number (%)	109 (66.9)	100 (62.9)	0.176	98 (62.4)	118 (74.2)	0.010
Missing	Number (%)	11 (6.8)	4 (2.5)		12 (7.6)	13 (8.2)	
Strong opioids (units)	Median (IQR)	3 (8)	4.5 (9)	0.450[3]	3 (6)	3 (15)	0.441[c]
Side effects							
Nausea and vomiting	Number (%)	80 (49.1)	88 (55.4)	0.429	79 (50.3)	87 (54.7)	0.417
	Missing number (%)	10 (6.1)	4 (2.5)		12 (7.6)	12 (7.6)	
Antiemetics	Number (%)	19 (11.7)	20 (12.6)	0.916	16 (10.2)	21 (13.2)	0.391
	Missing number (%)	10 (6.1)	4 (2.5)		12 (7.6)	13 (8.2)	
Repeat femoral block	Number (%)	0 (0.0)	0 (0.0)	N/A	2 (1.3)	3 (1.9)	0.909
	Missing number (%)	10 (6.1)	4 (2.5)		12 (7.6)	12 (7.6)	
Sign of toxicity	Number (%)	1 (0.6)	0 (0.0)	0.497	1 (0.6)	0 (0.0)	0.313
	Missing number (%)	10 (6.1)	4 (2.5)		12 (7.6)	12 (7.6)	

N/A, not applicable.
a Between-arms comparisons were only conducted in the complete cases.
b Chi-squared test or Fisher-exact test.
c Wilcoxon–Mann–Whitney test.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 15 Prevalence of vomiting, nausea and analgesia intake during the first 48 hours after recovery for the APEX THR and TKR trial

Opioid intake, vomiting and nausea		Hips			Knees		
		Intervention ($n = 163$)	Standard care ($n = 159$)	p-value[a,b]	Intervention ($n = 157$)	Standard care ($n = 159$)	p-value[a,b]
Opioid intake							
Strong[c]	Median (IQR)	97 (88)	101 (105)	0.381[d]	120 (99)	130 (115)	0.324[d]
	Missing number (%)	10 (6.1)	12 (7.6)		13 (8.3)	13 (8.2)	
Weak[c]	Median (IQR)	0 (0)	0 (0)	0.625[d]	0 (0)	0 (0)	0.433[d]
	Missing number (%)	10 (6.1)	12 (7.6)		13 (8.3)	13 (8.2)	
Vomiting							
Day 1	Number (%)	47 (33.3)	51 (35.4)	0.711	32 (26.0)	51 (39.2)	0.025
	Missing number (%)	22 (13.5)	15 (9.4)		34 (21.7)	29 (18.2)	
Day 2	Number (%)	28 (17.2)	33 (20.8)	0.392	19 (15.1)	29 (20.4)	0.255
	Missing number (%)	24 (14.7)	24 (15.1)		31 (19.8)	17 (10.7)	
Day 3	Number (%)	10 (8.9)	10 (8.3)	0.888	9 (8.0)	14 (12.6)	0.261
	Missing number (%)	42 (27.1)	33 (21.6)		45 (28.7)	48 (30.2)	
Nausea							
Day 1	Number (%)	71 (50.4)	100 (69.4)	0.001	58 (47.5)	85 (64.9)	0.005
	Missing number (%)	15 (9.4)	22 (13.5)		35 (22.3)	28 (17.6)	
Day 2	Number (%)	67 (48.6)	77 (56.6)	0.181	52 (41.6)	72 (51.1)	0.123
	Missing number (%)	25 (15.3)	23 (14.5)		32 (20.4)	18 (11.3)	
Day 3	Number (%)	38 (33.6)	46 (38.3)	0.455	36 (32.1)	44 (39.6)	0.243
	Missing number (%)	42 (27.1)	33 (21.6)		45 (28.7)	48 (30.2)	

a Between-arms comparisons were only conducted in the complete-cases.
b Chi-squared test or Fisher-exact test.
c In oral morphine equivalent (mg).
d Wilcoxon–Mann–Whitney test.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 16 Intention-to-treat and per-protocol analyses[a] of the effect of the intervention on pain (WOMAC) at 3 and 6 months after surgery for the APEX THR and TKR trial

	ITT-CC		ITT-imputed		PP	
Analysis model	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value
Hips						
3 months						
Unadjusted	2.92 (–1.12 to 6.97)	0.156	3.38 (–0.76 to 7.53)	0.110	2.78 (–1.40 to 6.97)	0.192
Adjusted	1.71 (–2.32 to 5.74)	0.405	2.05 (–2.00 to 6.10)	0.321	1.49 (–2.57 to 5.56)	0.472
6 months						
Unadjusted	1.87 (–2.15 to 5.88)	0.362	2.84 (–1.00 to 6.67)	0.147	1.25 (–2.91 to 5.40)	0.556
Adjusted	0.61 (–3.31 to 4.53)	0.761	1.51 (–2.24 to 5.26)	0.431	–0.08 (–4.13 to 3.97)	0.968
Knees						
3 months						
Unadjusted	–0.52 (–4.85 to 3.79)	0.813	–0.80 (–5.12 to 3.52)	0.716	–0.26 (–4.72 to 4.20)	0.91
Adjusted	–0.32 (–4.52 to 3.88)	0.881	–0.42 (–4.62 to 3.79)	0.846	–0.26 (–4.61 to 4.09)	0.907
6 months						
Unadjusted	4.10 (–0.22 to 8.43)	0.063	4.37 (0.11 to 8.63)	0.044	4.34 (–0.15 to 8.83)	0.058
Adjusted	4.26 (0.04 to 8.48)	0.048	4.75 (0.61 to 8.90)	0.025	4.30 (–0.08 to 8.68)	0.055

a Baseline model.
Linear mixed regression adjusted for baseline pain score, surgical approach and measurement times. Interaction terms used between time and intervention effect to assess 3- and 6-months effects.
Adjusted model
Hip: baseline model + adjustments for sex, living arrangement and number of comorbidities.
Knee: baseline model + adjustments for working status, number of comorbidities, depression and anxiety.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 17 Intention-to-treat and per-protocol analyses[a] of the effect of the intervention on pain (WOMAC) at 3 and 6 months after surgery for the APEX THR trial

	ITT-CC		ITT-imputed		PP	
Analysis model	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
3 months post operation *(Moderate, mild or none) vs. reference = (severe)*						
Baseline	2.36 (0.54 to 10.37)	0.255	2.67 (0.60 to 11.92)	0.198	2.47 (0.52 to 11.78)	0.257
Adjusted	1.86 (0.43 to 8.00)	0.406	2.01 (0.46 to 8.81)	0.357	1.88 (0.41 to 8.74)	0.418
(Mild or none) vs. reference = (severe or moderate)						
Baseline	2.63 (0.95 to 7.29)	0.064	2.85 (1.02 to 7.94)	0.045	2.72 (0.90 to 8.24)	0.076
Adjusted	2.14 (0.79 to 5.79)	0.134	2.24 (0.83 to 6.08)	0.112	2.19 (0.75 to 6.42)	0.153
(None) vs. reference = (severe, moderate or mild)						
Baseline	2.61 (1.03 to 6.65)	0.044	2.61 (1.04 to 6.52)	0.040	2.84 (1.02 to 7.93)	0.046
Adjusted	2.05 (0.83 to 5.10)	0.122	2.04 (0.84 to 4.94)	0.113	2.15 (0.80 to 5.81)	0.130
6 months post operation *(Moderate, mild or none) vs. reference = (severe)*						
Baseline	6.52 (1.21 to 35.29)	0.030	7.19 (1.40 to 36.97)	0.018	5.66 (0.94 to 33.87)	0.058
Adjusted	5.04 (0.93 to 27.22)	0.06	5.32 (1.05 to 26.85)	0.043	4.26 (0.72 to 25.27)	0.111
(Mild or none) vs. reference = (severe or moderate)						
Baseline	2.28 (0.79 to 6.57)	0.128	2.50 (0.90 to 6.94)	0.079	2.26 (0.72 to 7.13)	0.165
Adjusted	1.74 (0.61 to 4.94)	0.297	1.92 (0.70 to 5.28)	0.206	1.69 (0.55 to 5.22)	0.361
(None) vs. reference = (severe, moderate or mild)						
Baseline	1.16 (0.47 to 2.86)	0.740	1.22 (0.50 to 2.99)	0.658	1.18 (0.44 to 3.16)	0.737
Adjusted	0.93 (0.38 to 2.23)	0.863	0.98 (0.41 to 2.33)	0.958	0.92 (0.35 to 2.39)	0.858

a Modelled with multilevel ordinal regression allowing for partial proportional odds. Baseline model adjusted for baseline pain score and surgical approach. Adjusted model: baseline model + adjustments for sex, living arrangement and number of comorbidities.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 18 Intention-to-treat and per-protocol analyses[a] of the effect of the intervention on pain (WOMAC) at 3 and 6 months after surgery for the APEX TKR trial

	ITT-CC		ITT-imputed		PP	
Analysis model	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
3 months post operation *(Moderate, mild or none) vs. reference = (severe)*						
Baseline	1.12 (0.35 to 3.60)	0.850	1.09 (0.37 to 3.26)	0.873	1.19 (0.36 to 4.01)	0.774
Adjusted	1.01 (0.32 to 3.19)	0.989	1.22 (0.41 to 3.63)	0.723	1.03 (0.31 to 3.42)	0.957
(Mild or none) vs. reference = (severe or moderate)						
Baseline	0.86 (0.32 to 2.32)	0.770	0.79 (0.31 to 2.02)	0.621	0.86 (0.31 to 2.40)	0.772
Adjusted	0.86 (0.32 to 2.27)	0.760	0.89 (0.35 to 2.26)	0.798	0.82 (0.30 to 2.26)	0.700
(None) vs. reference = (severe, moderate or mild)						
Baseline	1.45 (0.33 to 6.39)	0.623	1.77 (0.44 to 7.13)	0.425	1.47 (0.31 to 6.94)	0.628
Adjusted	1.58 (0.36 to 6.87)	0.540	1.98 (0.49 to 7.93)	0.335	1.57 (0.33 to 7.33)	0.570
6 months post operation *(Moderate, mild or none) vs. reference = (severe)*						
Baseline	2.95 (0.81 to 10.71)	0.100	2.80 (0.85 to 9.29)	0.091	3.08 (0.81 to 11.68)	0.097
Adjusted	2.48 (0.70 to 8.82)	0.161	2.73 (0.82 to 9.09)	0.101	2.55 (0.69 to 9.44)	0.162
(Mild or none) vs. reference = (severe or moderate)						
Baseline	1.83 (0.68 to 4.95)	0.235	1.84 (0.72 to 4.72)	0.205	1.92 (0.68 to 5.40)	0.217
Adjusted	1.70 (0.64 to 4.52)	0.289	1.98 (0.78 to 5.05)	0.151	1.71 (0.62 to 4.73)	0.303
(None) vs. reference = (severe, moderate or mild)						
Baseline	1.92 (0.58 to 6.29)	0.283	1.98 (0.63 to 6.23)	0.242	1.68 (0.49 to 5.75)	0.408
Adjusted	2.03 (0.63 to 6.55)	0.235	2.42 (0.76 to 7.66)	0.134	1.72 (0.51 to 5.81)	0.380

a Modelled with multilevel ordinal regression allowing for partial proportional odds. Baseline model adjusted for baseline pain score and surgical approach. Adjusted model: baseline model adjusted for working status, comorbidities, depression and anxiety.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 19 Intention-to-treat and per-protocol analyses of the effect of the intervention on pain (ICOAP)[a] at 3, 6 and 12 months after surgery in the APEX THR trial

	ITT-CC		ITT-imputed		PP	
Analysis model	RR (95% CI)	*p*-value	RR (95% CI)	*p*-value	RR (95% CI)	*p*-value
***3 months*[b]**	***(n = 259)***		***(n = 322)***		***(n = 246)***	
Baseline	0.58 (0.30 to 1.15)	0.120	0.56 (0.29 to 1.08)	0.086	0.59 (0.30 to 1.15)	0.122
Adjusted	0.66 (0.34 to 1.29)	0.222	0.65 (0.34 to 1.25)	0.195	0.66 (0.34 to 1.30)	0.233
***6 months*[b]**	***(n = 251)***		***(n = 322)***		***(n = 239)***	
Baseline	0.77 (0.37 to 1.62)	0.495	0.69 (0.35 to 1.38)	0.295	0.77 (0.35 to 1.68)	0.515
Adjusted	0.88 (0.41 to 1.86)	0.731	0.80 (0.40 to 1.60)	0.525	0.88 (0.40 to 1.92)	0.742
***12 months*[c]**	***(n = 265)***		***(n = 322)***		***(n = 251)***	
Baseline	0.40 (0.18 to 0.86)	0.020	0.49 (0.25 to 0.96)	0.038	0.42 (0.19 to 0.92)	0.031
Adjusted	0.44 (0.21 to 0.96)	0.038	0.58 (0.30 to 1.14)	0.115	0.47 (0.22 to 1.03)	0.059

RR, relative risk.

a Modelled as ICOAP pain (≥ 30, < 30).

b Modelled with an extension of the Poisson modified regression with robust variance estimation to account for repeated measurements.

c Modelled with a Poisson modified regression with robust variance estimation.

Note

Baseline model adjusted for baseline pain score and surgical approach. Adjusted model: baseline model plus adjustments for sex, living arrangement and number of comorbidities.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 20 Intention-to-treat and per-protocol analyses of the effect of the intervention on pain (ICOAP)[a] at 3, 6 and 12 months after surgery in the APEX TKR trial

	ITT-CC		ITT-imputed		PP	
Analysis model	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value
3 months[b]	***(n = 242)***		***(n = 316)***		***(n = 231)***	
Baseline	0.11 (–0.50 to 0.72)	0.725	0.13 (–0.44 to 0.71)	0.649	0.08 (–0.54 to 0.70)	0.801
Adjusted	0.12 (–0.48 to 0.72)	0.697	0.10 (–0.49 to 0.68)	0.746	0.11 (–0.49 to 0.72)	0.711
6 months[b]	***(n = 231)***		***(n = 316)***		***(n = 218)***	
Baseline	–0.46 (–1.08 to 0.15)	0.140	–0.38 (–0.98 to 0.21)	0.205	–0.47 (–1.10 to 0.16)	0.144
Adjusted	–0.45 (–1.06 to 0.16)	0.146	–0.42 (–1.01 to 0.16)	0.158	–0.45 (–1.07 to 0.17)	0.159
12 months[c]	***(n = 257)***		***(n = 316)***		***(n = 243)***	
Baseline	–0.15 (–0.76 to 0.48)	0.646	–0.06 (–0.68 to 0.57)	0.855	–0.16 (–0.81 to 0.50)	0.632
Adjusted	–0.29 (–0.90 to 0.34)	0.380	–0.20 (–0.81 to 0.42)	0.529	–0.30 (–0.95 to 0.35)	0.364

a Modelled as square root of ICOAP.
b Modelled with a linear mixed regression.
c Modelled with a linear regression.

Note
Baseline model adjusted for baseline pain score and surgical approach, Adjusted model: baseline model plus adjustments for working status, number of comorbidities, depression and anxiety.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 21 Intention-to-treat and per-protocol analyses of the effect of the intervention on function (WOMAC)[a] at 3, 6 and 12 months after surgery in the APEX THR trial

	ITT-CC		ITT-imputed		PP	
Analysis model	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value
3 months[b]	***(n = 257)***		***(n = 322)***		***(n = 244)***	
Baseline	636.04 (71.40 to 1200.68)	0.027	632.0 (40.01 to 1223.99)	0.036	614.4 (42.3 to 1186.5)	0.035
Adjusted	487.9 (–59.29 to 1035.1)	0.081	472.8 (–102.7 to 1048.3)	0.107	443.9 (–108.0 to 995.9)	0.115
6 months[b]	***(n = 254)***		***(n = 322)***		***(n = 241)***	
Baseline	326.6 (–239.28 to 892.40)	0.258	425.9 (–141.8 to 993.5)	0.141	265.1 (–308.0 to 838.2)	0.365
Adjusted	188.2 (–361.7 to 738.1)	0.502	266.7 (–286.5 to 819.9)	0.344	106.6 (–447.5 to 660.7)	0.706
12 months[c]	***(n = 266)***		***(n = 322)***		***(n = 252)***	
Baseline	500.6 (–80.6 to 1081.9)	0.091	623.4 (46.1 to 1200.7)	0.034	400.7 (–192.2 to 993.6)	0.184
Adjusted	459.4 (–97.3 to 1016.13)	0.105	499.4 (–58.61 to 1057.5)	0.079	363.2 (–201.3 to 930.7)	0.209

a Modelled as WOMAC function.
b Modelled with a linear mixed model.
c Modelled with a linear model.

Note
Baseline model adjusted for baseline pain score and surgical approach. Adjusted model: baseline model plus adjustments for sex, living arrangement and number of comorbidities.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 22 Intention-to-treat and per-protocol analyses of the effect of the intervention on function (WOMAC) at 3, 6 and 12 months after surgery in the APEX TKR trial

	ITT-CC		ITT-imputed		PP	
Analysis model	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value
3 months[a]	***(n = 233)***		***(n = 316)***		***(n = 223)***	
Baseline	0.19 (–4.12 to 4.50)	0.931	–0.68 (–4.99 to 3.64)	0.759	0.60 (–3.86 to 5.07)	0.790
Adjusted	0.71 (–3.44 to 4.86)	0.738	0.04 (–4.13 to 4.21)	0.985	0.97 (–3.32 to 5.26)	0.658
6 months[a]	***(n = 227)***		***(n = 316)***		***(n = 215)***	
Baseline	2.54 (–1.79 to 6.88)	0.250	1.76 (–2.56 to 6.09)	0.425	2.82 (–1.67 to 7.32)	0.218
Adjusted	2.97 (–1.21 to 7.15)	0.164	2.48 (–1.72 to 6.67)	0.247	3.11 (–1.21 to 7.44)	0.159
12 months[b]	***(n = 258)***		***(n = 316)***		***(n = 246)***	
Baseline	1.20 (–3.24 to 5.65)	0.594	1.81 (–3.38 to 7.00)	0.491	1.22 (–3.41 to 5.86)	0.604
Adjusted	1.88 (–2.49 to 6.24)	0.398	3.03 (–2.22 to 8.28)	0.256	1.85 (–2.69 to 6.40)	0.422

a Modelled with a linear mixed regression.
b Modelled with a linear regression.

Note
Baseline model adjusted for baseline pain score and surgical approach. Adjusted model: baseline model plus adjustments for working status, number of comorbidities, depression and anxiety.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 23 Intention-to-treat and per-protocol analyses of the effect of the intervention on stiffness (WOMAC)[a] at 3, 6 and 12 months after surgery for the APEX THR trial

	ITT-CC		ITT-imputed		PP	
Analysis model	RR (95% CI)	*p*-value	RR (95% CI)	*p*-value	RR (95% CI)	*p*-value
***3 months*[b]**	***(n = 258)***		***(n = 322)***		***(n = 245)***	
Baseline	0.87 (0.50 to 1.53)	0.634	0.80 (0.46 to 1.37)	0.414	0.97 (0.55 to 1.72)	0.920
Adjusted	0.96 (0.55 to 1.67)	0.881	0.86 (0.51 to 1.45)	0.566	1.08 (0.62 to 1.90)	0.784
***6 months*[b]**	***(n = 246)***		***(n = 322)***		***(n = 233)***	
Baseline	0.99 (0.45 to 2.19)	0.990	0.96 (0.46 to 2.00)	0.921	1.01 (0.44 to 2.30)	0.983
Adjusted	1.03 (0.48 to 2.21)	0.942	1.03 (0.50 to 2.13)	0.927	1.05 (0.47 to 2.34)	0.907
***12 months*[c]**	***(n = 266)***		***(n = 322)***		***(n = 252)***	
Baseline	0.60 (0.29 to 1.24)	0.167	0.55 (0.29 to 1.04)	0.068	0.68 (0.33 to 1.44)	0.318
Adjusted	0.64 (0.31 to 1.35)	0.246	0.64 (0.34 to 1.21)	0.173	0.73 (0.34 to 1.56)	0.414

RR, relative risk.

a Modelled as stiffness (WOMAC) (≤ 50, > 50).

b Modelled with an extension of the Poisson modified regression with robust variance estimation to account for repeated measurements.

c Modelled with a Poisson modified regression with robust variance estimation.

Note

Baseline model adjusted for baseline pain score and surgical approach. Adjusted model: baseline model plus adjustments for sex, living arrangement and number of comorbidities.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 24 Intention-to-treat and per-protocol analyses of the effect of the intervention on stiffness (WOMAC) at 3, 6 and 12 months after surgery in the APEX TKR trial

	ITT-CC		ITT-imputed		PP	
Analysis model	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value	Coefficient (95% CI)	*p*-value
3 months[a]	***(n = 237)***		***(n = 316)***		***(n = 227)***	
Baseline	2.94 (–2.05 to 7.94)	0.248	1.23 (–3.85 to 6.30)	0.635	2.89 (–2.24 to 8.02)	0.270
Adjusted	3.53 (–1.44 to 8.49)	0.164	2.10 (–3.04 to 7.24)	0.423	3.20 (–1.91 to 8.30)	0.219
6 months[a]	***(n = 228)***		***(n = 316)***		***(n = 216)***	
Baseline	4.03 (–1.02 to 9.08)	0.117	3.22 (–2.06 to 8.52)	0.234	3.68 (–1.52 to 8.89)	0.166
Adjusted	4.54 (–0.47 to 9.55)	0.076	4.09 (–1.18 to 9.36)	0.128	3.93 (–1.24 to 9.09)	0.136
12 months[b]	***(n = 256)***		***(n = 316)***		***(n = 242)***	
Baseline	1.78 (–3.21 to 6.78)	0.483	1.81 (–3.38 to 7.00)	0.491	1.77 (–3.40 to 6.94)	0.500
Adjusted	2.70 (–2.37 to 7.77)	0.296	3.03 (–2.22 to 8.28)	0.256	2.63 (–2.63 to 7.89)	0.325

a Modelled with a linear mixed regression.
b Modelled with a linear regression.

Note
Baseline model adjusted for baseline pain score and surgical approach. Adjusted model: baseline model plus adjustments for working status, number of comorbidities, depression and anxiety.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 25 Intention-to-treat and per-protocol analyses of the effect of the intervention on neuropathic pain as measured by painDETECT (< 13, ≥ 13) at 12 months after surgery[a] in the APEX THR trial

	ITT-CC ($n = 267$)		ITT-imputed ($n = 322$)		PP ($n = 253$)	
Analysis model	RR (95% CI)	*p*-value	RR (95% CI)	*p*-value	RR (95% CI)	*p*-value
Baseline	0.17 (0.04 to 0.76)	0.021	0.21 (0.05 to 0.83)	0.027	0.17 (0.04 to 0.77)	0.022
Adjusted	0.17 (0.03 to 0.82)	0.028	0.22 (0.05 to 0.90)	0.035	0.16 (0.03 to 0.83)	0.030

RR, relative risk.

a Modelled with a Poisson modified regression with robust variance estimation.

Note

Baseline model adjusted for baseline pain score and surgical approach. Adjusted model: baseline model plus adjustments for sex, living arrangement and number of comorbidities.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 26 Intention-to-treat and per-protocol analyses of the effect of the intervention on neuropathic pain as measured by painDETECT (< 13, ≥ 13) at 12 months after surgery[a] in the APEX TKR trial

	ITT-CC ($n = 254$)		ITT-imputed ($n = 316$)		PP ($n = 241$)	
Analysis model	RR (95% CI)	*p*-value	RR (95% CI)	*p*-value	RR (95% CI)	*p*-value
Baseline	0.92 (0.60 to 1.42)	0.715	0.99 (0.67 to 1.47)	0.973	0.94 (0.60 to 1.47)	0.792
Adjusted	0.95 (0.61 to 1.49)	0.834	1.05 (0.69 to 1.61)	0.796	0.98 (0.62 to 1.53)	0.918

RR, relative risk.

a Modelled with a Poisson modified regression with robust variance estimation.

Note

Baseline model adjusted for baseline pain score and surgical approach. Adjusted model: baseline model plus adjustments for working status, number of comorbidities depression and anxiety.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 27 Patient complications and serious adverse events in the APEX THR trial

Patient complications and SAE	Intervention ($N = 163$)	Standard care ($N = 159$)	p-value[a]
Deceased patient, *n* (%)	0 (0.0)	6 (3.8)	N/A
Patient with an infection, *n* (%)[b]	3 (1.8)	3 (1.9)	1.000
Patients with SAE, *n* (%)	41 (25.2)	55 (34.6)	0.090
Patients by count of SAEs, *n* (%)			0.611
1	29 (17.8)	44 (27.7)	
2	10 (6.1)	9 (5.7)	
3	2 (1.2)	2 (1.3)	
Total SAEs, *n*	55	68	
Expedited SAEs, %	85.5	82.4	0.640

N/A, not applicable; SAE, serious adverse event.
a Chi-squared test or Fisher-exact test.
b Superficial or deep surgical site infection.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 28 Patient complications and serious adverse events for the APEX TKR trial

Patient complications and SAE	Intervention ($N = 157$)	Standard care ($N = 159$)	p-value[a]
Deceased patient, *n* (%)	3 (1.9)	1 (0.6)	0.369
Patient with an infection, *n* (%)[b]	5 (3.2)	3 (1.9)	0.500
Patients with SAE, *n* (%)	63 (40.1)	58 (36.5)	0.505
Patients by count of SAEs, *n* (%)			0.685
1	48 (30.6)	48 (30.2)	
2	11 (7.0)	8 (5.0)	
3	4 (2.6)	2 (1.3)	
Total SAEs, *n*	82	69	
Expedited SAEs, %	85.4	82.9	72

SAE, serious adverse event.
a Chi-squared test or Fisher-exact test.
b Superficial or deep surgical site infection.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 29 Pre-operative hip X-ray form

Study ID						Initials				DOB							

A1a. Reader: Reader1 Other (Please Specify)……

A2. Date X-ray read: ……/……/……

A3. Date X-ray taken: ……/……/……

B1. Technical problem- film cannot be assessed accurately No ☐ Yes ☐

B2. Severe rotation (position of greater trochanters) No ☐ Yes ☐

B3. Severe tilt of film (Coccyx overlap >3mm with symphysis) No ☐ Yes ☐

	(i) Right	(ii) Left
B4. Intra-articular implant (0/1)		
B5. Kellgren and Lawrence (0-4)		
B6. Superior acetabular ostephyte (0-3)		
B7. Superior femoral osteophyte (0-3)		
B8. Inferior acetabular osteophyte (0/1)		
B9. Inferior femoral osteophyte (0/1)		
B10. Acetabular sclerosis (0/1)		
B11. Acetabular cysts (0/1)		
B12. Acetabular flattening (0/1)		
B13. Femoral sclerosis (0/1)		
B14. Femoral cysts (0/1)		
B15. Femoral flattening (0/1)		
B16. Superior joint space narrowing (0-3)		
B17. Medial joint space narrowing (0-3)		
B18. Chondrocalcinosis (0/1)		
B19. Migration: None = 0; Superolateral = 1 Concentric = 2		
B20. No pattern = 0; hypertrophic = 1; atrophic = 2		
B21. Protrusio (0/1)		
B22. FAI Bump (0/1)		

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 30 Pre-operative knee X-ray form

Study ID						Initials				DOB					19		

A1a. Reader : Reader1 Other[2] A1b. If other, please specify ……..

A2. Date X-ray read: ……/……/……

A3. Date X-ray taken: ……/……/……

AP Knees

B1. Technical problem – film cannot be assessed accurately No[0] ☐ Yes[1] ☐

B2. Severe rotation of film No[0] ☐ Yes[1] ☐

B3. Severe tilt of film (Medial tibial plateau superimposition >1mm) No[0] ☐ Yes[1] ☐

		(i) Right	(ii) Left
B4.	Intra-articular knee implant (0/1)		
B5.	Kellgren & Lawrence (0-4)		
B6.	Medial tibial osteophyte (0-3)		
B7.	Medial femoral osteophyte (0-3)		
B8.	Lateral tibial osteophyte (0-3)		
B9.	Lateral femoral osteophyte (0-3)		
B10	Medial joint space narrowing (0-3)		
B11.	Lateral joint space narrowing (0-3)		
B12.	Medial subchondral sclerosis (0/1)*		
B13	Lateral subchondral sclerosis (0/1)*		
B14	Medial bony attrition (0/1)*		
B15	Lateral bony attrition (0/1)*		
B16	Chondrocalcinosis (0/1)		

Lateral Knees

C1. Technical problem – film cannot be assessed accurately No[0] ☐ Yes[1] ☐

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

C2. Severe rotation of film No[0] ☐ Yes[1] ☐

		(i) Right	(ii) Left
C3.	Intra-articular knee implant (0/1)		
C4.	Superior osteophyte (0-3)		
C5.	Inferior osteophyte (0-3)		
C6.	Joint space narrowing (0-3)		

Skyline Knees

		(i) Right	(ii) Left
D1.	Not done (=0), Available (=1)		
D2.	Medial PFJ narrowing (0/1)		
D3.	Lateral PFJ narrowing (0/1)		
D4.	PFJ subluxation (absent=0, lateral=1, medial=2)		

		(i) Right	(ii) Left
E	**Pattern:** 0=No OA, 1=Medial, 2=Lateral, 3=Patellofemoral, 4=Bicompartmental/tricompartmental		

E . Notes

*either femur, tibia or both

Appendix 31 Pre-surgical exercise and educational interventions before total hip and knee replacement: Cochrane risk-of-bias table

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data addressed (attrition bias)	Lack of selective reporting (reporting bias)	Lack of other sources of bias	Our evaluation
Aoki and colleagues 2009[509]	~	~	✓	✓	✓	✓	Low risk of bias (allocated by odd or even last digit of hospital number; no losses to follow-up described)
Beaupre and colleagues 2004[510]	✓	✓	✓	~	✓	✓	Unclear: no reason to assume bias (10 intervention and six control patients excluded from analyses as they did not have joint replacement eligible for Review A. It is possible that the intervention was 'highly effective' in improving function and pain)
Berge and colleagues 2004[487]	✓	~	✓	~	✓	✓	Unclear: no reason to assume bias (two control group patients decided to delay joint replacement and were excluded from analyses; three control patients had operation early and lost to follow-up)
Bitterli and colleagues 2009[488]	✓	✓	✓	~	✓	~	Unclear: no reason to assume bias (two intervention group patients had joint replacement brought forward. 9/41 intervention and 9/39 control patients lost to follow-up)
Bondy and colleagues 1999[526]	✓	~	✓	✗	✓	✓	Possible bias (6/17 intervention and 8/15 control patients lost to follow-up)
Börjesson and colleagues 1996[511]	~	~	✓	✓	✓	✓	Low risk of bias
Brown and colleagues 2012[512]	~	✓	✓	✗	✓	✓	Possible bias (6/17 intervention and 8/15 control patients lost to follow-up)
Butler and colleagues 1996[489] and from McDonald and colleagues 2004[83]	~	✓	✓	✗	✓	✓	Possible bias (data analysed for primary replacement but all hip replacement patients randomised; no follow-up of 8/80 patients)
Clode-Baker and colleagues 1997[490] and from McDonald and colleagues 2004[83]	✓	~	✓	✗	✓	✓	Possible bias (no details on distribution between randomised groups of 13 patients with cancelled operations)
Cooil and Bithell 1997[491]	✓	~	✓	✓	✓	✓	Low risk of bias

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data addressed (attrition bias)	Lack of selective reporting (reporting bias)	Lack of other sources of bias	Our evaluation
Crotty and colleagues 2009[527]	✓	✓	✓	✓	✓	✓	Low risk of bias
Crowe and Henderson 2003[528]	✓	✓	✓	~	✓	✓	Unclear: no reason to assume bias (5/65 losses to follow-up – discharge destination – in intervention but none in control groups, other losses not shown)
Cuñado Barrio and colleagues 1999[529]	✓	✓	✓	✗	✓	✓	Possible bias (1/42 intervention and 7/42 control patients lost to follow-up)
Daltroy and colleagues 1998[530]	✓	~	✓	✓	✓	✓	Low risk of bias
D'Lima and colleagues 1996 cardiac[513]	✓	~	~	✗	✓	✗	Possible bias (small numbers of patients: baseline demographic differences)
D'Lima and colleagues 1996 physical therapy[513]	✓	~	~	✗	✓	✗	Possible bias (small numbers of patients: baseline demographic differences)
Doering and colleagues 2000[492]	~	~	✓	✓	✓	✓	Low risk of bias
Evgeniadis and colleagues 2008[514]	✓	✓	✓	~	✓	✓	Unclear: no reason to assume bias (5/48 patients lost to follow-up)
Ferrara and colleagues 2008[493]	✓	~	✓	~	✓	✓	Low risk of bias (0/11 and 2/12 control patients lost to 3-month follow-up)
Gilbey and colleagues 2003[494]	~	✓	~	✓	✓	~	Unclear: no reason to assume bias (alternate allocation within blocks of patient age, 2/37 intervention patients chose to delay surgery)
Giraudet Le Quintrec and colleagues 2003[495]	✓	✓	✓	✓	✓	~	Low risk of bias. Possible bias for anxiety outcome (imbalance in baseline anxiety between groups)
Gocen and colleagues 2004[496]	✓	~	✓	✓	✓	✗	Possible bias (intervention patients significantly younger than controls)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data addressed (attrition bias)	Lack of selective reporting (reporting bias)	Lack of other sources of bias	Our evaluation
Gstoettner and colleagues 2011[515]	✓	✓	~	✓	✓	✗	Possible bias (control group baseline pain and function values used for comparison with post-intervention pre-surgical outcome)
Heikkinen and colleagues 2008[516]	✓	~	✓	✓	✓	✓	Low risk of bias
Hoogeboom and colleagues 2010[497]	✓	✓	✓	✓	✓	✓	Low risk of bias (one control patient lost to follow-up unexplained)
Huang and colleagues 2012[517]	~	~	~	✓	✓	✓	Unclear: no reason to assume bias (randomly allocated by chart number)
Johansson and colleagues 2007[498]	✓	✓	✓	~	✓	✓	Unclear: no reason to assume bias (length of stay data from hospital notes, 18/123 lost to follow-up)
Lewis and colleagues 2002[531]	~	~	~	✓	✓	✓	Unclear: no reason to assume bias
Lilja and colleagues 1998[499]	~	~	✓	~	✓	✓	Unclear: no reason to assume bias (one patient refused to participate after randomisation and 3/22 intervention and 1/28 control patients withdrawn for medical reasons
Liu and Lu 2004[532]	~	~	✓	✓	✓	✓	Low risk of bias
Mancuso and colleagues 2008 hips[500]	~	✓	✓	✓	✓	✓	Low risk of bias (class was unit of randomisation)
Mancuso and colleagues 2008 knees[500]	~	✓	✓	✓	✓	✓	Low risk of bias (class was unit of randomisation)
McDonald and colleagues 2001[533]	✓	✓	✓	✗	✓	✓	Possible bias (7/20 intervention and 2/20 control patients lost to follow-up)
McDonald and Molony 2004 communication[518]	✓	✓	✓	✓	✓	~	Unclear: no reason to assume bias (recruitment to control group stopped early)

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data addressed (attrition bias)	Lack of selective reporting (reporting bias)	Lack of other sources of bias	Our evaluation
McDonald and Molony 2004 pain management[518]	✓	✓	✓	✓	✓	~	Unclear: no reason to assume bias (recruitment to control group stopped early)
McGregor and colleagues 2004[501]	✓	✓	✓	✗	✓	✓	Possible bias (4/19 intervention patients lost to review)
McKay and colleagues 2012[519]	✓	✓	✓	✗	✓	✗	Possible bias (baseline differences in WOMAC pain and function, 5/22 lost to 12-week follow-up)
Mitchell and colleagues 2005[520]	✓	✓	✓	~	✓	✓	Unclear: no reason to assume bias (45/160 withdrawals including 24 patients with surgery cancelled). No evidence that study withdrawal varied by group or WOMAC scores
Nuñez and colleagues 2006[521]	✓	✓	✓	~	✓	✓	Low risk of bias (20% loss to follow-up but no evidence that the loss of patients was related to baseline characteristics or to group)
Oosting and colleagues 2012[502]	✓	✓	✓	~	✓	✓	Low risk of bias (0/15 and 2/15 lost to pre-surgical follow-up)
Pellino and colleagues 1998[534]	✓	✓	✓	~	✓	✗	Possible bias (recruitment into intervention quicker than control group, surgery delayed more frequently in control group)
Rooks and colleagues 2006 hips[503]	✓	✓	✓	~	✓	✗	Possible bias (14/63 lost to follow-up, dropouts had a higher level of function than completers)
Rooks and colleagues 2006 knees[503]	✓	✓	✓	~	✓	✓	Low risk of bias (16/45 lost to follow-up but baseline characteristics similar)
Sandell 2008[504]	✓	✓	✓	✗	✓	✓	Possible bias (22/89 patients had surgery before follow-up)
Santavirta and colleagues 1994[505] and McDonald and colleagues 2004[83]	~	~	✗	~	✓	✓	Unclear: no reason to assume bias (postponement or other loss to follow-up similar in intervention 7/27 and control 6/33)

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data addressed (attrition bias)	Lack of selective reporting (reporting bias)	Lack of other sources of bias	Our evaluation
Sjöling and colleagues 2003[522]	~	~	✓	✓	✓	✓	Low risk of bias (alternate allocation after first chosen at random)
Swank and colleagues 2011[523]	✓	✓	~	✓	✓	✓	Unclear: no reason to assume bias (outcomes on patients who completed both testing sessions)
Vukomanovic and colleagues 2008[506]	✓	✓	✓	~	✓	✓	Low risk of bias (5/23 intervention and 4/22 lost to longer-term follow-up)
Weidenhielm and colleagues 1993[524]	~	~	~	✓	✓	✓	Unclear: no reason to assume bias (allocation by drawing lots)
Wijgman and colleagues1994[507] and McDonald and colleagues 2004[83]	~	~	~	✓	~	✓	Unclear: no reason to assume bias
Williamson and colleagues 2007[525]	✓	✓	✓	✗	✓	✓	Possible bias (before surgery there were 7/60 intervention and 2/61 control patients lost to follow-up, large losses to follow-up after surgery)
Wong and Wong 1985[508]	~	~	✓	✗	✓	✓	Low risk of bias

✓, low risk of bias; ✗, possible risk of bias; ~, unclear: no reason to assume bias.

Note

Extra information provided by Bitterli and colleagues,[488] Ackland and colleagues,[494] Hoogeboom and colleagues,[497] McDonald and Molony,[518] McDonald colleagues,[533] Núñez and colleagues [521] and Aoki and colleagues.[509]

Appendix 32 Occupational therapy in total hip replacement: Cochrane risk-of-bias table

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data addressed (attrition bias)	Lack of selective reporting (reporting bias)	Lack of other sources of bias	Our evaluation
Butler and colleagues 1996[489] and McDonald and colleagues 2004[83]	~	✓	✓	✗	✓	✗	Possible bias (data analysed for primary replacement but all hip replacement patients randomised; no follow-up of 8/80 patients)
Ferrara and colleagues 2008[493]	✓	~	✓	~	✓	✓	Low risk of bias in short term. Unclear: no reason to assume bias in long-term (small study with 3/12 control patients lost to follow-up)
Gocen and colleagues 2004[496]	✓	~	✓	✓	✓	✗	Unclear: no reason to assume bias (intervention patients were significantly younger than control patients)
McGregor and colleagues 2004[501]	✓	✓	✓	✗	✓	✓	Possible bias (4/19 intervention patients were lost to review)
Munin and colleagues 1998[567]	✓	✓	~	✗	✓	✓	Possible bias (9/35 patients lost to follow-up)
Sandell 2008[504]	✓	✓	✓	✗	✓	✓	Possible bias (large loss to follow-up mainly owing to 22 patients having surgery before follow-up)
Siggeirsdottir and colleagues 2005[568]	✓	✓	✓	~	✓	✓	Low risk of bias (3/23 controls lost to 6-month follow-up)

✓, low risk of bias; ✗, possible risk of bias; ~, unclear: no reason to assume bias.

Appendix 33 PROOF-THR detailed summary of European Quality of Life-5 Dimensions scale

Topic	Baseline ($n = 44$)	4 weeks ($n = 36$)	12 weeks ($n = 37$)	26 weeks ($n = 36$)
Mobility				
I have no problems in walking about	0%	44%	68%	72%
I have some problems in walking about	100%	56%	32%	28%
I am confined to bed	0%	0%	0%	0%
Self-care				
I have no problems with self-care	36%	60%	76%	94%
I have some problems washing or dressing myself	64%	40%	21%	6%
I am unable to wash or dress myself	0%	0%	3%	0%
Usual activities				
I have no problems with performing my usual activities	14%	31%	54%	74%
I have some problems with performing my usual activities	77%	47%	41%	26%
I am unable to perform my usual activities	9%	22%	5%	0%
Pain/discomfort				
I have no pain or discomfort	0%	29%	43%	60%
I have moderate pain or discomfort	57%	66%	54%	40%
I have extreme pain or discomfort	43%	6%	3%	0%
Anxiety/depression				
I am not anxious or depressed	66%	71%	84%	78%
I am moderately anxious or depressed	34%	29%	13%	22%
I am extremely anxious or depressed	0%	0%	3%	0%

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 34 PROOF-THR detailed summary of ICECAP scale (baseline data)

Topic	Baseline ($n = 44$)	4 weeks ($n = 36$)	12 weeks ($n = 37$)	26 weeks ($n = 36$)
Love and friendship				
I cannot have any of the love and friendship that I want	5%	3%	3%	3%
I can have a little of the love and friendship that I want	9%	8%	5%	3%
I can have a lot of the love and friendship that I want	23%	40%	22%	19%
I can have all the love and friendship that I want	64%	49%	70%	75%
Thinking about the future				
I can only think about the future with a lot of concern	9%	6%	5%	3%
I can only think about the future with some concern	11%	11%	14%	11%
I can think about the future with only a little concern	55%	44%	38%	43%
I can think about the future without any concern	25%	39%	43%	43%
Doing things that make you feel valued				
I am unable to do any of the things that make me feel valued	5%	3%	2%	0%
I am able to do a few of the things that make me feel valued	23%	17%	11%	6%
I am able to do many of the things that make me feel valued	48%	54%	38%	36%
I am able to do all of the things that make me feel valued	25%	26%	49%	58%
Enjoyment and pleasure				
I cannot have any of the enjoyment and pleasure that I want	2%	3%	3%	0%
I can have a little of the enjoyment and pleasure that I want	43%	36%	16%	5%
I can have a lot of the enjoyment and pleasure that I want	39%	36%	46%	42%
I can have all of the enjoyment and pleasure that I want	16%	25%	35%	53%
Independence				
I am unable to be at all independent	2%	3%	3%	0%
I am able to be independent in a few things	23%	13%	5%	3%
I am able to be independent in many things	45%	65%	43%	36%
I am able to be completely independent	30%	19%	49%	61%

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 35 Physiotherapy interventions after total knee replacement: Cochrane risk-of-bias table

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data addressed (attrition bias)	Lack of selective reporting (reporting bias)	Lack of other sources of bias	Our evaluation
Evgeniadis and colleagues 2008[514]	✓	✓	✓	✗	✓	✓	Possible bias (9/24 intervention and 4/24 control patients lost to follow-up
Frost and colleagues 2002[588]	✓	~	✓	✗	✓	✓	Possible bias (7/23 intervention and 13/24 control patients lost to follow-up)
Fung and colleagues 2012[589]	✓	✓	✓	✓	✓	✓	Low risk of bias
Harmer and colleagues 2009[590]	✓	✓	✓	✓	✓	✓	Low risk of bias (small losses to follow-up)
Kauppila and colleagues 2010[591]	✓	~	✗	✗	✓	✗	Possible risk of bias (8/44 intervention and 3/42 control patients lost to follow-up, owing to uneven losses to follow-up, baseline differences in prevalence of comorbidities and WOMAC score)
Kramer and colleagues 2003[592] and Minns Lowe 2007[84]	~	~	✓	✗	✓	✓	Possible risk of bias ('medical issue' losses to follow-up differed between groups, 7.5% in clinic and 15% in home-based groups)
Liebs and colleagues 2010[593]	✓	✓	✓	✗	✓	✓	Possible risk of bias (10/85 intervention and 14/74 control patients lost to follow-up)
Madsen and colleagues 2013[594]	✓	✓	✓	✗	✓	✓	Possible risk of bias (4/40 intervention and 8/40 control patients lost to follow-up)
Minns Lowe and colleagues 2012[595]	✓	✓	✓	✓	✓	✓	Low risk of bias (low losses to follow-up at 12 months)
Mitchell and colleagues 2005[520]	✓	✓	✓	✓	✓	~	Low risk of bias (randomisation before surgery with pre-surgical intervention component). Surgery cancelled for 24 patients
Mockford and colleagues 2008[596]	✓	✓	✓	✓	✓	✓	Low risk of bias (4.7% patients excluded from analysis as lost to follow-up)
Moffet and colleagues 2004[597]	✓	✓	✓	~	✓	✓	Low risk of bias. Possible risk of bias for 12 month outcomes (uneven loss to follow-up)

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data addressed (attrition bias)	Lack of selective reporting (reporting bias)	Lack of other sources of bias	Our evaluation
Monticone and colleagues 2013[598]	✓	✓	✓	✓	✓	✓	Low risk of bias
Piqueras and colleagues 2013[599]	✓	✓	✓	✓	✓	✓	Low risk of bias
Piva and colleagues 2010[600]	✓	✓	✓	~	✓	✓	Unclear: no reason to assume bias (3/21 intervention and 5/22 control patients lost to follow-up)
Rajan and colleagues 2004[601]	✓	~	✓	✓	✓	✓	Low risk of bias
Tousignant and colleagues 2011[602]	✓	✓	✓	~	✓	~	Unclear: no reason to assume bias (3/24 randomised to control withdrew owing to knowledge of group allocation. 3/24 intervention and 4/24 control patients lost to follow-up)

✓, low risk of bias; ✗, possible risk of bias; ~, unclear: no reason to assume bias.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 36 Telephone survey questionnaire for current provision of physiotherapy following discharge after total hip replacement and total knee replacement

The University of Bristol and North Bristol NHS Trust are running a research project investigating current post-operative physiotherapy received by patients following total hip and knee replacement after discharge from hospital.
Would it be possible to ask you questions about the current physiotherapy practice at your unit?

Part A - Physiotherapy provision following THR

Q1. What standard Physiotherapy intervention are patients offered following discharge after a total hip replacement?

Intervention	Tick
None offered	
Leaflet/booklet/exercise sheet	
Outpatient physiotherapy	
Circuit/group exercises	
Hydrotherapy	
Domiciliary	
Telephone consultation	
Drop in service	
Other (*please state*);	

Additional comments;

……
……
……
……
……

If patients are not referred for Physiotherapy

What is the referral process for patients to receive post-operative physiotherapy treatment?

……
……
……
……
……

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Physiotherapy Outpatient Intervention (*only*)

Q1. At what time point are patients referred to outpatients?

Time point	Tick
Within 2 weeks	
2-4 weeks	
4-8 weeks	
8 or more weeks	

Q2. On average how many treatment sessions do they receive?

Number of sessions	Tick
1	
2-4	
5-8	
9-12	
More than 12	
variable	

Q3. What is the typical treatment approach?

Treatment	Tick
Advice	
Specific joint exercises	
Functional exercises	
Manual therapy	
Electrotherapy	
Ice/Heat	
Acupuncture	
Pain management (CBT)	

Additional Information

.....

.....

.....

Group or exercise class-based physiotherapy (*only*)

Q1. At what time point are patients referred to exercise group/class?

Time point	Tick
Within 2 weeks	
2-4 weeks	
4-8 weeks	
8 or more weeks	

Q2. How many sessions do they receive?

Number of sessions	Tick
1	
2-4	
5-8	
9-12	
More than 12	

Q3. How long is each session?

Duration of sessions	Tick
0-30 mins	
30-45 mins	
45-60 mins	
More than 60 mins	

Q4. How many members of staff are involved in the sessions?

Q5. What grades are the staff involved in the sessions?

Q6. What treatment/exercises are involved in the sessions?

Treatment	Tick
Advice	
Specific joint strengthening	
Specific joint stretches	
Functional exercises	
Task-related exercises	
Cardiovascular exercises	
Relaxation	
Individualised exercises	
1:1 treatment component	

Additional information

.....

.....

.....

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Leaflet / Booklet / Exercise sheet provision

Q1. What is the content of the material handed out to patients with THR?

Content	Tick
Precautions	
Advice	
Range of motion exercises	
Strengthening exercises	
Stretching exercises	
Functional tasks/exercise	
Gait re-education	

Additional information

.....

.....

.....

Precautions following THR

What **precautions** are advised for patients following a primary total hip replacement? Please include ***time frames***.

.....

.....

.....

.....

.....

.....

.....

Part B - Physiotherapy provision following TKR

Q1. What standard Physiotherapy intervention are patients offered following discharge after a total knee replacement?

Intervention	Tick
None offered	
Leaflet/booklet/exercise sheet	
Outpatient physiotherapy	
Circuit/group exercises	
Hydrotherapy	
Domiciliary	

Telephone consultation	
Drop in service	
Other.....	

Additional comments;

.....
.....
.....
.....
.....

If patients are not referred for Physiotherapy

What is the referral process for patients to receive post-operative physiotherapy treatment?

.....
.....
.....
.....
.....
.....
.....
.....

Physiotherapy Outpatient Intervention (*only*)

Q1. At what time point are patients referred to outpatients?

Time point	Tick
Within 2 weeks	
2-4 weeks	
4-8 weeks	
8 or more weeks	

Q2. On average how many treatment sessions do they receive?

Number of sessions	Tick
1	
2-4	
5-8	
9-12	
More than 12	
variable	

Q3. What is the typical treatment approach?

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Treatment	Tick
Advice	
Specific joint exercises	
Functional exercises	
Manual therapy	
Electrotherapy	
Ice/Heat	
Acupuncture	
Pain management (CBT)	

Additional Information

.....

.....

.....

Group or exercise class-based physiotherapy (*only*)

Q1. At what time point are patients referred to exercise group/class?

Time point	Tick
Within 2 weeks	
2-4 weeks	
4-8 weeks	
8 or more weeks	

Q2. How many sessions do they receive?

Number of sessions	Tick
1	
2-4	
5-8	
9-12	
More than 12	

Q3. How long is each session?

Duration of sessions	Tick
0-30 mins	
30-45 mins	
45-60 mins	
More than 60 mins	

Q4. How many members of staff are involved in the sessions?

Q5. What grades of staff are used in the sessions?

Q6. What treatment/exercises are involved in the sessions?

Treatment	Tick
Advice	
Specific joint strengthening	
Specific joint stretches	
Functional exercises	
Task-related exercises	
Cardiovascular exercises	
Relaxation	
Individualised exercises	
1:1 treatment component	

Additional information

.....

.....

.....

Leaflet / Booklet / Exercise sheet provision

Q1. What is the content of the material handed out?

Content	Tick
Precautions	
Advice	
Range of motion exercises	
Strengthening exercises	
Stretching exercises	
Functional tasks/exercise	
Gait re-education	

Additional information

.....

.....

.....

What **precautions** are advised for patients following a primary total knee replacement? Please include ***time frames***.

.....

.....

.....

.....

.....

Thank you for taking the time to answer these questions.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 37 Job title of the respondent at each of the twenty-four orthopaedic centres surveyed

Orthopaedic unit	Procedure surveyed (THR/TKR)	Position of staff member surveyed
1	Both	Clinical therapies manager
2	Both	Orthopaedic therapy team lead
3	Both	Clinical lead
4	Both	Extended scope physiotherapy practitioner
5	Both	Clinical lead
6	Both	Team lead
7	Both	Therapy lead
8	Both	Senior physiotherapist
9	Both	Clinical lead
10	TKR only	Senior physiotherapist
11	Both	Clinical lead
12	Both	Senior physiotherapist
13	Both	Clinical lead
14	Both	Extended scope physiotherapy practitioner
15	TKR only	Senior orthopaedic physiotherapist
16	TKR only	Senior OT
17	TKR only	Senior physiotherapist
18	TKR only	Senior physiotherapist
19	TKR only	Senior physiotherapist
20	TKR only	Clinical lead
21	TKR only	Clinical lead
22	TKR only	Senior outpatient physiotherapist
23	TKR only	Senior orthopaedic physiotherapist
24	THR only	Outpatient manager

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Appendix 38 Study feedback reports for patients

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

WHAT'S NEXT?

The study team is now looking in more detail at the information. The results will be presented in academic journals, which ensure that policy makers and healthcare professionals hear about the research. They will also be available to all members of the public through our website.

We would like to thank you again for taking part. We hope that the research that is done at the Musculoskeletal Research Unit helps to provide better healthcare in the UK, and your participation was vital in this.

Contact details

If you have any questions about this study, please telephone Vikki Wylde on [redacted] or email mru-restore@bristol.ac.uk

Address:
Musculoskeletal Research Unit, Avon Orthopaedic Centre, Southmead Hospital, Bristol, BS10 5NB

http://www.bristol.ac.uk/clinicalsciences/research/musculoskeletal/orthopaedic/research/restore/

North Bristol NHS Trust

University of BRISTOL

Summary of findings

Apex study
Arthroplasty Pain Experience Study

DOI: 10.3310/pgfar04120

Thank you for being involved in the APEX study (Arthroplasty Pain Experience study). You were one of 322 people who kindly took part in this study.

BACKGROUND

The APEX study aimed to find out if an injection of local anaesthetic during a hip replacement operation could reduce pain in the first year after surgery.

STUDY DESIGN

Of the 322 people in the study, 159 people were chosen at random to have the 'usual care' that patients at Southmead normally receive. 163 other people were chosen at random to have an injection of local anaesthetic during their operation, in addition to 'usual care'. This was important as research needs to be able to compare the experiences of people having the 'usual care' with experiences of people having something new. Comparing both treatments provides information about which is best.

We asked everyone in the study to fill in questionnaires before their operation, in the first few days after their operation and then at 3-months, 6-months and 12-months after their operation. People were also invited to attend a research appointment at 12-months after their operation.

SOME KEY FINDINGS

- Most people in both groups had excellent pain relief at one year after their hip replacement. People in both groups generally experienced the biggest improvements in pain during the first 3 months after their operation.
- Patients who had the injection of local anaesthetic were less likely to have a high level of pain in their replaced hip one year after their operation.
- There was no difference in pain levels at 3 months and 6 months after surgery between patients who did and did not have the injection of local anaesthetic.
- We will be recommending that an injection of local anaesthetic is given to patients having a hip replacement. This is because our study suggests it can reduce the number of people who have a high level pain after their operation.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

WHAT'S NEXT?

The study team is now looking in more detail at the information. The results will be presented in academic journals, which ensure that policy makers and healthcare professionals hear about the research. They will also be available to all members of the public through our website.

We would like to thank you again for taking part. We hope that the research that is done at the Musculoskeletal Research Unit helps to provide better healthcare in the UK, and your participation was vital in this.

Contact details

If you have any questions about this study, please telephone Vikki Wylde on [redacted] or email mru-restore@bristol.ac.uk

Address:
Musculoskeletal Research Unit, Avon Orthopaedic Centre, Southmead Hospital, Bristol, BS10 5NB

http://www.bristol.ac.uk/clinicalsciences/research/musculoskeletal/orthopaedic/research/restore/

North Bristol NHS Trust

University of BRISTOL

Summary of findings

Apex study
Arthroplasty Pain Experience Study

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

DOI: 10.3310/pgfar04120

Thank you for being involved in the APEX study (Arthroplasty Pain Experience study). You were one of 316 people who kindly took part in this study.

BACKGROUND

The APEX study aimed to find out if an injection of local anaesthetic during a knee replacement operation could reduce pain in the first year after surgery.

STUDY DESIGN

Of the 316 people in the study, 159 people were chosen at random to have the 'usual care' that patients at Southmead normally receive. 157 other people were chosen at random to have an injection of local anaesthetic during their operation, in addition to 'usual care'. This was important as research needs to be able to compare the experiences of people having the 'usual care' with experiences of people having something new. Comparing both treatments provides information about which is best.

We asked everyone in the study to fill in questionnaires before their operation, in the first few days after their operation and then at 3-months, 6-months and 12-months after their operation. People were also invited to attend a research appointment at 12-months after their operation.

SOME KEY FINDINGS

- Most people in both groups had good pain relief at one year after their knee replacement. People in both groups generally experienced the biggest improvements in pain during the first 3 months after their operation.
- Patients who had the injection of local anaesthetic reported slightly less pain in their replaced knee at one year after their operation compared to patients who did not have the injection.
- There was no difference in pain levels at 3 months and 6 months after surgery between patients who did and did not have the injection of local anaesthetic.
- We will be recommending that an injection of local anaesthetic is given to patients having a knee replacement. This is because our study suggests it can slightly reduce the amount of pain people have in their replaced knee at one year after their operation.

NIHR Journals Library www.journalslibrary.nihr.ac.uk

Contact details

If you have any questions or you would like more information about this study, please telephone Vikki Wylde (study co-ordinator) on [redacted] or email mru-restore@bristol.ac.uk

Address:
Musculoskeletal Research Unit, Avon Orthopaedic Centre, Southmead Hospital, Bristol, BS10 5NB

http://www.bristol.ac.uk/clinical-sciences/research/musculoskeletal/orthopaedic/research/restore/

Some members of the ADAPT research team

North Bristol NHS Trust

University of BRISTOL

Summary of findings

ADAPT

Assessing disability after partial and total joint replacement

DOI: 10.3310/pgfar04120

Thank you for being involved in the ADAPT study. You were one of 254 people who kindly took part in this study which is one of the largest studies of this type.

BACKGROUND

The aim of the ADAPT study was to compare different ways that mobility can be measured in people who are having joint surgery. The study compared the information that can be collected though questionnaires with information that can be collected through mobility tests and joint examinations.

Everyone taking part in the study was asked to come for a research appointment before their operation, and then at 3 months and 1 year after their operation.

STUDY DESIGN

People who took part in the ADAPT study filled in a number of questionnaires about mobility and then completed the following mobility tests:

- Walking 20 metres down a corridor
- Getting up from a chair
- Stepping on and off a box
- Balancing on one leg

A researcher also looked at how much everyone's joint moved.

FINDINGS

Early findings suggest that questionnaires, mobility tests and joint examinations all provide different results. A person's level of joint pain clearly affected the results of all the different ways of measuring mobility.

This may seem obvious, but in fact this study is new because until now it was not clear that doctors needed to ask about pain to understand information about mobility collected in questionnaires and through tests in clinics.

The study team is working to analyse the information further. We expect findings to be available in the next two years, and these will be publicly available through our website (please see overleaf).

WHAT'S NEXT?

We would like to thank you again for taking part. The research that is done at the Musculoskeletal Research Unit helps to inform better healthcare in the UK, and your participation was vital in this. The results will now be presented in academic journals and at research conferences, which ensures that policy makers and healthcare professionals hear about the research.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

WHAT'S NEXT?

The study team is now looking in more detail at the information. We expect findings to be available in 2014 and these will be publicly available through our website.

We would like to thank you again for taking part. The research that is done at the Musculoskeletal Research Unit helps to inform better healthcare in the UK, and your participation was vital in this.

The results will now be presented in an academic journal, which ensures that policy makers and healthcare professionals hear about the research.

Contact details

If you have any questions or would like more information about this study, please telephone Vikki Wylde on [redacted] or email mru-restore@bristol.ac.uk

Address:
Musculoskeletal Research Unit, Avon Orthopaedic Centre, Southmead Hospital, Bristol, BS10 5NB

http://www.bristol.ac.uk/clinical-sciences/research/musculoskeletal/orthopaedic/research/restore/

University of BRISTOL

ARTHRITIS CARE

Summary of findings

Spiral Study

Self-managing pain in arthritis and arthroplasty

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

DOI: 10.3310/pgfar04120

Thank you for being involved in the SPIRAL study. You were one of 88 people who kindly took part in this study.

BACKGROUND

The SPIRAL study aimed to find out whether we could run a study of a pain self-management course for people having a hip replacement.

STUDY DESIGN

Of the 88 people in the study, 45 people were chosen at random to have 'standard care' that patients at Southmead normally receive. 43 other people were chosen at random to be invited to attend a new pain self-management course. This was important as research needs to be able to compare the experiences of people having the 'standard care' with experiences of people having something new.

We asked everyone in the study to fill in questionnaires before their operation, and then at 1-month, 3-months and 6-months after their operation. We needed to find out whether people would be willing to fill these in.

We also talked to 57 additional people who did not wish to take part in the study to find out why.

SOME KEY FINDINGS

We would like to share three key findings with you:

- Between 81% and 91% of people completed the questionnaires at each time point. This is a very high completion rate compared with other studies. Some people thought the questions could be improved, and future research could make them better.

- People who attended the course gave it an average satisfaction rating of 7/10. In particular, people gave positive feedback about the group-based format of the course because it provided the opportunity to engage with other people having a hip replacement. This means that there is the potential to run further research about the impact of the course.

- One of the main reasons that people chose not to take part in this study was because of difficulties with getting to the hospital. This shows that future research and pain self-management groups may need to be run in places that are easier to get to.

NIHR Journals Library www.journalslibrary.nihr.ac.uk

WHAT'S NEXT?

The findings have informed an application for funding to run a larger study of physiotherapy after knee replacement. The results will also be presented in an academic journal, which ensures that policy makers and healthcare professionals hear about the research. We expect findings to be available in 2014 and these will be publicly available through our website.

We would like to thank you again for taking part. The research that is done at the Musculoskeletal Research Unit helps to inform better healthcare in the UK, and your participation was vital in this.

Contact details

If you have any questions or would like more information about this study, please telephone Samantha Dixon on [redacted] or email mru-restore@bristol.ac.uk

Address:
Musculoskeletal Research Unit, Avon Orthopaedic Centre, Southmead Hospital, Bristol, BS10 5NB

http://www.bristol.ac.uk/clinical-sciences/research/musculoskeletal/orthopaedic/research/restore/

North Bristol NHS Trust

University of BRISTOL

Summary of findings

ARENA *study*

Activity orientated rehabilitation following knee arthroplasty

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

DOI: 10.3310/pgfar04120

Thank you for being involved in the ARENA study. You were one of 46 people who kindly took part in this study.

BACKGROUND

The ARENA study aimed to find out whether we could run a study of a physiotherapy class for people having a knee replacement.

STUDY DESIGN

Of the 46 people in the study, 23 people were chosen at random to have 'standard care' that patients at Southmead normally receive. 23 other people were chosen at random to be invited to attend a new 6 week physiotherapy class. This was important as research needs to be able to compare the experiences of people having the 'standard care' with experiences of people having something new.

We asked everyone in the study to fill in questionnaires before their operation, and then at 2 weeks, 3 months and 6 months after their operation. We needed to find out whether people would be willing to fill these in.

SOME KEY FINDINGS

We would like to share three key findings with you:

- 37% of people who we talked to about the study agreed to take part. Of the people who agreed to take part in the study, 91% completed the 6 month follow-up of the study. This is a very good completion rate compared with other studies.

- One of the main reasons that people chose not to take part in this study was because of difficulties with getting to the hospital. This shows that future research and physiotherapy classes may need to be run in places that are easier to get to.

- People who attended the physiotherapy classes gave them an average satisfaction rating of 9/10. In particular, people gave positive feedback about the group-based format of the course because it provided the opportunity to engage with other people having a knee replacement. This means that there is the potential to run further research about the impact of the course.

Contact details

If you have any questions or you would like more information about this study, please telephone Emma Johnson (researcher) on [redacted] or email mru-restore@bristol.ac.uk

Address:
Musculoskeletal Research Unit, Avon Orthopaedic Centre, Southmead Hospital, Bristol, BS10 5NB

http://www.bristol.ac.uk/clinical-sciences/research/musculoskeletal/orthopaedic/research/restore/

Some members of the RESTORE research team

North Bristol NHS Trust

University of BRISTOL

Summary of findings

Apex study
Arthroplasty Pain Experience Study

A study into minimising pain after joint replacement

An interview study



Thank you for being involved in the interview study that was part of the APEX trial. You were one of 24 people who kindly took part in this sub-study.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

DOI: 10.3310/pgfar04120

BACKGROUND

The interview study aimed to learn more about why people chose to take part in the APEX trial and what they thought of it. We were also interested in learning about people's journeys to hip or knee replacement and how they had managed their pain before and after their operation.

APEX is one part of the RESTORE Research Programme. The programme is made up of several research projects focusing on improving patient experiences of joint replacement surgery.

STUDY DESIGN

Emma Johnson visited you after your operation. Emma talked with you about your experiences of taking part in the trial and of surgery.

All interviews were audio recorded and these recordings were typed up. We then looked at them to find any similarities and differences in people's experiences.

FINDINGS

Participants took part in APEX for many reasons including:

- wanting to help others
- the value of research to advance knowledge

This information will be useful to improve future trials. We also looked at what people thought of pain relief medication. People told us that:

- although in pain before the operation they often chose to limit how much pain relief they took
- having the operation changed their thoughts about and use of pain relief

This information is helpful to health professionals. The study team is now looking in more detail at the information. Findings will be publically available in the next two years through our website (please see overleaf).

WHAT'S NEXT?

We would like to thank you again for taking part. The research that is done at the Musculoskeletal Research Unit helps to inform better healthcare in the UK, and your participation was vital in this. The results will be presented in academic journals and at research conferences, which ensures that policy makers and healthcare professionals hear about the research.

Contact details

If you have any questions or you would like more information about this study, please telephone Emma Johnson (researcher) on [redacted] or email mru-restore@bristol.ac.uk

Address:
Musculoskeletal Research Unit, Avon Orthopaedic Centre, Southmead Hospital, Bristol, BS10 5NB

http://www.bristol.ac.uk/clinical-sciences/research/musculoskeletal/orthopaedic/research/restore/

Some members of the RESTORE research team

North Bristol NHS Trust

University of BRISTOL

Summary of findings

Having a joint replacement

You and your joint replacement

© Queen's Printer and Controller of HMSO 2016. This work was produced by Blom *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

DOI: 10.3310/pgfar04120

Thank you for being involved in the 'You and your joint replacement' study. You were one of 34 people who kindly gave up their time to take part.

BACKGROUND

The aim of the 'You and your joint replacement' study was to learn more about people's experiences and 'journeys' through hip or knee replacement surgery.

The study is one part of the RESTORE Research Programme. The programme is made up of several research projects focusing on improving patient experiences of joint replacement surgery.

STUDY DESIGN

Taking part in this study involved you meeting with Emma Johnson before you had your joint replacement surgery. Emma asked you questions about your history of joint problems, experiences of pain and your thoughts about the operation. A member of the research team also aimed to talk to you again 2-4 weeks, 6 months and 12 months after the operation to learn about your recovery from surgery.

All interviews were audio recorded. These recordings were then typed up. We then looked at them to find any similarities and differences in people's experiences.

FINDINGS

Many of you told us that you had to wait a long time to have your operation. It was also a common experience to learn that your operation had been cancelled or delayed. We have been interested in studying the impact that this had on you and the potential ways to limit this for other patients in the future.

We were able to learn a great deal about the support that you received from health professionals before, during and after joint replacement. You also gave us useful suggestions about input that you felt was missing. This information will be useful in helping to improve the support provided to others having joint replacement.

The study team is now looking in more detail at the information. Findings will be publically available in the next two years through our website (please see overleaf).

WHAT'S NEXT?

We would like to thank you again for taking part. The research that is done at the Musculoskeletal Research Unit helps to inform better healthcare in the UK, and your participation was vital in this. The results will be presented in academic journals and at research conferences, which ensures that policy makers and healthcare professionals hear about the research

EME
HS&DR
HTA
PGfAR
PHR

Part of the NIHR Journals Library
www.journalslibrary.nihr.ac.uk

This report presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health

Published by the NIHR Journals Library