FULL TITLE OF PROJECT
The role of hospital organisation, surgical factors, and the enhanced recovery pathway, on patient outcomes and NHS costs following primary hip and knee replacement surgery: spatial and longitudinal analysis of routine data

SUMMARY OF RESEARCH

RESEARCH QUESTION
To determine the effect of hospital organisation, surgical factors, and the enhanced recovery pathway on patient outcomes and NHS costs of hip/knee replacement

AIMS
(1) Identification of hospital organisation, surgical factors and the enhanced recovery pathway, as determinants of geographical variation in patient outcomes and NHS costs
(2) Natural experiment to determine the clinical and cost-effectiveness of the enhanced recovery treatment pathway
(3) Qualitative study (process evaluation) on implementation of enhanced recovery pathways in four hospital settings

POPULATION
Primary hip/knee replacement for osteoarthritis

PATIENT FORUM
Elicit patient's views on the outcomes of surgery most important to them (patient identified outcomes). Findings from the forum will inform selection of the primary and secondary outcomes of the study.

DATA SOURCES
UK Clinical Practice Research Datalink; Hospital Episode Statistics; National Joint Registry; NHS Patient Reported Outcome Measures; NHS Hospital and Community Health Service Workforce Statistics; NHS Quarterly Bed Availability and Occupancy data; Supporting Facilities data

OUTCOMES
Length of stay, readmission, reoperation, complications, PROMs, mortality, NHS resource use and costs, cost-effectiveness

EXPOSURES
Patient (age, gender, BMI, deprivation, ethnicity, comorbidity, ASA grade);
Hospital organisation (operating theatres, day case theatres, available and occupied beds, specialist consultants, hospital volume, day case surgery);
Surgical (surgeon volume, operative time, surgeon grade, surgical approach, type of surgery (open, minimally invasive));
Enhanced recovery pathway (1) pre-op planning; 2) reduce physical stress; 3) post-op management; 4) early mobilisation)

GEOGRAPHICAL VARIATION IN OUTCOMES
Multilevel regression modeling of HES/NJR/PROM linked data will describe the association of hospital organisation, surgical factors and the enhanced recovery pathway on patient outcomes of surgery, adjusting for patient case-mix. Random intercept models will explore geographical variation in outcomes across hospital trusts and Clinical Commissioning Groups. Geographical Information Systems will be used to produce maps depicting variation in outcomes, and graphically display the influence these factors have on explaining such variation.

QUALITATIVE PROCESS EVALUATION
Ethnographic research in four different hospital settings (specialist orthopaedic centre, teaching hospital, district general hospital, private hospital) selected to represent the main organisational contexts in which hip/knee replacement takes place. A qualitative researcher will approach and recruit health professionals and patients at the hospitals and collect information about enhanced recovery pathways by observing and recording practice and processes, conducting interviews, and collecting relevant documentation.

ENHANCED RECOVERY PATHWAY
CPRD/HES linked data will be used to estimate the hospital and non-hospital costs following hip/knee replacement. A disease specific Markov model will simulate the costs and health-related quality of life of hip/knee replacement patients before and after introduction of the pathway. A cost-effectiveness analysis will be performed using outcome measures such as Quality-Adjusted Life Years (QALYs) gained. Relative effectiveness measures will be applied to the transition probabilities to model the impact of the new treatment pathway. Interrupted time series analysis will be used to evaluate the impact of the enhanced recovery pathway on trends in rates of outcomes, adjusting for socioeconomic status and case-mix.

TIME PLAN
Month -6 to 0: Approvals for CPRD and NJR data; Month 0-1: Patient forum; Month 0-6: Obtain HES, CPRD, NJR, PROMs data; Month 3-22: Process evaluation; Month 3-9: Data cleaning and coding; Month 9-18: Statistical analysis; Health economics analysis; Months 18-24: Submission for publication and study close

BENEFIT TO NHS
The study will provide information to commissioners of healthcare, NHS managers and clinicians on the clinical and cost-effectiveness of the enhanced recovery pathway, together with small area data on geographical variation in surgical outcomes, and knowledge of modifying factors to minimise inappropriate variation

BACKGROUND AND RATIONALE
Osteoarthritis presents an important health burden as the population becomes older and increasingly obese(1). Almost half of those aged over 75 seek medical care for osteoarthritis with a large impact on healthcare costs and health-related quality of life(2). It is a leading cause of worldwide disability, with an estimated annual loss of productivity cost of £3.2 billion in the UK(3), with pain being the primary symptom that causes people to seek out medical care such as physiotherapy, pain management, and in severe cases, joint replacement surgery. Over 160,000 people with severe hip or knee pain caused by osteoarthritis have joint replacement surgery each year in the NHS and this number is expected to increase(4).

A recent White Paper(5) outlined the future of the NHS, making it more accountable to patients through greater choice and information, with a strong focus on clinical outcomes. To shift decision-making as close as possible to individual patients, the Government have devolved power and responsibility for commissioning services to GPs and their practice teams working in consortia. The National Health Service Act 2006, as amended by the Health and Social Care Act 2012, places duties on the NHS Commissioning Board and clinical commissioning groups to have regard to the need to reduce variations in access to, and outcomes from, health care services for patients, and to assess and report on how well they have fulfilled this duty. There is a commitment to increasing value from the budget allocated to healthcare, requiring that unwarranted variations in patient outcomes are addressed.

There are well known geographical variations in the uptake of common surgical procedures including hip and knee replacement(6, 7), as publicised through the NHS Atlas of Variation(8). A recent study found evidence of significant unexplained variation among hospitals in both health outcomes and resource use following hip and knee replacement(9), but little is known about factors that can explain why such variation exists. In the NHS, as part of the Patient Choice Agenda(10), patients can choose which hospital they want to have their surgery in. Information on the outcomes of surgery between different hospitals would help patients in making their decision. Outcomes of surgery will vary across different hospitals and areas of the country(9). This may be explained by a hospital treating more complex and sicker patients, and this must be accounted for. However, differences in patient outcomes could also be explained by how hospitals organise their services(6), such as bed availability, numbers of operating theatres and specialist surgeons, using new surgical techniques such as minimally invasive surgery(11), or centralising care into specialist high volume hospitals(12, 13). Knowledge of this would help NHS managers to change the way services are organised and reduce variation in outcomes between hospitals.

In some areas of healthcare the Department of Health has driven NHS wide changes to specific care pathways to reduce variations in patient care and introduce quality standards(14). Between April 2009

and March 2011 the Department of Health established an Enhanced Recovery Partnership Programme(15) to support the NHS to implement and realise the benefits of enhanced recovery in colorectal, musculoskeletal, gynaecology and urology major elective surgical pathways. Hip and knee replacement is a high volume elective surgical procedure that lends itself well to standardising best practice and improving patient outcomes, and was the focus of enhanced recovery in musculoskeletal care. Through the Department of Health led programme a new "enhanced recovery" patient pathway for hip and knee replacement has now been introduced across all NHS hospitals(16). Enhanced recovery is a complex intervention(17, 18) that focuses on key areas of care across the pathway in order to improve patient care: *pre-operatively* (for the patient to be in the best possible condition for surgery); *peri-operatively* (the patient has the best possible management during and after their operation); *post-operatively* (the patient experiences the best rehabilitation). It is hoped this will benefit patients through patient education before and after surgery, which includes making changes around the home, exercises to strengthen the joint and changes to diet to help reduce the risk of complications and speed up a patient's recovery time. For patients in whom it is suitable, they will further benefit by being able to return home earlier to continue their recuperation at home with appropriate support. This in turn will benefit the hospital by freeing up space for other patients on the waiting list. A greater number of frail older people with complex co-morbid conditions now receive hip/knee replacement surgery. The new enhanced recovery pathway for orthopaedics could specifically benefit these patient groups(19). Through reducing the time a patient spends in hospital, with fewer complications of surgery and a decrease in readmissions to hospital, introduction of the pathway should be cost-effective for the NHS.

There is limited evidence concerning the effectiveness of enhanced recovery programmes in hip and knee replacement surgery(20). Particularly when applied nationwide across a healthcare system. It may be implemented differently and variably across different hospital settings. There is a need for information on what the core active ingredients are, and how they are exerting their effect(18). This is important because, when implemented in diverse hospital settings, the intervention may be adapted to local circumstances that inhibit its effectiveness(21). A recent synthesis of evidence about effectiveness and implementation of enhanced recovery programmes highlights 'barriers' and 'facilitators' to implementation(20). Barriers included resistance to change, inadequate funding, lack of support from management, high staff turnover, poor documentation, and shortness of time. Facilitators included a dedicated enhanced recovery lead, presence of multidisciplinary team working and ongoing education for staff and patients. Studies of patients' experiences of enhanced recovery have taken place in colorectal surgery, indicating that patients are willing to provide feedback about enhanced recovery(22-24), but we know little about experiences for hip and knee replacement. Whilst it is known that delays during the wait for joint replacement surgery impacts on patients' psychological wellbeing(25), we do not know elements of pathway-driven care that patients like most and least. We know that organisational processes and collaboration between professionals are crucial to the delivery of safe and satisfactory care, for instance around discharge planning(26), but the organisational contexts that can support or inhibit delivery of enhanced recovery have not been explored, and previous studies have tried to identify discrete factors rather than process. Successful implementation relies on working practices within organisations and needs to incorporate patients' experiences and preferences.

EVIDENCE EXPLAINING WHY THIS RESEARCH IS NEEDED NOW

Osteoarthritis is a leading cause of pain and disability(1). Over 160,000 people with severe hip or knee pain caused by osteoarthritis have joint replacement surgery each year in the NHS and this number is expected to increase(27). The annual NHS budget for dealing with orthopaedic patients is approximately £10 billion a year, set in the context of an ageing population and rising levels of obesity. Despite the success of joint replacement surgery up to 20% of patients have a poor outcome(28, 29) and the ongoing care and treatment of such patients increases the burden to the NHS.

Our proposed research addresses two areas of the commissioning brief and we have chosen to focus specifically on hip/knee replacement for osteoarthritis:

(1) Variation in access, quality and safety in surgery

It is well known there are variations in the uptake of hip/knee replacement as publicised by the NHS Atlas of Variation(8). Much less is known about variations in outcomes of surgery and why they exist(9). As suggested in the commissioning brief we will conduct a robust analysis of routine data

from NJR/HES/PROMs, to explore variation in patient outcomes of hip/knee replacement surgery. Adjusting for patient case mix, we will explore whether surgical and hospital organisational factors can explain geographical variation in patient outcomes. Factors we will explore include centralisation of services, use of minimally invasive surgical techniques, and numbers of available beds, operating theatres, and specialist surgeons. Using Geographical Information Systems we will produce maps showing variation in outcomes across hospital trusts and CCGs, adjusted for case-mix.

(2) New pathways and services for changing patient profile
Increasing numbers of patients are receiving joint replacement surgery(4), reflecting an ageing and increasing obese population alongside improvements in peri-operative techniques. This has led to a significant change in the profile of patients undergoing this surgery. Greater numbers of younger patients and frail older people with complex co-morbid conditions now receive hip/knee replacement. The enhanced recovery pathway can benefit all patients but is especially relevant to these older patient groups(19). However there is heterogeneity in the way hospitals organise enhanced recovery services and it is unclear which way is best. We will use a natural experimental study design(30) using routine data (NJR/HES/PROMs) to see if introduction of the pathway has led to improved patient outcomes, reduced length of stay and freed up hospital capacity, with a health economics analysis to examine the cost and cost-effectiveness to the NHS.

AIMS AND OBJECTIVES

RESEARCH QUESTION
To determine the effect of hospital organisation, surgical factors, and the enhanced recovery pathway on patient outcomes and NHS costs of hip/knee replacement

AIMS
(1) Identification of hospital organisation, surgical factors, and the enhanced recovery pathway as determinants of geographical variation in patient outcomes and NHS costs
(2) Natural experiment to determine the clinical and cost-effectiveness of the enhanced recovery treatment pathway
(3) Qualitative study (process evaluation) on implementation of enhanced recovery pathways in four hospital settings

Statistical analysis of national linked data from the NJR/HES/PROMs databases will allow identification of hospital organisation and surgical factors that explain geographical variations in patient outcomes of surgery, after adjustment for patient level case-mix. We will provide data at the small area level presented as maps to describe variation in outcomes, before and after accounting for these organisational and surgical factors. We will also focus on variation in outcomes of specific patient groups (old and frail with co-morbidities and obese) and provide evidence as to whether the introduction of new surgical innovations (e.g. minimally invasive surgery), and centralisation of services, has led to improved patient outcomes.

The project will then use a natural experimental study design to specifically examine the impact that the new enhanced recovery treatment pathway has had on NHS resource use, NHS costs and patient outcomes (PROMs, length of stay, complications, readmission). Interrupted time series analysis will examine changes in secular trends in outcomes and NHS costs before and after the introduction of the new treatment pathway. There will be a focus on the benefit of the new enhanced recovery pathway to specific patient groups such as frail older people with complex co-morbid conditions. A process evaluation to explore the way enhanced recovery is implemented will enable us to achieve more depth in our interpretation of effects on patient outcomes, to understand how context influences outcomes, and provide insights to aid future implementation. An economic evaluation will describe the hospital and non-hospital NHS costs, patient health-related quality of life and cost effectiveness that reflect the new treatment pathway for hip/knee replacement surgery.

The study will inform patients, NHS managers, commissioners and health professionals of the NHS costs, patient outcomes and cost-effectiveness associated with the enhanced recovery treatment pathway, and the key elements that are most clinically and cost effective. It will provide patients with information on variation in outcomes of surgery to inform patient choice and decision-making. We will provide commissioners with evidence of modifiable hospital organisational factors that can explain unwarranted geographical variation in patient outcomes of surgery.

RESEARCH PLAN / METHODS

SUMMARY OF RESEARCH PLAN

The project comprises of a patient forum and two main work packages (WP). The project will begin with a patient forum to identify the outcomes that matter most to hip and knee replacement patients (patient identified outcomes). Findings from the forum will inform the primary and secondary outcomes of the study.

WP1 will address our aim to explore geographical variation in patient outcomes of surgery. Using large linked national datasets (NJR/HES/PROMs) we will identify whether hospital organisational factors (e.g. staff, beds, operating theatres) and surgical factors (e.g. minimally invasive technique, surgeon volume, operative time, implant fixation, thromboprophylaxis) can explain geographical variation in patients outcomes, adjusting for patient case-mix. Results will be displayed as maps highlighting the level of variation in patient outcomes across hospitals and CCGs before and after accounting for these factors.

WP2 focuses specifically on the enhanced recovery care pathway:

- *Process evaluation.* To characterise the enhanced recovery intervention as used in practice in different hospital settings (specialist orthopaedic centre, teaching hospital, district general hospital, private hospital) and understand organisational processes that enable or impede implementation of the enhanced recovery pathway. The qualitative work will use an ethnographic approach and will be informed by extended Normalisation Process Theory.
- *Natural experiment.* Evaluate the impact the enhanced recovery pathway has had on NHS resource use, NHS costs and patient outcomes (PROMs, length of stay, complications, readmission). Interrupted time series analysis will examine changes in secular trends in outcomes and NHS costs before and after the introduction of the new treatment pathway.
- *Economic evaluation.* To describe the hospital and non-hospital NHS costs, patient health-related quality of life and cost effectiveness that reflect the new treatment pathway for hip/knee replacement surgery.

DETAILED RESEARCH PLAN

PATIENT FORUM

Among priorities identified through the work of the James Lind Alliance (JLA) Priority Setting Partnership for Hip/Knee Replacement was the need to involve patients to identify the outcomes that matter most to them (patient identified outcomes)(31, 32). We will assemble a patient forum comprising 8-10 hip/knee replacement patients to identify outcomes, from the list of outcomes available in the routine datasets that we have available to us in this study. We will utilise the University of Bristol's Musculoskeletal Research Unit's (MRU) patient involvement group: the 'Patient Experience Partnership in Research' (PEP-R)(32). PEP-R comprises twelve patients with musculoskeletal conditions, most of whom have had joint replacement, all of whom have had experience of long-term pain.

The forum will be conducted at the start of the study, made possible by the well established PEP-R patient group. At the forum session, patients will be provided with a plain English description of the project and the outcome measures available in the datasets, sent out in advance, along with information on patient and public involvement in research. In the session the PPI co-ordinator will foster discussion about the different outcome variables and using consensus techniques will capture patients views about the outcomes that matter most to them. Views will be linked to service users own individual experiences that they will be encouraged to share with others. The group discussion will be recorded on flip-charts and in notes by a scribe who will be present.

At the end of the meeting, the group's views will be collated and drafted into a brief report that will be sent out to group members after the meeting. The meeting will last around 2 and a half hours, and include a comfort break, refreshments and chance for discussion. Patients will be reimbursed for their time and expenses. Findings from the forum will inform the primary and secondary outcomes of the study.

WORK PACKAGE 1: Identification of hospital organisation and surgical factors as determinants of geographical variation in patient outcomes and NHS costs

POPULATION
National sample of all patients undergoing primary hip/knee replacement for osteoarthritis in the NHS

ROUTINE DATA SOURCES
This study will use routinely collected large national datasets that capture actual NHS patient activity within primary and secondary care settings, allowing us to contextualise changes and trends affecting all organisations during this period.

Starting in 2003 the *National Joint Registry (NJR)*(4) for England, Wales and Northern Ireland collects information on all hip and knee replacements performed each year in both public and private hospitals in England, Wales and, since 2012, Northern Ireland. Data are entered into the NJR using forms completed by surgeons at the time of surgery, and revision operations are linked using unique patient identifiers. Data recorded in the NJR includes prosthesis and operative information (including prosthesis type, approach and thromboprophylaxis use); patient information (age, gender, BMI, American Society of Anaesthesiologists (ASA) grade); surgical and unit information (including surgeon and unit caseload and public/private status).

The *Hospital Episode Statistics (HES)* database holds information on all patients admitted to NHS hospitals in England, including diagnostic ICD codes providing information about a patient's illness or condition and OPCS4 procedural codes for surgery. It covers a smaller geographical area than the NJR (excluding patients operated upon in Wales and Northern Ireland), and does not include privately-funded operations. However, HES provides additional information for every patient (including detailed comorbidity information and deprivation indices), and about every procedure (including length of stay and need for blood transfusion or critical care). Additional records contain details of readmissions, reoperations, and revisions not recorded in the NJR database. Data for all-cause mortality are provided by the ONS and linked to the HES database.

Since April 2009, Patient-Reported Outcome Measure (PROM)(33) data has been collected on hip and knee replacements performed in public hospitals in England. Pre-operative and 6 month quality of life questionnaires (the EuroQol five domain (EQ5D)(34)) and joint-specific PROMs (the Oxford Hip Score (OHS)(35) and Oxford Knee Score (OKS)(36)) are collected along with patient-reported measures of preoperative disability and post-operative satisfaction. Data are collected by the NHS trusts under whose care the procedure is performed, and co-ordinated by the Health and Social Care Information Centre on behalf of the Department of Health.

For this analysis we will use NJR records linked to data from the HES and PROMs databases on all hip and knee replacement operations over a 5-year period (2009/10 to 2014/15). Analyses will be restricted to patients receiving elective primary hip or knee replacement surgery for osteoarthritis. Such data linkage has already been undertaken for previous collaborative research projects(37-40). In terms of the process, the HES and PROMS datasets are already linked and obtained through the Health and Social Care Information Centre (HSCIC). To preserve anonymity of the patients within the NJR, patients in the HES database are matched to those in the NJR by the HSCIC Linkage Service. They used patient identifiers to identify matching patients and each HES record was supplied with an NJR identifier to allow matching. As an example, there are currently 69,749 TKR patients with linked NJR-HES-PROMs data collected between 2009/10 to 2012/13 with completed pre and post-operative PROM questionnaires.

PATIENT LEVEL CHARACTERISTICS (CASE-MIX)
Age, gender, body mass index (BMI), area deprivation, rurality, ethnicity, Charlson co-morbidity index, ASA grade

HOSPITAL ORGANISATION FACTORS
As a measure of centralisation of services in specialist centres, we can calculate the annual volume of procedures performed in each acute hospital trust(13). We will identify whether or not the enhanced recovery care pathway was in place at the time of operation. The *NHS Hospital and Community Health Service (HCHS) Workforce Statistics* in England provide details on workforce within NHS organisations including numbers of consultants (e.g. Trauma and Orthopaedic, Anesthetists), registrars and other doctors in training. The *NHS Quarterly Bed Availability and Occupancy Data Set (KH03)* gives data on the number of available beds and occupied beds, whilst the *Supporting*

Facilities dataset (KH12) provides information on operating theatres and dedicated day case theatres. The data are published quarterly and can be linked to HES data through the hospital provider code(6) and reflect service organisation for patients at the time of operation.

SURGICAL FACTORS
Data from the NJR provide additional information on: whether or not a minimally invasive technique was used; annual surgeon volume/case load, operative time, grade of operating surgeon, surgical approach, patient position, implant fixation, type of mechanical or chemical thromboprophylaxis, unit type (public, private, independent sector treatment centre).

OUTCOMES
Length of stay, readmission, reoperation, complications and mortality (ONS linked data). PROMS linked data provides information on patient reported outcomes: Oxford hip score (OHS), Oxford Knee Score (OKS), EQ5D, satisfaction.

SAMPLE SIZE
To account for clustering within the data (patients nested within CCGs) we need to inflate the required sample size by the design effect [1 + (n-1)p] (p is the intra-cluster correlation (ICC) and n the mean cluster size). From our previous work the ICC was 0.0135 for hip and 0.014 for knee replacement(41). There are 209 CCGs in England and the CCG is the cluster. If we expect to have 100 patients from each CCG group, the design effect is (1 + 99*0.014) = 2.4.

For Oxford hip and knee score outcomes, the minimally important difference between groups(42, 43) has been estimated to be 5, with a standard deviation of 10. Using a 2-sided 2-sample t-test, with 90% power, at a 5% level of significance, to detect a difference in mean OHS/OKS of 5, requires a sample size of 85 in each exposure group. Assuming a 50% response rate to the 6-month follow up OHS/OKS questionnaires, inflates the sample size to 170 per exposure group. The required sample size per exposure group (or consider as 1 degree of freedom) adjusted for clustering is 2.4*170 = 408. Several exposure variables will be considered in the model. Including up to 50 degrees of freedom would require a sample size of around 20,000 patients. Hence we are more than adequately powered.

For the other binary outcomes, for complications of both THR and TKR, within 6-months of operation, rates of stroke and MI were under 0.5%, anaemia, UTI, wound infection and PE/DVT were below 3%[4](44). The NJR annual report shows 90-day mortality of 0.5% and 1-year mortality of 1.5%. Rates of revision are around 5% at 10-years, and revision/re-operation higher at up to 20%[5](39).

For the rarest outcomes, to detect a difference in proportions of 0.5% versus 1%, using a 2-sided, 2-sample chi-squared test, with 90% power at a 5% level of significance, requires 6650 patients per exposure group. As HES encompasses elective admissions to all English hospital we expect no loss to follow up as this information would be captured. For the design effect of 2.4 the sample size increases to 15,960 per degree of freedom. Hence even for these rarest outcomes, with an actual sample size of > 350,000, we can still include over 20 degrees of freedom in the model.

STATISTICAL ANALYSIS
The hierarchical structure of the data will consist of patients (level 1), nested within hospitals (level 2), within health regions (Clinical Commissioning Groups (CCG)) (level 3). Multilevel regression models will describe the association of hospital organisation and surgical factors on patient outcomes of surgery, adjusting for patient level case mix. This controls for evidence of clustering in the data, by allowing outcomes to vary across hospitals and CCGs. Failure to control for evidence of clustering can lead to estimates of standard errors that are spuriously precise and be a potential source of bias. Analyses are conducted separately for hip and knee replacement.

Proportional hazards regression will be used to examine survival outcomes (e.g. revision, revision/reoperation, and mortality). Because mortality can be regarded as a competing risk for revision surgery, we will use competing risk regression when examining revision and revision/reoperation(45); and Cox regression for the mortality comparison. We examine continuous outcomes (e.g. length of stay, OHS, OKS) using linear regression and binary outcomes (complications during the primary admission) using logistic regression, and readmission rates using a zero-inflated Poisson model.

To produce predicted rates of outcome in each hospital and CCG, the regression models are re-fitted using the Bayesian software WinBUGS to provide estimates of precision around the predictions that incorporate uncertainty arising from the joint estimation of model parameters(6, 46). Small-area predictions are produced by adding the mean of the linear predictor in each hospital to the estimate of residual hospital variation to obtain the overall predicted rate in each hospital. Geographical Information Systems will be used to produce maps depicting geographical variation in outcomes across CCGs, and graphically display the influence hospital process factors have on explaining such variation.

WORK PACKAGE 2: Process evaluation, natural experiment and economic evaluation of the enhanced recovery treatment pathway

Enhanced recovery is a complex intervention(17, 18). MRC guidance on the evaluation of complex interventions emphasise the importance of integrating data on process and outcome evaluation(18, 21). Using a mixed methods approach in this study as a whole, learning generated from qualitative work will be use to inform our interpretation of data from the statistical analysis on the effect of the intervention on patient outcomes from the natural experimental study. Including information from the health economic analysis will further make the results of the evaluation much more useful for decision-makers.

PROCESS EVALUATION
The aims are to provide: 1) a description of the care pathway in each context, including reasons for its adoption, refinements made to elements of the pathway, and the role of staff in its delivery, 2) analysis of any issues that make the pathway challenging to implement, whether due to organisational or patient-related factors, 3) an understanding of the elements of healthcare that enable the pathway to be delivered, 4) a detailed analysis of patients' experience of care within the structure of the pathway and their preferences for care at key points in the pathway.

To achieve the necessary depth about processes and practices, we will conduct a focused study including relevant care settings that can deliver high-quality findings that will be transferable to other locations. We will conduct in-depth ethnographic research in four hospitals in a region of England. These will be a specialist orthopaedic centre, a teaching hospital, a district general hospital and a private hospital, which represent the main organisational contexts in which hip and knee replacement takes place(47, 48).

A qualitative researcher will spend three intensive one-week phases of fieldwork in each hospital, allowing for time in between phases for interim analysis that will inform ongoing data collection. In total, data collection fieldwork will total 12 weeks and will include weekends and nights as appropriate. A purposive sample will comprise health professionals involved in delivering care, and patients undergoing hip or knee replacement. Within each setting the study will include 20-30 professionals and patients. This is likely to comprise 10-15 professionals and 10-15 patients and will enable us to develop case descriptions of patients and treating professionals, providing a total sample of 80-120 participants.

Before the qualitative data collection starts we will introduce the study to professionals at the four settings. To initiate data collection, the study's qualitative researcher will negotiate access with gatekeepers and will approach and recruit health professionals working across all aspects of care. We will approach all key professionals including nursing staff, physiotherapists, occupational therapists, surgeons and anaesthetists. To ensure that all key professions are included we will also use snowball sampling by asking participants in the early phases of data collection to suggest any further participants. Professionals who agree to take part (as participants) will be asked to provide their written informed consent to do so, including to be interviewed and audio-recorded. These professionals will then be asked to identify patients who are potential participants. This is a more complex recruitment process as we must allow for time in-between the initial approach and decision-making phase, but shall achieve this by contacting a purposive and diverse sample of patients in advance of their admission for surgery. The sample will include a range of ages, men and women and also a range of co-morbidities identified as important by professionals as having potential to influence length of stay in hospital, care and discharge processes. These characteristics will be used to define a sampling matrix by the researcher team and to ensure achievement of an appropriate sample that

includes patients from across the matrix. To do so there will be regular communications between the study's qualitative researcher and participating health professionals.

Data collection will comprise observation, interviews and collection of documentation. First, the researcher will 'shadow' participating professionals in their work and discuss with them reasons for their decisions and practice. While this might seem obtrusive, this type of approach is widely used and can be liked by participants, also known as 'go-along' interviewing(49). Through this, the researcher will access practice at pre-operative clinics, at admission for surgery, in recovery after surgery and on wards offices and staff rooms. The researcher will also observe routine aspects of practice, such as completion of documentation, ward and drug rounds, and staff meetings. During observation, the researcher will take field notes(50), using a structured approach to provide focus on aspects of implementation guided by extended Normalisation Process Theory (eNPT) and to facilitate analysis. In between observations, professionals will be interviewed about their experiences of delivering enhanced care pathways, including any changes that it has meant for their working days, their workload and views about organisational structures and processes that may influence ability to deliver the pathway. These semi-structured interviews will be audio-recorded and are likely to take place in phases 2 and 3 of fieldwork as interview questions will be developed according to early findings from observation. The researcher will also collect hospital documentation (not patient notes), including polices and checklists, these will be discussed with professionals and will be included in analysis.

Patients who agree to participate will be interviewed about their experience of care, with focus on their transition through care from pre-operative care to discharge. Interviews will be in-depth, using a topic guide and will be audio-recorded with patients' consent. Topic guides will be developed with PPI input and will be refined as the study progresses, but we would expect to ask patients to describe their journeys through healthcare in a narrative format, and then ask further questions about this. We considered whether to conduct longer-term follow up of patients after discharge, but decided that the focus of this study should be a detailed evaluation of the delivery of the elements of care to the point of discharge, though which our focus is on how the enhanced care pathway has been implemented by services. In addition to interviews, interaction between participating patients and professionals will also be observed, to inform interview questions and as a data source in their own right. These interactions will be recorded in field notes.

Written field notes, transcripts of interviews and hospital documentation will be anonymised and imported in to QSR NVivo analysis software. Interview transcripts and field notes of will be analysed initially using a thematic approach(51). This will enable the themes to emerge from the data, and the themes will then be mapped against constructs from eNPT. As data collection will be informed by eNPT, the material should have a reasonable fit, but a thematic more inductive approach also enables us first to identify, describe and explore concepts from the data that may challenge or not match the constructs of eNPT. Data from each hospital will be analysed as a discrete dataset, but we will work as team to double code the data to foster certainty about the analysis and to devise a single overarching set of codes and themes to enable comparison and contrast between the hospital contexts. Early analysis will inform ongoing data collection through the development of matrices summarising early findings and refinement of interview topic guides as the study progresses.

In the final stages of this work, we will develop summary models of the different contexts, with key factors clearly identified and described in case study formats as well as using the constructs of eNPT to provide structure. These findings will be further explored in light of results from the four hospitals in the natural experimental study (as described below). This will enable us to examine whether the effect of the intervention on outcomes is related to the different hospital settings, and will be used to explain any discrepancies between expected and observed outcomes more fully, to understand how context influences outcomes.

NATURAL EXPERIMENT

A Natural Experimental study design(30) will be used to evaluate the impact that introduction of the enhanced recovery pathway has had on a range of patient outcomes, NHS costs and health related quality of life. A natural experimental design is a valid methodological approach to evaluate the impact of a range of events, policies and interventions which are not under the control of researchers, but which are amenable to research which uses the variation in exposure that they generate to analyse their impact on health outcomes(30). It is an approach recommended within the IDEAL

recommendations for surgical innovation and evaluation(52). The model will incorporate a 'lag time' from the intervention date to allow time for it to take effect.

The primary exposure ('intervention') is the date the new enhanced recovery pathway was introduced. Back in 2009 the adoption of enhanced recovery was fragmented across the NHS. The Department of Health in partnership with NHS Improvement, the National Cancer Action Team (NCAT) and the NHS Institute for Innovation and Improvement led a two-year programme between April 2009 to March 2011, to accelerate and provide support for the spread and adoption of enhanced recovery in colo-rectal, musculoskeletal, gynaecology and urology major elective surgical pathways(15). By the end of the programme enhanced recovery had become widely adopted by the majority of NHS provider organisations.

From the four different hospital settings included in the process evaluation more detailed information will be available such as dates of any changes to different elements of the pathway and details of the clinical team leading the programme (e.g. partnership of consultant surgeon, nurse, consultant anaesthetist, pain management expert, nurse facilitator).

DATA SOURCES

Routine data on hospitals in the region will be extracted from the NJR/HES/PROMs linked data (as described earlier) through the hospital provider code. Further data will be obtained from the *Clinical Practice Research Datalink (CPRD)*(53) that contains computerised records of all clinical and referral events in primary and secondary care and comprehensive demographic information, medication prescription data, clinical events, specialist referrals, hospital admissions and their major outcomes.

STATISTICAL ANALYSIS

Data will be analysed using an interrupted times series design(54, 55), using repeated measures before and after the intervention to control for secular changes. The intervention is the date the hospital introduced its enhanced recovery service. Each hospital will be analysed separately. Using this design, each hospital acts as its own control. In interrupted times series studies, sample size calculations are related to the estimation of the number of observations or time points at which data will be collected(54). According to the quality criteria of Ramsey et al, at least 10 pre- and 10 post-data points would be needed to reach at least 80% power to detect a change (if the autocorrelation is >0.4)(56). Our outcomes will be estimated at monthly intervals and, as autocorrelation is unknown, we will allow at least 2 years either side of the date of interest (24 pre and 24 post-data points).

Data on outcomes are measured at equally spaced intervals over the time period of interest (financial years 2009/10 through to 2014/15). Outcomes of interest include those described earlier (see section OUTCOMES), measured at monthly intervals (e.g. mean length of stay, proportion of deaths). Using the interrupted times series approach, we estimate the trend in outcome prior to the intervention, and after the intervention, and test for changes pre- and post- intervention in a) the overall (absolute level) of outcome, and b) the slope of the trend in level of outcome. Analyses will control for case-mix including adjustment for a wide range of confounding variables (see section PATIENT LEVEL CHARACTERISTICS).

Segmented linear regression models will be used to estimate the monthly outcomes. Controlling for baseline level and trend, the models estimate changes in levels and trends after the change (introduction of enhanced recovery care pathway). The regression model includes terms to estimate the pre-existing level for each outcome in the first month of the observation period (intercept), trend in the outcome before the intervention was introduced, change in level of the outcome after the intervention, and change in trend after the intervention. The models can cope in situations when the intervention takes time to affect the outcome (lag times), and in this situation we will consider taking that time period out of the analysis(56, 57). For each time series model we will include an extensive pre-intervention period to control for biases in level and trend at baseline.

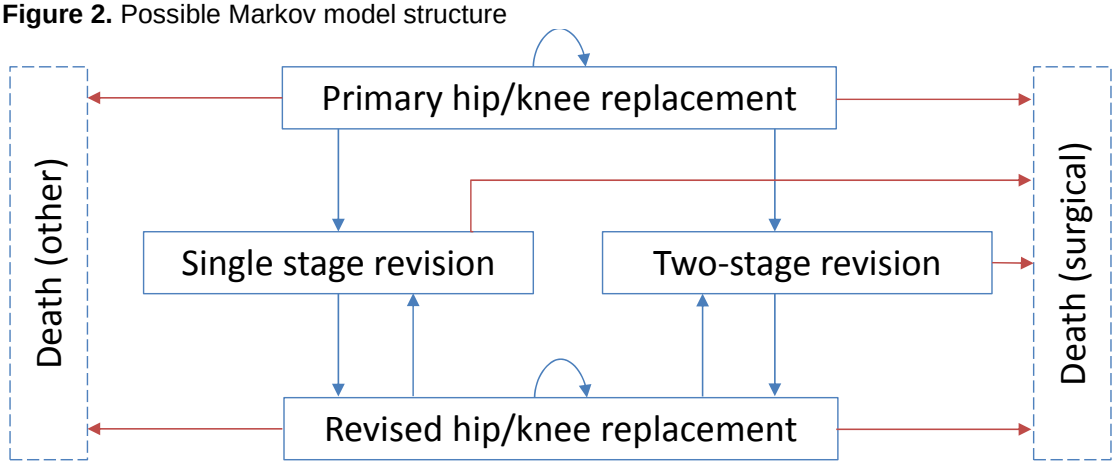
Cox proportional hazards regression modeling will be used to obtain incidence rates for outcomes of time to revision, reoperation, and mortality. Analyses will be repeated on two separate cohorts of primary hip/knee replacement patients – a pre-intervention cohort and post-intervention cohort. Analyses will be adjusted for potential confounding variables. Patients are censored on date of the outcome of interest, date of death, date of loss to follow up, or end of study period.

ECONOMIC EVALUATION

Data from the NJR, HES, ONS mortality, and CPRD will be used to estimate the hospital and non-hospital costs associated with primary hip and knee replacement and posterior revisions within the year and subsequent years of occurrence. Hospital costs will be derived by grouping each hospital episode into a Health Resource Group (HRG). HRGs are a method of classifying episodes with similar levels of resource consumption into the same group. National average costs for each HRG are published annually by the Department of Health(58). The sensitivity of the HRG coding system to capture savings from potential reductions of length of stay will also be assessed. The unit costs for several non-hospital categories (e.g. GP visits) will be derived from readily available national databases and will be multiplied by the respective use of NHS resources. Panel data regression analysis (e.g. fixed effects, random effects)(59-61) will be undertaken to estimate hospital and non-hospital costs conditional on patient characteristics (e.g., age, sex and area deprivation score), co-morbidities (e.g. Charlson co-morbidity index, American Society of Anesthesiologists grade for physical status), and reason for revision (e.g. single stage or two-stage). These will inform the costs of the different stages of the Markov model described below.

A disease specific Markov model(62) will be developed to evaluate the costs, (quality-adjusted) life expectancy and cost-effectiveness of the different models of the Enhanced Recovery Pathway. Patients reside in one of a finite number of health states and make transitions between those states over time. The Markov health states will be defined according to good practice modelling guidelines.(63, 64) These will reflect the relevant states of health associated with hip and knee replacement (e.g., primary replacement, revision carried out in a single operation, revision carried out as two operations due to deep infection, death) and the impact of the different Enhanced Recovery Pathway models (e.g., reduction in length of stay, reduction in complications/revisions, etc). Figure 2 shows an example of the possible structure of the Markov model. The specification of the health states will be informed by the analysis of the NJR/HES/CPRD linked datasets, targeted literature searches as well as from discussion with clinical experts. Transition probabilities will determine the probability of remaining in a particular state or transiting into another (e.g. hip replacement to single stage revision, mortality following revision). These will be informed by the NJR/HES/ONS linked datasets using survival analysis methods (e.g. piecewise constant survival model, parametric survival model, logistic model, etc.)(65) and relevant targeted literature searches, if necessary. Relative effectiveness measures will be applied to the transition probabilities to simulate the impact of the different models of Enhanced Recovery Pathway as well as items of NHS resource use (e.g. length of stay at primary replacement), if justified. The choice of cycle length will be determined by the timing of events concerning the natural history of patients with hip and knee replacement. The structure of the Markov model, the data used, and any simplifying assumptions made during its construction will also be checked with clinical experts.

Figure 2. Possible Markov model structure



Costs and utility scores will be assigned to each health state. Costs associated with primary hip and knee replacement and revisions will be obtained from the NJR/HES and CPRD linked datasets as described above. Costs associated with the different Enhanced Recovery Pathways will be estimated using the survey of hospitals in the region. NHS resource use associated with the provision of these models will be identified and valued using appropriate data sources. Utility scores provide the weights

required to calculate the Quality-adjusted Life Years (QALYs) of the different Enhanced Recovery Pathways under evaluation(66). These scores express the quality of life associated with a health state on a scale from 0 (dead) to 1 (perfect health). The quality of life after primary hip/knee replacement and revision will be informed by the analysis of the NHS Patient Reported Outcome Measures (PROM) dataset which reports preoperative and postoperative EQ-5D-3L results. We will also search the literature for data sources on utility scores and consider their synthesis to inform the different health states being modelled.

Once the Markov model is built, we will simulate the transition of a cohort of hip/knee replacement patients through the health states over time, to estimate expected costs and outcomes. All costs and effects will be discounted beyond the first year of simulation using recommended discount rates. Probabilistic sensitivity analysis will be used to propagate parameter uncertainty and quantify it in the resulting pairs of costs and effects(67). Cost and effect results will be reported as means with 95% credible intervals. Incremental cost-effectiveness ratios (ICERs) for the different Enhanced Recovery Pathways will be calculated by dividing the difference in costs by the difference in effects and will be depicted on the cost-effectiveness plane. Cost-effectiveness acceptability curves will also be used to represent the decision uncertainty(68). These show the probability that a model of care is cost-effective for given values of the amount that the decision maker is willing to pay for an additional unit of outcome. The value of information approach will be used to identify key model inputs for which there would be gain from reducing uncertainty by collecting more data in a subsequent study(69).

The Markov model will be evaluated following the recommendations from modeling guidelines(63, 64). Face validity will be performed by checking whether its assumptions, structure and results are reliable, sensible and can be explained intuitively. Internal validation will be performed by undertaking sensitivity analyses using extreme or null values of parameter inputs to assess whether the results are reasonable. Further validation will entail comparing model outputs with data used to inform it. External validation will be performed by comparing the results of our model with those from other independent models that have addressed similar questions.

INTEGRATION OF DATA ON PROCESS AND OUTCOME

Further to calls for increased integration of data on process and outcome evaluation(18, 70) we propose to use a mixed methods approach to integrate our findings at the interpretation and reporting level(71). Data collection will take place on a parallel rather than sequential basis, with qualitative data from the process evaluation, and quantitative data from the statistical analyses and economic evaluation, will be collected at the same time and analysed separately, before being merged together for analysis and comparison. Although we have considered a sequential approach, this would expand the project's timeframe to the point where the work will take considerably longer to influence NHS practice, and we consider that collecting data in parallel still enables us to answer key questions about the impact of enhanced recovery pathways on patient outcome, and key issues in implementation.

To integrate the data we will develop summary representations of key findings from each strand of work, and work as a team to bring the qualitative and quantitative findings together on a theme by theme basis. Further integration using joint displays will bring the data together through a visual means to draw out new insights by organising related data in figures and tables. At the end of the project our report will include these displays and our account of the findings will highlight where strands of work have enhanced the interpretation of one another: for instance where findings from the qualitative work provide explanation for findings from the natural experiment.

DISSEMINATION AND PROJECTED OUTPUTS

PLANS FOR DISSEMINATING FINDINGS OF THIS RESEARCH

Throughout all stages of this project, we will engage with key stakeholders including NHS managers, healthcare professionals, patients and the public for interpretation, dissemination and direct communication of the main findings.

This project is informed by results from the recent James Lind Alliance (JLA) Priority Setting Partnership (PSP) for Hip/Knee Replacement. We see working with the partners who have and continue to work on these projects as important to our dissemination plans. We recognise the importance of meaningful PPI involvement and have worked collaboratively with the PPI Officer at

NIHR RDS to identify individuals to become involved, and our Director of Patient Involvement at the Oxford NIHR BRC. We have identified two lay people who understand the needs and problems of hip and knee replacement patients, and have agreed to be patient representatives and co-applicants on this study. Through their involvement we will listen to their ideas regarding the dissemination of findings so they are readily available and interpretable to the wider patient and public community.

We shall disseminate findings in peer-reviewed journals, at national and international conferences, and inform learned societies that include the British Orthopaedic Association, The British Association for Surgery of the Knee (BASK), Arthritis Research UK, rheumatology (British Society for Rheumatology), geriatrics (British Society of Geriatrics). Based on our experience of previous related projects, the research is likely to generate media interest, and this will form a platform for dissemination. We will work alongside charities and learned societies to disseminate the findings of this study using established platforms that include social media such as Twitter and a study website, as more patients are now turning to these resources for information about planned surgery.

EXPECTED OUTPUT OF RESEARCH AND IMPACT

IMPACT
We will produce maps highlighting how patient outcomes of hip/knee replacement vary across different hospitals and clinical commissioning groups. This would be informative to patients in making a choice of where to have surgery. We will identify whether differences in the way hospitals organise their services, such as bed availability, numbers of operating theatres and specialist surgeons, using new surgical techniques, or centralising care into specialist hospitals, can explain why such variation exists. Knowledge of this would inform NHS managers of changes that can be made to the way services are organised, that lead to improved patient outcomes, and reduce unwarranted variation in outcomes between hospitals.

We will provide evidence of the clinical and cost-effectiveness of the new enhanced recovery pathway for hip/knee replacement surgery. The study will identify which elements and ways of organising these services are best in terms of NHS cost and improved patient outcomes. The future benefit to patients will be through improving and standardising their care before, during and after surgery, helping reduce the risk of complications and speeding up their recovery time. NHS managers will benefit through knowledge of the best ways to organise enhanced recovery services that lead to improved patient outcomes.

OUTPUT
Throughout all stages of this project, we will engage with key stakeholders including NHS managers, healthcare professionals, patients and the public for interpretation, dissemination and direct communication of findings. This will be facilitated through involvement of NHS management, collaboration with the James Lind Alliance, support of learned societies, and PPI representation. We will identify areas needing more exploration, including further qualitative research. Findings will be published in peer-reviewed journals and at national conferences. A final and full research report detailing all the work undertaken and supporting technical appendices, an abstract and an executive summary will be provided at the end of the study. A set of PowerPoint slides will be provided presenting the main findings from the research for use of members of the research team and others in disseminating research findings to the NHS. We will publish a full and complete account of that research in the NIHR HS&DR Journal, ensuring the research is reported fully, and publicly available via the NIHR Journals Library website and Europe PubMed Central.

PLAN OF INVESTIGATION AND TIMETABLE

The project will take two years to complete:

1. APPROVALS (Months -6 to 0)
Stage 1.1: ISAC (Independent Scientific Advisory Committee) application form and protocol for research using CPRD data
Stage 1.2: Application to use data from the National Joint Registry (NJR) for the purposes of research
Stage 1.3: HES data request service application form using Health and Social Care Information Centre (HSCIC) data extract service

Stage 1.4: National Information Governance Board (NIGB) for Health and Social Care, Ethics and Confidentiality Committee application for approval of linkage of HES and PROMs data to NJR
Stage 1.5: Ethics and R&D approvals for process evaluation
Milestone 1.1: Month 0: Approvals and permissions for use and linkage of routine data
Milestone 1.2: Month 0: Ethical approvals and permissions for qualitative process evaluation

2. DATA (Months 0 to 6)
Stage 2.1: Linkage of HES and PROMS data to NJR data using the Health and Social Care Information Centre (HSCIC) trusted data linkage service
Milestone 2.1: Month 6: Obtain the NJR-HES-PROMs linked data, and CPRD dataset

3. PATIENT FORUM (Months 0 to 1)
Stage 3.1: Send plain English description of the project and the outcome measures available out in advance
Stage 3.2: Conduct forum with the PEP-R patient group
Milestone 3.1: Month 1: Brief report sent out to group members summarising group's views

4. DATA CLEANING (Months 3 to 9)
Milestone 4.1: Month 9: Completion of cleaning and coding of routine datasets by data manager

5. WP1 VARIATION IN OUTCOMES (Months 9 to 18)
Stage 5.1: Link in data on hospital organisational factors to HES dataset through hospital provider code
Stage 5.2: Prepare NJR/HES/PROMs data ready for Multilevel regression analysis (national cohort and regional hospitals detailed cohorts)
Stage 5.3: Run regression models to identifying predictors (hospital organisation and surgical) of outcomes
Stage 5.4: Fit models in WINBUGS to predict outcomes in each hospital and CCG
Stage 5.5: Produce maps of patients' outcomes across CCGs using GIS software
Milestone 5.1: Month 18: Write up findings for report and paper for publication

6. WP2 PROCESS EVALUATION (qualitative) (months 3 to 22)
Stage 6.1: Design study materials
Stage 6.2: Fieldwork in 3 phases, with interim analysis in between fieldwork (4 weeks of fieldwork and 4 weeks of analysis).
Milestone 6.1: Month 18: Full analysis and production of reports
Milestone 6.2: Month 20: Report to relate findings with quantitative and economic data
Milestone 6.3: Month 22: Final write up and submission to journals

7. WP2 NATURAL EXPERIMENT (Statistics) (months 9 to 18)
Stage 7.1: Prepare NJR/HES/PROMs data ready for interrupted time series analysis
Stage 7.2: Run regression models for effect of pathway on range of outcomes
Milestone 7.1: Month 18: Write up findings in a report and write paper for publication

8. WP2 NATURAL EXPERIMENT (Health economics) (months 9 to 18)
Stage 8.1: Targeted literature search for specification of Markov model
Stage 8.2: Discussion with clinical experts
Stage 8.3: Define health states and structure of Markov model
Stage 8.4: Estimate NHS costs associated with hip and knee replacement
Stage 8.5: Estimate transition probabilities for Markov model
Stage 8.6: Simulation of Markov model to estimate expected costs and outcomes
Stage 8.7: ICERs estimated and probabilistic sensitivity analysis
Milestone 8.1: Month 18: Write up findings in a report and write paper for publication

9. DISSEMINATION (Months 18 to 24)
Milestone 9.1: Month 24: Complete dissemination including final report

PROJECT MANAGEMENT

The project will be sponsored by the University of Oxford. Dr Judge will be responsible for the overall leadership of the project and will be assisted by a part time project manager. The PI and project manager will communicate regularly through weekly meetings. Dr Leal will lead the health economics and Dr Gooberman-Hill the qualitative research and both will meet regularly with Dr Judge. Prof Price will work closely with Dr Judge for work on the enhanced recovery pathway. Throughout the project, the PI and project manager will communicate with the Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences finance department to oversee financial management. In addition to regular meetings between project staff, we will hold project oversight meetings to monitor progress and achievement of milestones and oversee analysis. The committees will also monitor adherence to research governance policies. The oversight meetings will include:

- 3-monthly Project Management meetings with all co-applicants and project staff. This will allow effective communication between applicants at different institutions and ensure the whole team are directly involved in the management of the project.
- 6-monthly Steering Committee meetings. The steering committee will consist of the PI, a patient representative, an orthopaedic surgeon, a statistician, a health economist and a public health specialist. The majority of members will be external to the project.

APPROVAL BY ETHICS COMMITTEES

To conduct qualitative ethnographic research with NHS staff and patients we will obtain NHS REC approval, and necessary permissions from the University of Oxford's Research Ethics Committee and local R&D offices. In all outputs from the project for the hospitals will be anonymised and only members of the study team will be allowed access to the collected data identified by hospital. We will allow the hospitals access to their own data if requested. We will produce maps of outcomes by Clinical Commissioning Groups (CCGs) and we have considered the impact of this. However, we do not foresee problems here; firstly, we are using area level geography to demonstrate variations in outcomes and not targeting specific hospitals, and secondly, this type of information is very helpful for CCGs and can be used to inform changes in clinical practice. Dissemination will involve work with patient groups and stakeholders. We will work with experienced facilitators through links already in place at the University of Oxford to manage patient expectations and ensure everyone is understanding and given the opportunity to contribute. ISAC approval will be obtained for the use of CPRD data in this project, and we will obtain the necessary linkage approvals for NJR-HES-PROMs databases. All data will be stored in line with the University of Oxford data security policies and those laid out in the data re-use agreements. Data will be deleted at the end of the study.

PATIENT AND PUBLIC INVOLVEMENT

AIMS OF ACTIVE INVOLVEMENT IN THIS PROJECT

Within this project patients and the public will be actively involved in: Design of the research; Management of the research (steering group); Developing participant information resources; Contribute to reporting of research; Dissemination of research findings. We recognise the importance of meaningful PPI involvement and have worked collaboratively with the PPI Officer at NIHR RDS to identify individuals to become involved, and our Director of Patient Involvement at the Oxford NIHR BRC. We have identified two lay people who understand the needs and problems of hip and knee replacement patients. Through their involvement we will listen to their ideas regarding the dissemination of findings so they are readily available and interpretable to the wider patient and public community.

DESCRIPTION OF PATIENTS TO BE INVOLVED

We have identified two lay people who have agreed to be patient representatives and co-applicants on this study. Patient representative 1 cares for his wife, patient representative 2 who has extensive arthritis and is himself currently recovering at home following a recent hip replacement operation. He is a patient representative for other research projects and member of the James Lind Alliance (JLA) Priority Setting Partnership for Hip/Knee Replacement. He thought this was a worthwhile and important project, but cautioned that the enhanced recovery pathway could be perceived as a way for hospitals to discharge patients early to save money. To defend against this, it was necessary to have more explicit descriptions of the benefits to patients and precautions taken to prevent early discharge for those in whom it is unsuitable. From patient representative 1's experience, as he needs to care for his wife, arrangements for her care were in place prior to his surgery from a local care organisation. This highlights the need for social care and support mechanisms to be in place when returning home

from surgery, as part of pre-operative planning in the enhanced recovery pathway. Patient representative 2 has previously had hip replacement surgery. She has experience of attending a 'hip school' (patient education before surgery) and was on an enhanced recovery pathway. She is a patient representative for the National Joint Registry (NJR) and has written a blog about her pre and post-operative experiences. Patient representative 2 has experience of reading research proposals for the NJR, has given a patient view on research at the British Orthopaedics Association (BOA), and has access to a patient network through the NJR and Arthritis Care with whom she also works. Patient representative 2 has agreed to help with the study as a co-applicant, and believes this to be very important research that will offer significant benefit to patients.

We met (May 2014) with the patient involvement group: 'Patient Experience Partnership in Research' (PEP-R), comprising twelve patients with musculoskeletal conditions, most of whom had joint replacement. During the meeting we discussed their thoughts and experience on patient choice of where to have surgery, and what they think is most important about the four areas of the enhanced recovery pathway. In discussion of patient choice the group spoke of their experiences of using private treatment centres compared to NHS hospital trusts. One patient had experience of both for two hip operations, where the treatment centre was quicker with a shorter waiting time, a better experience when being discharged, and was consistent with elements of enhanced recovery, unlike the NHS hospital. Other patients were unaware they had this choice of using an alternative private provider. One patient also spoke about choice of anaesthetic (epidural versus general), with mixed feelings in the group about being awake during surgery but benefits of being able to be up and walking only 4 hours after the operation were seen as desirable. This was not something we had previously considered in this project, and have now included this based on feedback.

A patient shared an experience of being inappropriately discharged after her most recent operation in 2013. The patient lives at home and felt appropriate care at home was necessary when discharged. The patient was in agreement about having someone at home to help when coming out of hospital, particularly if you already care for someone else at home. Others reflected on early discharge as being put in a departure lounge and being forced out of the hospital. Further concerns on early discharge revolved around pain medication, with that prescribed at home being generally less effective as that administered in the hospital. Findings from the patient group highlight clear concerns over pre-operative planning and early discharge in the enhanced recovery pathway, and the importance of the study to evaluate these different elements.

DESCRIPTION OF METHODS OF INVOLVEMENT
The two patient representatives have been given information on how they can be involved, the type of support available to them and we have ascertained if they require any further support or training, to help in this role. Using the INVOLVE guidance, we have identified a variety of resources to help them in this role and have offered payment for both time and expenses. They have provided feedback on the application and reviewed the summary. They have agreed to be co-applicants on the grant and are willing to be involved in the steering group.

Among priorities identified through the work of the James Lind Alliance was the need to involve patients to identify the outcomes that matter to them (patient identified outcomes). We have taken this on board and will assemble a patient forum comprising 8-10 hip/knee replacement patients. We will use the well established PEP-R patient group for this forum, as described earlier. An experienced facilitator is essential to ensure all patients have their say. The session will be organised and facilitated by the PPI co-ordinator based at the University of Bristol's MRU.

EXPERTISE AND JUSTIFICATION OF SUPPORT REQUIRED

Dr Judge (20%) is an Associate Professor and Senior Statistician. He will be responsible for the overall leadership of the project. He will lead the statistical analyses. Dr Leal (10%) is a senior health economist and will lead the health economics work. Dr Gooberman-Hill (3%) is Reader in Applied Health Research and is a senior qualitative methodologist and will lead the qualitative research. Prof Price (5%) is Professor of Orthopaedic Surgery and Consultant Orthopaedic Knee Surgeon. He has worked with NHS England and the MSK Clinical Leaders Network on implementation of enhanced recovery. He will provide input on enhanced recovery (WP2) and contribute to interpretation of data analysis and report writing (WP1 and 2), and support dissemination activities through NHS England, and his positions on the NJR, BASK and BOA research committees. Dr Daniel Prieto-Alhambra (3%)

is a NIHR Clinician Scientist and primary care physician and has extensive experience in primary care research, particularly in the use of CPRD data for research purposes. He will provide input to statistical and health economic analysis of CPRD data (WP2), and will facilitate data analysis and report writing (WP1 and 2). Prof Carr (3%) is Professor of Orthopaedics, Head of Department, and Director of the Oxford NIHR Musculoskeletal BRU. He has expertise in PROMs and involvement of patients in assessing outcomes of surgery. He will provide input into analyses of variation in patient outcomes following surgery (WP1), and contribute to data analysis and report writing (WP1 and 2). Prof Arden (3%) is Professor of Rheumatology and has led research in prediction of patient outcomes of hip/knee replacement, with expertise in CPRD data analysis. He will contribute to interpretation and report writing of findings in WP1 and 2, and dissemination activities through his role on OARSI guidelines committee. Prof Cooper (3%) is Professor of Rheumatology and Director of the MRC Lifecourse Epidemiology Unit, University of Southampton. He leads internationally competitive programme of research into the epidemiology of musculoskeletal disorders. He will provide input to data analysis and report writing (WP1 and 2), and expertise and experience in engagement and dissemination activities to wider public bodies and stakeholder groups. Prof Peat (3%) is a physiotherapist and Professor of Clinical Epidemiology, Keele University. He will provide epidemiological expertise, with experience of research into osteoarthritis and research using CPRD and contribute to data analysis and report writing (WP1 and 2). Dr Barker (3%) is an experienced divisional director for orthopaedics working as NHS manager at Nuffield Orthopaedic Centre. She will provide input into interpretation of findings from an NHS management perspective will assist in communication of findings to NHS management. Prof Fitzpatrick (3%), Professor of Public Health and Primary Care, directs a programme of research in health services research and the measurement of health outcomes. He has research expertise in patient outcomes of joint replacement (WP1), and mixed methods methodology for design and analysis (MRC guidance) of complex interventions (WP2), and will contribute to data analysis and report writing. Dr Old and Ms Musson are patent representatives and will assist in interpretation and dissemination of findings from a lay perspective, and communication of findings through their wider PPI activities with the James Lind Alliance, NJR and Arthritis Care.

In additional to support for costs for time committed to the project by the team assembled above, we are seeking costs to appoint a data manager (50% year 1), study coordinator (40% years 1 and 2), statistician (50% years 1 and 2), health economist (50% year 1 and 2), and qualitative researcher (80% years 1 and 2). Further support is requested for the costs of obtaining NJR-HES-PROMs linked data, PPI representation, computer software, meetings such as the Project Advisory Group, conference and publication fees, and dissemination of findings to stakeholders including NHS managers, health professionals and commissioners.

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