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UK poSt Arthroplasty Follow-up rEcommendations (UK SAFE): what does analysis of linked, routinely collected national data sets tell us about mid-late term revision risk after hip replacement? Retrospective cohort study

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ABSTRACT

Objective To identify patients at risk of mid-late term revision of hip replacement to inform targeted follow-up.

Design Analysis of linked national data sets from primary and secondary care (Clinical Practice Research Datalink (CPRD-GOLD); National Joint Registry (NJR); English Hospital Episode Statistics (HES); Patient-Reported Outcome Measures (PROMs)).

Participants Primary elective total hip replacement (THR) aged≥18.

Event of interest Revision surgery≥5 years (mid-late term) after primary THR.

Statistical methods Cox regression modelling to ascertain risk factors of mid-late term revision. HR and 95% CI assessed association of sociodemographic factors, comorbidities, medication, surgical variables and PROMs with mid-late term revision.

Results NJR-HES-PROMs data were available from 2008 to 2011 on 142 275 THR; mean age 70.0 years and 61.9% female. CPRD GOLD-HES data covered 1995–2011 on 17 047 THR; mean age 68.4 years, 61.8% female. Patients had minimum 5 years postprimary surgery to end 2016. In NJR-HES-PROMS data, there were 3582 (2.5%) revisions, median time-to-revision after primary surgery 1.9 years (range 0.01–8.7), with 598 (0.4%) mid-late term revisions; in CPRD GOLD, 982 (5.8%) revisions, median time-to-revision 5.3 years (range 0–20), with 520 (3.1%) mid-late term revisions.

Reduced risk of mid-late term revision was associated with older age at primary surgery (HR: 0.96; 95% CI: 0.95 to 0.96); better 6-month postoperative pain/function scores (HR: 0.35; 95% CI: 0.27 to 0.46); use of ceramic-on-ceramic (HR: 0.73; 95% CI: 0.56 to 0.95) or ceramic-on-polyethylene (HR: 0.76; 95% CI: 0.58 to 1.00) bearing surfaces.

Increased risk of mid-late term revision was associated with the use of antidepressants (HR: 1.32; 95% CI: 1.09 to 1.59), glucocorticoid injections (HR: 1.33; 95% CI: 1.06 to 1.67) and femoral head size≥44 mm (HR: 2.56; 95% CI: 1.09 to 6.02)

No association of gender, obesity or Index of Multiple Deprivation was observed.

Conclusion The risk of mid-late term THR is associated with age at primary surgery, 6-month postoperative pain and function and implant factors. Further work is needed to explore the associations with prescription medications observed in our data.

Strengths and limitations of this study

- This study is part of a wider programme of work to identify potential patient groups for follow-up after hip and knee replacement and used large national routine data sets from primary and secondary care.
- The linkage of data sets allowed us to explore the impact of multiple risk factors on the mid-late term risk of revision of hip replacement.
- This study identifies predictors of mid-late term revision risk for hip replacement from real-world data and contributes to the discussion on follow-up.
- A limitation of the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man, the Hospital Episode Statistics and Patient-Reported Outcome Measures linked data was limited long-term follow-up—only data from 2009 to 2011 could be included to allow for revision rates at least 5 years after primary surgery.
- Data were missing for some of the variables in our data sets and this required us to use imputation to account for this in our analyses.

INTRODUCTION

Total hip replacement (THR) continues to provide many thousands of patients each year with a clinically effective treatment for end stage osteoarthritis of the hip joint. The surgical procedure has been shown to produce good outcomes for the patient and

to be cost effective.[1] The latest report from the National Joint Registry for England, Wales, Northern Ireland (NJR) and the Isle of Man recorded over 100 000 hip replacements in the preceding year;[2] the lifetime risk of undergoing a THR is estimated to be 11.6% for women and 7.1% for men.[3] Although it is a highly successful procedure, the cost associated with THR places an increasing burden on healthcare resources of funding and capacity, and the numbers are projected to grow with an ageing and increasingly obese population.[4]

Until relatively recently, care for patients with a THR included follow-up over the longer term; British Orthopaedic Association guidelines recommended outpatient follow-up at 1 and 7 years, and every 3 years thereafter for implants with well-documented survival statistics, namely the Orthopaedic Data Evaluation Panel 10A implants.[5] These services were intended to provide early detection of patients with failing implants. However, many hospitals face pressure to reduce the number of outpatient appointments due to longer waiting lists for orthopaedic treatment and there is evidence that follow-up services have been declining for some time.[6] With the additional challenges of the COVID-19 pandemic, waiting lists for orthopaedic treatment have increased further, placing additional pressure on outpatient services.[7] In the current healthcare environment where outpatient services face multiple threats, evidence is needed of the impact of disinvestment on follow-up of THR.

Although current evidence suggests that the proportion of THR that require a revision surgery is relatively low (7.53% at 15 years), the patient experience and costs vary with the cause of revision.[2 8] Periprosthetic fractures, which occur when the bone fractures adjacent to the THR, are one of the most expensive and traumatic categories, and it is estimated that numbers of this type of revision surgery are increasing.[9] As disinvestment in follow-up services has a potential effect on patient safety through early detection of failing implants, it is of interest to identify those groups of patients who may be at increased risk of revision of THR if no follow-up is provided. The James Lind Alliance work with groups of patients, public and health professionals to establish priorities in research.[10] In March 2014, they established that defining the ideal postoperative period and the best long-term model of care were among the top 10 priorities for people with osteoarthritis and a hip replacement. This emphasises a need to identify which patient groups will be most impacted by disinvestment in follow-up services.

This study forms part of a larger research programme, UK SAFE, that was designed to address the research question: Is it safe to disinvest in mid-late term follow-up of hip and knee replacement? (see protocol in online supplemental file 1).[11] The UK SAFE programme consisted of four work-packages using a mixed-methods design and took place between 1 December 2016 and 30 November 2020. The aim of this study (one of the four) was to identify which groups of patients with THR may require follow-up based on their mid-late term revision risk, five or more years postprimary surgery.

METHODS

Study design

This was an observational retrospective study based on existing national primary care and linked secondary care data sets aiming to identify factors that may be predictive for revision of hip replacement. The data sets included the Clinical Practice Research Datalink (CPRD) GOLD, the NJR, the Hospital Episode Statistics (HES) and Patient-Reported Outcome Measures (PROMs) for hip replacement.

Sources of data

CPRD GOLD-HES

The CPRD GOLD comprises the entire computerised medical records of a sample of patients attending general practitioners (GPs) in the UK.[12] It contains information on over 14 million patients registered at over 700 general practices in the UK that are representative of the population in terms of demographics such as age and sex.[13] The CPRD is administered by the Medicines and Healthcare products Regulatory Agency (MHRA). GPs in the UK play a key role in the delivery of healthcare, and each GP practice records any available medical information for their registered patients. This includes all clinical and referral events in both primary and secondary care in addition to comprehensive demographic information, prescription data and hospital admissions. Data are stored using Read codes[14] for diseases that are cross-referenced to the International Classification of Diseases (ICD-10).[15] Read codes are used as the standard clinical terminology system within UK primary care. Only practices that pass quality control are used as part of CPRD GOLD. CPRD ensures patient confidentiality by providing anonymised healthcare records.

CPRD GOLD data were linked to data for all-cause mortality, provided by the Office for National Statistics (ONS).[16] CPRD GOLD data were also linked to the Index of Multiple Deprivation (IMD) and to the HES database (described later). CPRD already provide access to HES data for England that is held under the CPRD Data Linkage Scheme, available for around 60% of patients in the database.

NJR-HES-PROMs

Starting in 2003, the NJR collected information on all hip and knee replacements performed each year in both public and private hospitals in England, Wales, Northern Ireland and the Isle of Man.[2] Data are entered into the NJR using forms completed at the time of surgery, and revision operations are linked to primaries using unique patient identifiers. Data recorded in the NJR includes prosthesis and operative information (prosthesis type, approach and thromboprophylaxis); patient information (age, gender, body mass index (BMI), American Society

of Anaesthesiologists (ASA) grade); surgeon and unit information (including caseloads, public/private status).

The HES data set holds information on all patients admitted to National Health Service (NHS) hospitals in England, including diagnostic ICD codes providing information about a patient's illness or condition and NHS national clinical procedural codes (OPCS4) for surgery.[17] It covers a smaller geographical area than the NJR and does not include privately funded operations. However, HES provides additional information for every patient, including detailed comorbidity information and deprivation indices, and 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. We used the Admitted Patient Care data set.

Since April 2009, PROMs have been collected on all hip replacements performed in public hospitals in England.[18] A health-related quality of life questionnaire (the EuroQol five domain (EQ-5D-3L)[19]) and a joint-specific outcome score (the Oxford Hip Score (OHS)[20]) are collected preoperatively and at 6 months after surgery, along with patient-reported measures of preoperative disability and postoperative satisfaction.

For this analysis, we used NJR records linked to data from the HES and PROMs databases on all hip operations.

Participants

Anonymised records were extracted for all patients over 18 years of age if they had THR for osteoarthritis. Inflammatory arthropathies were excluded as follow-up would commonly be managed by their rheumatologist. We excluded patients who had a total joint replacement of unspecified fixation, and those with a metal-on-metal THR or a hip resurfacing procedure as these groups have specific follow-up protocols in place. In addition, the following exclusions were made to remove potential case-mix issues: diagnostic codes indicating fracture or cancer of the hip bones; other injuries due to trauma, such as transport accidents and falls; non-elective admissions; a diagnosis other than primary hip osteoarthritis.

Primary outcome

The primary outcome was a mid-late term revision of the THR, defined as more than 5 years postprimary surgery. Revision is defined as the removal, exchange or addition of any of the components of arthroplasty. Revision before 5 years usually involves a symptomatic condition such as dislocation, infection or fracture.[2] The symptomatic nature will prompt the patient to seek medical help and will not be reliant on a screening service, as in follow-up clinics, to identify the failing THR.

In the NJR-HES-PROMS linked data sets, operative details are completed using the NJR data set, rather than the OPCS4 coding used by the HES data set. The NJR collects operative data using two forms, one for primary operations, and the other for revision operations. In both cases, all component labels from the surgery are attached to the form and it is from these that the component details are collected. Revision operations are linked to primaries using unique patient identifiers and so two operations on the same knee/hip could be linked using this system. The combination of the separate coding at source and the secondary linkage gives confidence that primary and revision operations are correctly identified. In the CPRD GOLD data set, subjects with a revision surgery procedure are identified using the Read codes, and for those with HES-linked data, OPCS4 codes can be used as well.

Predictors

Primary care predictors

The CPRD GOLD database provided information on age, gender, BMI, joint replaced, year of joint replacement operation, recorded diagnosis of osteoarthritis (yes/no), fracture presurgery (yes/no), calcium and vitamin D supplements, use of bisphosphonates, use of selective oestrogen receptor modulators, oral glucocorticosteroid therapy, smoking status and alcohol intake recorded closest to the date of the primary surgery, region of UK, comorbid conditions registered by the physician (asthma, malabsorptive syndromes, inflammatory bowel disease, hypertension, hyperlipidaemia, ischaemic heart disease, stroke, chronic obstructive pulmonary disease, chronic kidney failure, neoplasms and diabetes) and use of drugs which can affect fracture risk (proton pump inhibitors, antiarrhythmics, anticonvulsants, antidepressants, anti-Parkinson drugs, statins, thiazide diuretics and anxiolytics).

Secondary care predictors

Patient-level characteristics available in NJR and HES and included in the analysis were age, gender, BMI, area deprivation, rurality, ethnicity, Charlson comorbidity index[21] (calculated from HES using ICD-10 codes) and ASA grade. Additional data from the NJR provided surgical and operative factors: 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). Data from the PROMs database provided information on symptoms of pain, function and health-related quality of life preoperatively and at 6 months postsurgery. Pain and function were measured using the OHS. The EQ-5D-3L consists of five questions (assessing mobility, self-care, ability to conduct usual activities, degree of pain/discomfort and degree of anxiety/depression), ranging from 1 (best state) to 3 (worst state). EQ-5D-3L can be expressed as an overall index (graded from −0.594 to 1), or as ordinal responses for each category.

Sample size

We included all patients receiving planned elective THR within a specified time period; for CPRD GOLD-HES data, the time span covered the years 1995–2017; for

NJR-HES-PROMS data, it covered the years 2009–2017, which was specified to allow the linkage with PROMs data which commenced in 2009. For both data sets we excluded patients receiving a primary joint replacement after 2011 to ensure all patients had at least 5 years follow-up, as we were interested in revisions occurring 5 years or more after the primary replacement surgery.

Statistical analysis methods

Survival analysis was used to model time to revision. To identify patients most likely to require revision, proportional hazards regression modelling was used to identify preoperative, perioperative and postoperative predictors of mid-late term revision. The date of the first incidence of a subject's hip replacement was used as the start time. The event of interest in all time-to-event models was the first-recorded revision operation. Linearity of continuous predictors was assessed using fractional polynomial regression modelling. Proportionality assumptions were checked using Schoenfeld residuals. Fine and Grey regression modelling was used to account for the competing risk of death. Missing data were handled by using multiple imputation methods using the ICE (Imputation by Chained Equations) procedure.[22] SEs were calculated using Rubin's rules. We included all predictor variables in the multiple imputation process, together with the outcome variable (Nelson Aalen estimate of survival time and whether or not the patient had the outcome) as this carried information about missing values of the predictors.

For the CPRD GOLD-HES primary care, we generated 10 imputed data sets for THR. Data were imputed for the variables BMI, deprivation index, smoking and drinking risk factors. For secondary care NJR-HES-PROMS data set, we generated a single imputed data set for THR. Variables imputed were BMI, deprivation index, rurality, ethnicity, OHS baseline scores and EQ-5D-3L item for anxiety and depression. A full regression model was fitting including all variables, and then backward selection of variables with likelihood ratio tests was used to identify variables to keep in the final model risk factors. Fine and Grey regression models are used to account for the competing risk of death. For the CPRD GOLD-HES primary care data set, we present two final models, one with medication use as yes/no variables, and the other model with daily defined doses (DDDs) calculated from 1 year prior to the primary surgery and divided in tertiles. Harrell's C statistic is used as a measure of discriminatory ability of the survival regression models.

Patient and public involvement

Members of the National Institute for Health Research (NIHR) Leeds Biomedical Research Centre and Bristol patient and public involvement (PPI) groups were involved in developing the UK SAFE research question and work programme based on experiences of arthroplasty and preferences for care. The steering committee includes a PPI coapplicant who has contributed to interpretation of the results and will be involved in production of the final report that will be disseminated to the public, patients and NHS staff.

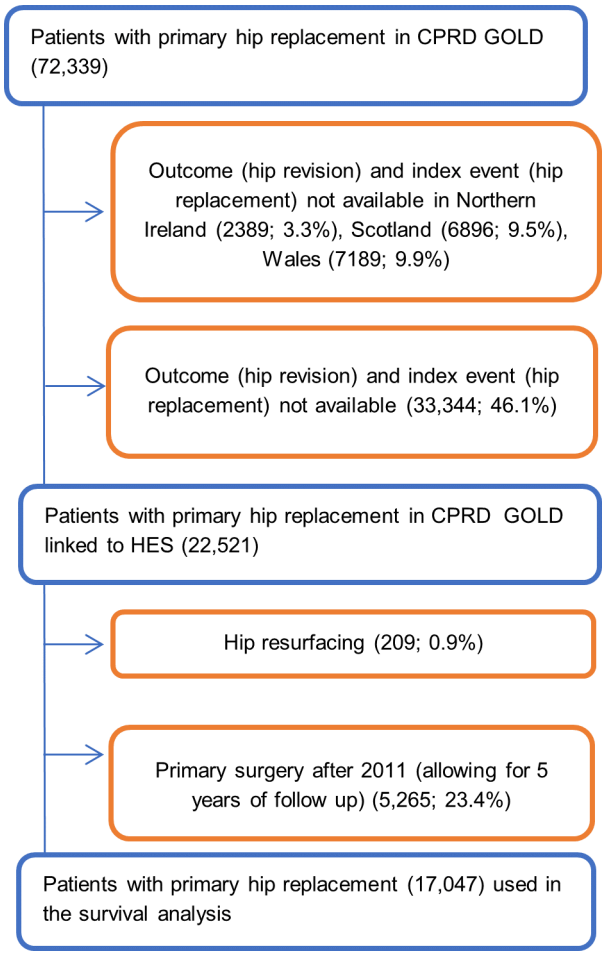

Figure 1 Selection of patient data for inclusion in survival analysis. Primary care data (inclusion in blue, exclusion in orange boxes). CPRD, Clinical Practice Research Datalink; HES, Hospital Episode Statistics.

RESULTS

The results of this study have been reported in accordance with the STROBE checklist (supplementary file 2)

Participants

The extraction of records from national data sets for inclusion in data for analysis is recorded in figure 1 (primary care records) and figure 2 (secondary care records). The CPRD GOLD-HES data (primary) covered a longer time period from 1995 to 2011 and yielded a total of 17 047 records. The NJR-HES-PROMs data (secondary) were available from 2009 to 2011 on 142 275 THR.

The age and gender distribution of patients were similar across both data sets, with a mean age of 68.4 years, 61.8% female in the CPRD GOLD-HES data, and 70.0 years, 61.9% female in the NJR-HES-PROMs data, respectively. These data, additional demographic data plus details of patient case-mix, surgical factors, operative details and primary care prescribing data are presented in online

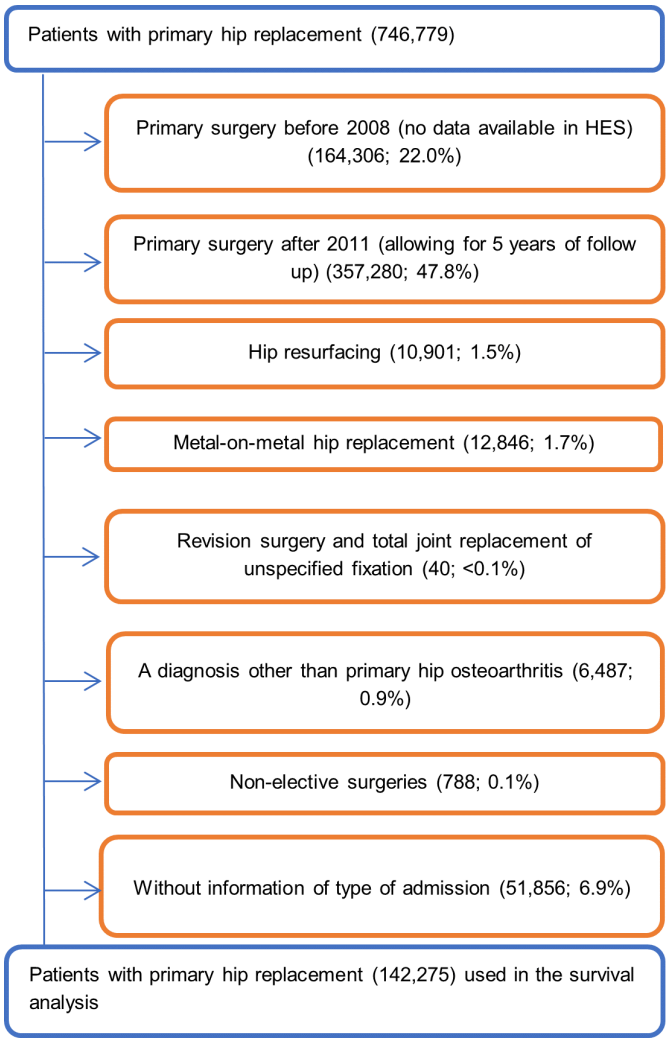

Figure 2 Selection of patient data for inclusion in survival analysis. Hospital data (inclusion in blue, exclusion in orange boxes). HES, Hospital Episode Statistics.

supplemental file 3: additional data (table A, CPRD-HES and table B, NJR-HES-PROMs).

The time from primary THR to revision in the CPRD GOLD-HES data was longer than in the NJR-HES-PROMs data; there were 982 (5.8%) revisions over a median time-to-revision of 5.3 years (range 0–20 years), with 520 (3.1%) mid-late term revisions. In the NJR-HES-PROMs data, there were 3582 (2.5%) revision procedures over a median time-to-revision of 1.9 years (range 0.01–8.7 years), of which 598 (0.4%) were mid-late term revisions.

Predictors of mid-late term revision

Patient demographics

Older age at the time of primary operation was associated with a lower risk of mid-late revision (tables 1 and 2). The association of age was linear; for a 1-year increase in age at surgery, the risk of mid-late term revision reduced by 3% and this finding was consistent across the CPRD-HES and NJR-HES data sets. There was no association for gender, obesity or IMD deprivation on the primary outcome. An association was observed for smoking where current smokers were at reduced risk of revision.

Co-morbidities

Of the comorbidities recorded in the CPRD GOLD-HES data set, two conditions were associated with increased risk of revision—malabsorption and previous non-hip fracture—and one with reduced risk—hypertension (table 1). Poorer health state at primary surgery, as indicated by ASA grade, was associated with reduced risk of revision (table 2).

Medication use

Analysis of preoperative medication in the CPRD GOLD-HES data (table 1) showed that the use of an antidepressant was associated with a higher revision risk. Analgesics considered for the model included narcotics (opioid pain relief) and non-narcotics, listed as non-steroidal anti-inflammatories (NSAIDs), NSAID cox (celecoxib, etoricoxib and rofecoxib), paracetamol, partial opiates and total opiates. Intra-articular glucocorticoid steroid injections were analysed as a separate predictor variable and were associated with an increased revision risk in final backwards selected regression models.

When examining associations of medication use by looking at DDDs calculated from 1 year prior to the primary surgery and divided into tertiles, further patterns emerged. The use of statins was associated with increased risk of revision in those with DDD<370 compared with no medication use. The association of injected glucocorticoid steroid use was only apparent in the higher dose category of>55 DDD (table 1).

Preoperative and 6-month postoperative scores

There was no association between preoperative PROMs and risk of mid-late revision. However, worse 6-month postoperative pain and function (OHS) was associated with an increased risk of revision (table 2).

Implant factors

Two of the implant factors in the NJR-HES-PROMs data (table 2) were associated with risk of mid-late term revision: the bearing surface and the head size. When compared with metal-on-polyethylene (MoP) implants, those patients with a ceramic-on-ceramic (CoC) or a ceramic-on-polyethylene (CoP) bearing surface had a reduced risk of outcome. Those with a femoral head size≥44 mm were at significantly increased revision risk (table 2 and online supplemental table C), with the risk being lowest in the smaller head sizes (≤28 mm).

Subgroup analysis

Within the NJR-HES-PROMS secondary care data set, analyses were repeated in the subset of patients with a MoP or CoP bearing surface (n=112 609), in order to reflect the most commonly used bearing surfaces. The variables identified in the final backward selection regression models were similar, with the exception that ASA grade was no longer selected, and comorbidities

Table 1 Cox regression model identifying risk factors of revision after 5 years of primary total hip replacement (THR) for osteoarthritis: primary care data

	Patients undergoing THR (n=22 312) HR (95% CI); p-value				
Risk factors (reference category)	**Crude analysis**	**Adjusted analysis (drug yes/no)**	**Adjusted competing risk analysis (drug yes/no)**	**Adjusted analysis (drug DDD)**	**Adjusted competing risk analysis (drug DDD)**
Year of primary THR (2010–2011)					
1995–1999	4.34 (1.88 to 9.98); **p<0.01**	4.98 (2.14 to 11.59); **p<0.01**	7.31 (3.18 to 16.79); **p<0.01**	5.02 (2.14 to 11.76); p<0.01	7.22 (3.12 to 16.68); **p<0.01**
2000–2004	2.78 (1.22 to 6.32); **p=0.02**	3.16 (1.38 to 7.23); **p=0.007**	4.33 (1.91 to 9.80); **p<0.01**	3.22 (1.40 to 7.42); p=0.006	4.32 (1.90 to 9.83); **p<0.01**
2005–2009	2.59 (1.13 to 5.91); **p=0.02**	2.74 (1.20 to 6.28); **p=0.017**	3.46 (1.53 to 7.85); **p=0.003**	2.73 (1.19 to 6.25); **p=0.018**	3.40 (1.50 to 7.71); **p=0.003**
Age at primary THR (continuous variable)	0.97 (0.96 to 0.98); **p<0.01**	0.97 (0.96 to 0.98); **p<0.01**	0.96 (0.95 to 0.96); **p<0.01**	0.97 (0.96 to 0.98); **p<0.01**	0.96 (0.95 to 0.96); **p<0.01**
Smoking (non-smoker)					
Ex-smoker	1.31 (0.77 to 2.22); p=0.49	0.91 (0.72 to 1.17); p=0.47	0.88 (0.69 to 1.13); p=0.31	0.91 (0.71 to 1.16); p=0.44	0.88 (0.68 to 1.12); p=0.29
Current	1.31 (0.77 to 2.22); p=0.58	0.73 (0.54 to 0.99); **p=0.041**	0.67 (0.50 to 0.91); **p=0.01**	0.73 (0.54 to 0.98); **p=0.037**	0.67 (0.50 to 0.91); **p=0.009**
Fracture in pelvis, proximal/humerus, wrist/forearm, spine or rib	1.51 (0.96 to 2.40); p=0.08	1.68 (1.06 to 2.67); **p=0.027**	1.64 (1.04 to 2.61); **p=0.035**	1.76 (1.10 to 2.82); **p=0.018**	1.75 (1.09 to 2.79); **p=0.02**
Comorbidities					
Malabsorption	4.17 (1.24 to 14.01); **p=0.02**			3.97 (1.13 to 13.94); **p=0.032**	3.69 (1.05 to 12.95); **p=0.042**
Hypertension	0.72 (0.58 to 0.89); **p<0.01**	0.77 (0.61 to 0.96); **p=0.02**	0.77 (0.62 to 0.97); **p=0.025**	0.76 (0.60 to 0.95); **p=0.014**	0.77 (0.61 to 0.96): **p=0.021**
Antidepressants	1.40 (1.17 to 1.68); **p<0.01**	1.37 (1.14 to 1.65); **p=0.001**	1.32 (1.09 to 1.59); **p=0.004**		
Statins	1.07 (0.86 to 1.34); p=0.54	1.43 (1.12 to 1.81); **p=0.004**	1.37 (1.08 to 1.75); **p=0.01**		
Glucocorticoid steroid injections (intra-articular)	1.32 (1.06 to 1.65); **p=0.01**	1.32 (1.06 to 1.66); **p=0.015**	1.33 (1.06 to 1.67); **p=0.014**		
DDDs 1-year prior surgery					
Bisphosphonates (no dose)					
<140 DDD	1.02 (0.48 to 2.16); p=0.96			1.16 (0.54 to 2.48); p=0.70	0.99 (0.46 to 2.11); p=0.98
≥140–340 DDD	0.42 (0.16 to 1.12); p=0.08			0.43 (0.16 to 1.17); p=0.10	0.40 (0.15 to 1.09); p=0.072
>340 DDD	1.70 (0.84 to 3.45); p=0.14			2.03 (0.99 to 4.18); p=0.054	1.77 (0.85 to 3.68); p=0.13
Dose missing	0.42 (0.11 to 1.70); p=0.23			0.52 (0.13 to 2.09); p=0.35	0.43 (0.11 to 1.75); p=0.24
Antidepressants (no dose)					
<85 DDD	1.42 (0.97 to 2.06); p=0.07			1.35 (0.92 to 1.98); p=0.12	1.31 (0.90 to 1.92); p=0.16
≥85–365 DDD	1.67 (1.24 to 2.25); **p<0.01**			1.65 (1.22 to 2.24); **p=0.001**	1.57 (1.16 to 2.13); **p=0.003**
>365 DDD	1.57 (0.96 to 2.59); p=0.07			1.56 (0.93 to 2.61); p=0.089	1.46 (0.87 to 2.43); p=0.15

Continued

Table 1 Continued

Risk factors (reference category)	Patients undergoing THR (n=22312) HR (95% CI); p-value				
	Crude analysis	Adjusted analysis (drug yes/no)	Adjusted competing risk analysis (drug yes/no)	Adjusted analysis (drug DDD)	Adjusted competing risk analysis (drug DDD)
Dose missing	1.24 (0.96 to 1.59); p=0.09			1.21 (0.93 to 1.56); p=0.15	1.17 (0.90 to 1.51); p=0.23
Statins (no dose)					
<280 DDD	1.26 (0.88 to 1.81); p=0.20			1.61 (1.12 to 2.33); **p=0.01**	1.55 (1.07 to 2.23); **p=0.02**
≥280–370 DDD	1.16 (0.85 to 1.60); p=0.35			1.59 (1.14 to 2.23); **p=0.007**	1.51 (1.08 to 2.12); **p=0.016**
>370 DDD	1.01 (0.64 to 1.59); p=0.97			1.34 (0.84 to 2.15); p=0.22	1.32 (0.82 to 2.11); p=0.25
Dose missing	0.33 (0.10 to 1.01); **p=0.05**			0.44 (0.14 to 1.36); p=0.15	0.42 (0.13 to 1.31); p=0.13
NSAID cox (no treatment)					
<60 DDD	0.96 (0.53 to 1.74); p=0.89			0.97 (0.53 to 1.78); p=0.93	1.00 (0.55 to 1.83); p=0.99
≥60–280 DDD	0.51 (0.27 to 0.96); **p=0.04**			0.53 (0.28 to 1.01); p=0.053	0.55 (0.29 to 1.04); p=0.064
>280 DDD	1.10 (0.56 to 2.13); p=0.79			1.09 (0.56 to 2.12); p=0.80	1.15 (0.59 to 2.25); p=0.67
Dose missing	1.18 (0.80 to 1.74); p=0.42			1.26 (0.84 to 1.88); p=0.26	1.25 (0.84 to 1.87); p=0.27
Intra-articular steroids (no treatment)					
<55 DDD	1.18 (0.71 to 1.97); p=0.53			1.14 (0.68 to 1.93); p=0.62	1.14 (0.67 to 1.92); p=0.63
≥55 DDD	2.22 (1.15 to 4.31); **p=0.02**			2.28 (1.14 to 4.54); **p=0.019**	2.13 (1.07 to 4.25); **p=0.031**
Dose missing	1.29 (1.01 to 1.66); **p=0.04**			1.30 (1.01 to 1.67); **p=0.043**	1.31 (1.02 to 1.69); **p=0.037**

HR represents number of times to have a revision after 5 years compared with the reference group. A value>1 indicates that the group has higher risk for revision.
Variables included in the final regression model are those with at least one category with a p-value<0.05 for the 10 imputed data sets in a backward selection.
Year index is categorised because the continuous variable violates the proportional-hazards assumption for Cox models on the basis of Schoenfeld residuals.
Bold figures represent results with p values <0.05 in the final regression model
DDD, daily defined dose; NSAIDs, non-steroidal anti-inflammatories; THR, total hip replacement.

of mild diabetes (increased revision risk) and mild liver disease reduced revision risk) were included in the model (online supplemental table C). The effect of large femoral head size (≥44) showed a stronger effect size in this subgroup.

Model discrimination

The discriminatory ability of the primary care model using the CPRD-HES data was c-statistic 0.63 for the model with medication use (yes/no) and 0.65 with drug use defined as DDD. In the NJR-HES-PROMs secondary care data set the c-statistic was 0.64.

DISCUSSION

The risk of a mid-late revision operation 5 years after primary hip replacement surgery is very low. Within our CPRD GOLD-HES primary data set, we had up to 20 years patient follow-up from the start point of 5 years after the primary operation (so 25 years from the index operation date), and even then, the mid-late revision rate was only 3.1% for THR. The aim of the study was to identify groups of patients with THR that may require follow-up based on their mid-late term revision risk. We found that older age at primary surgery was associated with a lower risk of mid-late term revision; there was an increased risk of

Table 2 Cox regression model identifying risk factors of revision after 5 years of primary total hip replacement for osteoarthritis: hospital data

	Patients undergoing THR (n=142 275) HR (95% CI); p-value		
Risk factors (reference category)	Crude analysis	Adjusted analysis	Adjusted analysis (competing risk)
Age at primary THR (continuous variable)	0.98 (1.0 to 1.0); **p<0.01**	0.97 (0.97 to 0.98); **p<0.01**	0.97 (0.96 to 0.97); **p<0.01**
Sex (women)			
Men	1.17 (1.0 to 1.4); p=0.08	1.22 (1.02 to 1.45); **p=0.029**	1.17 (0.98 to 1.39); p=0.088
ASA grade (P1-fit and healthy)			
P2-Mild disease not incapacitating	0.93 (0.7 to 1.2); p=0.52	0.97 (0.76 to 1.22); p=0.77	0.95 (0.75 to 1.21); p=0.70
P3–P5	0.70 (0.5 to 1.0); **p=0.04**	0.67 (0.47 to 0.94); **p=0.022**	0.58 (0.41 to 0.82); **p=0.002**
Bearing surface (MoP)			
CoC	1.08 (0.9 to 1.3); p=0.44	0.73 (0.56 to 0.94); **p=0.015**	**p=0.02**
CoP	0.93 (0.7 to 1.2); p=0.57	0.75 (0.57 to 0.99); **p=0.039**	0.76 (0.58 to 1.00); **p=0.052**
CoM-MoC	2.28 (1.3 to 4.1); **p=0.01**	1.62 (0.87 to 2.99); p=0.13	1.65 (0.89 to 3.05); p=0.11
Head size (≤28 mm)			
32 mm	1.28 (1.0 to 1.6); **p=0.02**	1.33 (1.07 to 1.65); **p=0.012**	1.28 (1.03 to 1.60); **p=0.026**
36–42 mm	1.24 (1.0 to 1.5); p=0.05	1.21 (0.94 to 1.56); p=0.15	1.17 (0.91 to 1.51); p=0.23
≥44 mm	3.12 (1.4 to 7.0); **p=0.01**	2.63 (1.12 to 6.19); **p=0.027**	2.56 (1.09 to 6.02); **p=0.031**
OHS, 6-month score (0–9 points, worst score)			
(10–14 points)	0.75 (0.60 to 0.95); **p=0.02**	0.73 (0.58 to 0.91); **p=0.006**	0.73 (0.58 to 0.92); **p=0.007**
(15–18 points)	0.66 (0.52 to 0.83); **p<0.01**	0.61 (0.49 to 0.78); **p<0.01**	0.62 (0.49 to 0.79); **p<0.01**
(19–23 points)	0.39 (0.29 to 0.53); **p<0.01**	0.36 (0.26 to 0.49); **p<0.01**	0.36 (0.27 to 0.50); **p<0.01**
(24–48 points)	0.39 (0.30 to 0.51); **p<0.01**	0.34 (0.26 to 0.45); **p<0.01**	0.35 (0.27 to 0.46); **p<0.01**

HR represents number of times to have a revision after 5 years compared with the reference group. A value>1 indicates that the group has higher risk for revision.
Variables included in the final regression model are those with at least one category with a p-value<0.05 for a single imputed data set in a backward selection.
Bold figures represent results with p values <0.05 in the final regression model
ASA, American Society of Anaesthesiologists; CoC, ceramic-on-ceramic; CoM - MoC, ceramic-on-metal; CoP, ceramic-on-polyethylene; MoP, metal-on-polyethylene; OHS, Oxford Hip Score; THR, total hip replacement.

revision associated with implant factors (bearing surface and head size) and medication use, and worse pain/function 6 months after the surgery.

Strengths of this study include the use of large, national, routinely collected data sets where the NJR data are mandatory and have near complete coverage, and the CPRD GOLD data are nationally representative in respect of UK population demographic characteristics. Large sample sizes afforded us the ability to identify predictors of a rare long-term outcome such as revision

surgery. Additional strengths are the detailed surgical and hospital factors available in the NJR data and over 20 years of follow-up in the CPRD-GOLD data set as well as the ability to capture a wide range of primary and hospital factors. A limitation of the NJR-HES-PROMs linked data was limited long-term follow-up—we included only data on primary hip replacement from 2009 onwards (the commencement of PROMs data) up to 2011 to allow for revision rates after 5 years. A further limitation was the inability to define disease severity radiographically although the preoperative pain as measured on OHS (a patient reported assessment) was included within the models. We were also unable to analyse by type of revision as this data were not available in either of our data sets. We acknowledge that changes in anaesthesia and surgical techniques have taken place and current orthopaedic practice may differ. There were also missing data for some of the variables in our data sets and this required us to use imputation to account for this in our analyses.

One of the aims of our study was to understand when revision surgery happens to inform when follow-up should occur. In a previous study using data from the CPRD with over 20 years follow-up, the estimated smoothed hazard plots for hip and knee replacement combined showed consistently higher revision risks for men and younger patients at all timepoints.[23] Other studies have similarly shown that the risk of revision after THR is higher for younger patients.[24 25] Our finding in respect of age is consistent with this existing literature.

In our analysis of other patient factors, those who were current smokers (time of primary surgery) were at reduced risk of mid-late term revision.[26 26] Kapadia *et al* found an increased risk of revision in the early years for this group of patients; our emphasis on mid-late revision may be an explanation for this difference if there has been a higher frequency of early revision in this group. Similarly, other authors have found increased risk of early revision for patients with higher ASA grades at primary surgery,[27] whereas our results indicate reduced risk at mid-late revision, which may be related to a state of poorer general health. Fractures in the pelvis, proximal/humerus, wrist/forearm, spine or rib may be indicative of fragility, which are also known to increase risk of early revision;[28] patients without a history of these conditions may be at increased risk of mid-late term revision due to longevity. Other findings were a fourfold increased revision risk associated with malabsorption, but it is very rare with only 0.3% of patients having this comorbidity. Over 30% of patients had hypertension preoperatively, but it is unclear why this in itself would confer lower revision risk and we propose it is simply an association.

The OHS records pain and function and it has been found that a poor 6-month postoperative score reliably predicts the 5-year outcome trajectory for pain and function.[29] Our finding of an increased risk of mid-late revision associated with poorer scores 6 months after primary surgery is consistent with this trajectory and early identification of this group for targeted follow-up may be appropriate.

These findings require further investigation. Postoperative statin use has previously been suggested to reduce revision risk for hip replacement,[30] whereas the association seen here in our study on mid-late revision suggested an increased revision risk. Also, our study found an association between antidepressant use prior to primary surgery and increased risk of revision; however, we did not find that patient levels of anxiety and depression recorded in preoperative PROMS were a risk factor. In another study of hip and knee replacement, use of antidepressant medication preoperatively did not affect outcomes 1 year post-surgery,[31] but the effect on mid-late term revision was not discussed.

The use of intra-articular glucocorticoid steroid injections in 17% of the population was associated with a twofold increased risk of mid-late term revision following THR, which is the opposite of our finding following oral glucocorticosteroid prior to knee replacement (HR: 0.72 (95% CI: 0.53 to 0.99) (in press). Although the administration of the injected steroid was linked to the index hip, our data did not allow us to identify site of administration of this injection. We postulate the increased risk of infection following intra-articular injection of steroid and subsequent revision,[32] but cannot demonstrate this association from our study.

The MoP bearing surface was most commonly used (66% of patients) in the NJR data set over the time period studied. The bearing surfaces with a lower risk were the 20% of CoC patients, and 13% of CoP patients which is consistent with the non-inferiority shown in the network meta-analysis conducted by Lopez-Lopez *et al*.[33] Prior to analysis we had excluded patients who had hip resurfacing and metal-on-metal hip replacement, where larger head sizes are common, as we know revision risk is higher. However, we still observed an association where, in the remaining THR patients, a larger head size was associated with higher mid-late revision risks. In the 17th NJR annual report,[2] the associations of head size and bearing surface were examined for THR revision rates and reflect earlier work by Smith *et al*.[34] With MoP and CoP, large head sizes appear to be associated with higher failure rates particularly with 36 mm heads used with cemented fixation and heads>36 mm used with hybrid and uncemented fixation. In our study here, we also observe large head size as being associated with revision risk. Of concern is that, according to the 17th NJR report, in 2003, the vast majority of hip replacements utilised heads of 28 mm or smaller across all fixation methods but since 2003, there has been a progressive shift away from small heads in cemented hip replacements to larger head sizes (>28 mm) with alternative fixation methods (uncemented or hybrid). In respect of bearing surface, NJR Kaplan-Meier plots of revision rates also show lower revision risk for CoC and CoP bearing surfaces.[2] These implant factors are hence potentially relevant for making decisions about which patient groups to target for extended follow-up.

This is one of the first studies to specifically identify predictors of mid-late term revision risk for hip replacement surgery. It is clear that the risk factors we identified for hip replacement are different to those for knee replacement and suggests the need for different models of organisation of any follow-up. For THR, implant factors of bearing surface and head size, and 6-month postoperative pain and function scores, appear to be important and relevant factors in deciding which patients may require extended follow-up. Further work is needed to explore the associations with prescription medications observed in our data. In conclusion, we suggest that this analysis of routinely collected NHS data provides useful insights to consider in the design of any future hip arthroplasty follow-up.

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Disclaimer The views expressed represent those of the authors and do not necessarily reflect those of the NIHR, the NHS, the Department of Health and Social Care, the National Joint Registry Steering Committee or the Healthcare Quality Improvement Partnership (HQIP) who do not vouch for how the information is presented. HES data copyright 2016, re-used with the permission of the Health & Social Care Information Centre. All rights reserved.

Competing interests LS reports grants from National Institute for Health Research during the conduct of the study. AJ reports grants from National Institute for Health Research and has received consultancy fees from Freshfields Bruckhaus Derringer and Anthera Pharmaceuticals LTD unrelated to this work. AJ was supported by the NIHR Biomedical Research Centre at University Hospitals Bristol and Weston NHS Foundation Trust and the University of Bristol. NKA reports grants from Merck, personal fees from Pfizer/Lilly, unrelated to the submitted work. SRK, MS and PGC were supported in part by the NIHR Leeds Biomedical Research Centre.

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Ethical approval The CPRD has obtained ethical approval from a National Research Ethics Service Committee (NRES) for all purely observational research using anonymised CPRD data; namely, studies which do not include patient involvement. The study has been approved by ISAC (Independent Scientific Advisory Committee) for MHRA Database Research (protocol number 11_050AMnA2RA2).NJR-HES-PROMS linked data. Approval for NJR data was received on 3rd October 2016 (NJR internal reference: 'Is it safe to completely disinvest in TJR follow-up or will this expose people to harm?'). Health Research Authority Confidentiality Advisory Group section 251 approval was received on 24 February 2017 (CAG reference: 17/CAG/0030). A Data Access Request Service (DARS) application for a Data Sharing Agreement (DSA) between NHS Digital and by Oxford University Research Services was completed on 31 July 2018 (DARS-NIC-172121-G0Z1H-v0.11).

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Data sharing statement Access to data is available from the National Joint Registry for England and Wales, Northern Ireland and the Isle of Man, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data access applications can be made to the National Joint Registry Research Committee. Access to linked HES and PROMs data is available through data applications to NHS Digital.

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Open access Protocol

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Towards UK poSt Arthroplasty Follow-up rEcommendations (UK SAFE): protocol for an evaluation of the requirements for arthroplasty follow-up, and the production of consensus-based recommendations

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ABSTRACT

Introduction Hip and knee arthroplasties have revolutionised the management of degenerative joint diseases and, due to an ageing population, are becoming increasingly common. Follow-up of joint prostheses is to identify problems in symptomatic or asymptomatic patients due to infection, osteolysis, bone loss or potential periprosthetic fracture, enabling timely intervention to prevent catastrophic failure at a later date. Early revision is usually more straight-forward surgically and less traumatic for the patient. However, routine long-term follow-up is costly and requires considerable clinical time. Therefore, some centres in the UK have curtailed this aspect of primary hip and knee arthroplasty services, doing so without an evidence base that such disinvestment is clinically or cost-effective.

Methods Given the timeline from joint replacement to revision, conducting a randomised controlled trial (RCT) to determine potential consequences of disinvestment in hip and knee arthroplasty follow-up is not feasible. Furthermore, the low revision rates of modern prostheses, less than 10% at 10 years, would necessitate thousands of patients to adequately power such a study. The huge variation in follow-up practice across the UK also limits the generalisability of an RCT. This study will therefore use a mixed-methods approach to examine the requirements for arthroplasty follow-up and produce evidence-based and consensus-based recommendations as to how, when and on whom follow-up should be conducted. Four interconnected work packages will be completed: (1) a systematic literature review; (2a) analysis of routinely collected National Health Service data from five national data sets to understand when and which patients present for revision surgery; (2b) prospective data regarding how patients currently present for revision surgery; (3) economic modelling to simulate long-term costs and quality-adjusted life years associated with different follow-up care models and (4) a Delphi-consensus process, involving all stakeholders, to develop a policy document which includes a stratification algorithm to determine appropriate follow-up care for an individual patient.

Ethics and Dissemination Favourable ethical opinion has been obtained for WP2a (RO-HES) (220520) and WP2B (220316) from the National Research Ethics Committee. Following advice from the Confidentiality Advisory Group (17/CAG/0122), data controllers for the data sets used in WP2a (RO-HES) – NHS Digital and The Phoenix Partnership – confirmed that Section 251 support was not required as no identifiable data was flowing into or out of these parties. Application for approval of WP2a (RO-HES) from the Independent Group Advising on the Release of Data (IGARD) at NHS Digital is in progress (DARS-NIC-147997). Section 251 support (17/CAG/0030) and NHS Digital approval (DARS-NIC-172121-G0Z1H-v0.11) have been

Strengths and limitations of this study

- Our mixed-methods approach allows us to address a question that would not be feasible to answer with a randomised controlled trial.
- Our study will capture data from a mixture of teaching hospitals, district general hospitals and hospitals with a special interest in joint replacement and with a geographical spread, increasing the generalisability of our results.
- Our economic model will be populated with routinely collected National Health Service (NHS) data of patients attending primary and hospital care in the UK, ensuring that our analysis is based on actual patient use of services, outcomes such as health-related quality of life and costs to the NHS.
- While our analysis is based on data sources that reflect clinical practice in England only, we believe key cost-effectiveness findings are likely to be informative for decision-making in the whole of the UK.

obtained for WP2a (NJR-HES-PROMS). ISAC (11_050MnA2R2) approval has been obtained for WP2a (CPRD-HES).

INTRODUCTION

Arguably, total hip arthroplasty (THA) and total knee arthroplasty (TKA) are the most successful surgical interventions performed in modern times. Due to an ageing population, and an obesity epidemic, hip and knee replacement procedures increase annually, rising from less than 20 000/year in the UK in 1978 to around 200 000/year in 2017.[1] The current follow-up requirements are estimated at 500 000–1 000 000 annual outpatient attendances. With limitless resources, every patient undergoing a joint arthroplasty would incur routine lifetime follow-up. The rationale for follow-up is to ensure timely detection of complications or arthroplasty failure, such as aseptic loosening, osteolysis and potential periprosthetic fracture. The cost of revision for aseptic loosening is 35% lower than that for periprosthetic fractures and has a lower incidence of complications which impact recovery.[2] However, while routine long-term follow-up of joint prostheses may support timely revision for patients with asymptomatic complications, improving long-term health outcomes, it is also costly both clinically and financially.

Orthopaedic services are already one of the poorest performers across the National Health Service (NHS) by failing to meet waiting list targets, with an estimated 8000 orthopaedic NHS breaches each month.[3] With a rapidly ageing population and medical advances that mean less stringent criteria for surgery eligibility,[4] there is no sign that demand will recede in coming years and orthopaedic services will soon reach breaking point. To reduce the burden on orthopaedic services, evidence-based consensus guidelines are required to establish how, when and on whom follow-up should be conducted.

British Hip Society (BHS) and British Orthopaedic Association (BOA) guidelines recommend outpatient follow-up at 1 and 7 years, and every 3 years thereafter for Orthopaedic Data Evaluation Panel 10A (ODEP-10A) implants, with more frequent follow-up for novel implants.[5] However, recent work revealed considerable diversity across the UK in arthroplasty follow-up pathways, in timing, how follow-up is conducted and which health professionals are involved.[6]While some centres followed-up patients beyond 10 years, others did not have an established follow-up policy and in some centres follow-up services have been curtailed or stopped entirely after an early postoperative check.[6] Notably, we do not know whether long-term follow-up is cost-effective or whether disinvestment is safe for patients.

This project aims to determine the consequences of disinvestment in hip and knee arthroplasty follow-up. Given the timeline from joint replacement to revision, with a 7% revision rate for THA and 4% revision rate for TKA at 14 years, conducting a randomised controlled trial to address this question is not feasible. Moreover, the huge variation in follow-up practice across the UK limits the generalisability of the results of an RCT. We will therefore use a mixed-methods approach to comprehensively evaluate the requirements for arthroplasty follow-up and will use this evidence to inform the development of consensus-based recommendations and a policy document which includes a stratification algorithm to determine appropriate follow-up for individual patients. Disinvestment is a complex and often contentious issue. We plan to make use of published recommendations[7] to ensure that the results of this work are understood and considered as a genuine attempt to use the best evidence available to ensure that the NHS gets value for money and that patients remain safe.

METHODS AND ANALYSIS

Study objectives

A. Identify who needs follow-up and when this should occur for primary THA, TKA and unicompartmental knee arthroplasty (UKA) surgery by making use of routinely collected NHS data.
B. Understand the patient journey (in primary and secondary care) to revision surgery by recruiting patients admitted for elective and emergency hip and knee revision surgery.
C. Establish how and when patients are identified for revision, why some patients are missed from regular follow-up and present acutely with fracture around the implant (periprosthetic fracture), by using prospective and retrospective data.
D. Identify the most appropriate and cost-effective follow-up pathway to minimise potential harm to patients by undertaking cost-effectiveness modelling.
E. Provide evidence-based and consensus-based recommendations on how follow-up of primary THA and TKA should be conducted.

Design

This is a mixed-methods study using a variety of data sources consisting of four interconnected work packages (WP): (1) a systematic literature review; (2a) analysis of routinely-collected NHS data to understand when and which patient present for revision surgery; (2b) prospective data regarding how patients currently present for revision surgery collected on around 455 patients prior to elective or emergency revision surgery; (3) economic modelling to simulate long-term costs and quality adjusted life years associated with different follow-up models; (4) a Delphi-consensus process, incorporating all previous WPs and involving all stakeholders, to develop a policy document which includes a stratification algorithm to determine appropriate follow-up for an individual patient.

WP1: systematic review

The aim of the review is to evaluate different models of routine long-term follow-up care after TKA/THA/UKA. This systematic review will establish a robust evidence base

for the cost-effectiveness modelling (WP3) and consensus guideline development (WP4).

Registration

This systematic review will be undertaken following Cochrane Collaboration methods[8] and reported in accordance with Preferred Reporting Items for Systematic Review and Meta-analyses guidelines.[9] It has been prospectively registered with PROSPERO (CRD42017053017).

Searches

A comprehensive literature search will be undertaken with the aim of retrieving all relevant literature, published or unpublished, which evaluated the effectiveness of long-term follow-up after primary TKA/THA/UKA. A range of information sources will be searched: BIOSIS, CINAHL, ClinicalTrials.gov, The Cochrane Library, Embase, Health Management Information Consortium, IDEAS (RePEC), Ovid Medline(R), ProQuest Dissertations and Theses, PsycINFO, PubMed and Web of Science. Reference lists of included studies will be reviewed for potentially relevant articles. A sample search strategy is detailed in the online supplementary appendix A. No date or language restrictions will be applied.

Criteria for selection of studies

All study designs will be included which (1) consider the clinical and/or cost effectiveness of routine long-term (>5 years) follow-up care after primary THA, TKA or UKA; (2) describe patient safety issues associated with routine follow-up or (3) consider the acceptability of new care pathways from the perspective of the patient and/or practitioner. Studies will be excluded if they do not report specific patient-related outcome measures or appropriate health utility measures.

Selection of studies

Titles/abstracts of identified studies will be screened for eligibility by one experienced reviewer with a random selection (25%) independently screened by a second. Potential studies will be retrieved in full text and reviewed against the inclusion/exclusion criteria independently by the same two reviewers, with a third reviewer used to settle any disputes.

Data extraction

Data will be extracted by a single reviewer using a standardised proforma capturing (1) purpose and design; (2) methodological characteristics; (3) information relating to quality assessment and (4) outcome data relating to the clinical and cost-effectiveness of routine long-term follow-up care.

Quality assessment

The Cochrane Risk of Bias assessment tool will be used for experimental studies,[10] and the Newcastle-Ottawa scales for cohort and case–control studies.[11] Qualitative literature will be assessed using critical interpretive synthesis.[12] Economic evaluations will be assessed using the Drummond checklist.[13] Studies will be evaluated independently by two reviewers, with a third to settle any disputes. Studies at high risk of bias will not be excluded and conclusions will incorporate observed biases.

Evidence synthesis

The design, methodological characteristics, study quality and main findings will be summarised in narrative and tabular form. We anticipate substantial heterogeneity among included studies precluding the use of meta-analysis techniques.

WP2a: Analysis of routinely collected NHS data

This WP will use routinely collected NHS data to determine when revision happens and to identify patients most likely to require revision in order to target when and on whom follow-up should occur.

Data sources

Data from five national datasets will be used: (1) Clinical Practice Research Database (CPRD),[14] (2) ResearchOne (RO),[15] (3) Hospital Episode Statistics (HES),[16] (4) National Joint Registry (NJR)[17] and (5) patient reported outcome measures (PROMs).[18]

Three linked data sets will be constructed for analysis: (a) CPRD–HES–PROMS, which preexists at the University of Oxford, (b) RO–HES will be constructed and analysed at the University of Leeds. Linkage will be undertaken by NHS Digital on the basis of pseudonyms generated from NHS numbers by the data providers. (c) NJR–HES–PROMS will be constructed and analysed at the University of Oxford. Linkages will be undertaken by NHS Digital, using an agreed set of common patient identifiers, including NHS number. Data sets (a) and (b) provide a primary care view (eg, prior diagnoses, prescribing) and include different, representative patient populations for cross-validation; data set (c) provides a secondary care view (eg, surgeon, procedure details).

Data analysis

The primary outcome of the analysis will be mid-late term revision (>5 years post-primary surgery), defined as the removal, exchange or addition of any of the components of arthroplasty. Exposures will include secondary care predictors, including patient level characteristics recorded in NJR and HES (eg, age, body mass index (BMI)), surgical and operative factors and symptoms of pain, function and health-related quality of life preoperatively and 6 months post-surgery from PROMS, and primary care predictors, including patient demographics, comorbidities and use of drugs which can affect fracture risk. Survival analysis will be used to model time to revision.[19 20] The smoothed Nelson-Aalen cumulative hazard rate will be examined to identify any peak in the mid-long term risk of revision. Cox proportional hazards regression modelling will be used to identify preoperative, perioperative and postoperative predictors of mid-late term revision, for example, age, BMI, comorbidities, implant type, surgeon skill and postoperative problems. Competing risk

regression will be used, since mortality can be regarded as a competing risk for revision surgery.[21 22] To account for clustering within the data (such as patients nested within hospitals), a multilevel survival model will be fitted by extending the survival regression model to include a frailty term with a Gaussian distribution.[23]

WP2b part 1: multicentre observational prospective cohort

Prospective data collection from patients undergoing revision surgery.

Objectives:

- Identify all recent (previous 12 months) medical appointments and advice sessions related to the index joint in primary and secondary care.
- Establish if the patient has been seen by orthopaedic health professionals from 12 months after primary surgery until this hospital admission, that is, was the revision directed by routine follow-up.

Design

A multicentre, observational, single visit, prospective cohort study of patients admitted for revision hip or knee surgery.

Population

Patients presenting for elective and emergency revision surgery of a primary THA, TKA or UKA and who are able and willing to provide written informed consent will be included in the study. Patients will be excluded if they have had previous revision surgery; metal-on-metal primary joint replacement or hip hemiarthroplasty. Participants will be recruited from a sample of hospitals selected to provide geographical spread and representation of teaching hospitals, district general hospitals and hospitals with a special interest in joint replacement

Data collection

A participant case report form (CRF) will capture details of follow-up after primary surgery and pathway to current revision surgery, including symptom state. An investigator CRF will extract data from medical notes including demographics (age, gender, diagnosis leading to primary surgery, medical history), general practitioner and hospital appointments, details of primary and revision surgery (including implant type, complications, length of stay). The participant CRF will be piloted with the Leeds Biomedical Research Centre Patient and Public Involvement (PPI) group and the investigator CRF with two research nurses to ascertain the comprehension, usability and completeness of data subsequently extracted.

Sample size

We will use stratified sampling to recruit centres of varying size and anticipate that the average number of patients per centre will be 45 (based on NJR records and information from prospective centres). We initially anticipated the recruitment of 25 centres. With a recruitment rate of 60%, this gave 27 recruited patients from 25 centres (n=675). We do not know the intraclass correlation coefficient (ICC) for our primary outcome ('Was the revision a result of routine follow-up?'), but we anticipate it to be in the region of 0.01–0.05. To be conservative, we use ICC=0.05. This gives a design factor of 2.3 and hence an effective sample size of 293 after accounting for clustering within centre. The enrolment of 35 centres reduced the design factor to 1.6 and the total sample size required to 455. From previous research,[6] we estimate that the rate of our primary outcome is 20% so that the effective number of events will be 58. Hence, we will have sufficient power for our logistic regression to robustly estimate the coefficients of up to five potential risk factors derived from our brief patient survey.[24]

Analysis

The primary outcome will be 'revision identified through routine follow-up', and this will be modelled through a multilevel logistic regression model, with a centre-level random intercept of particular interest. The size of the centre-level effect will be assessed as the proportion of variance explained and will also be assessed through a likelihood ratio test. Up to five factors from the patient questionnaire will be explored as fixed effects at the patient level. This will adjust for case mix. Factors that are found to be both clinically and statistically significant could potentially contribute to a stratified approach to follow-up.

WP2b part 2: qualitative study

Building on previous work highlighting the changes in follow-up practice,[6] this WP aims to explore the rationale and motivating factors behind these changes, the facilitators and the evidence considered when implementing new pathways, including no follow-up.

Sampling

A sample of n=20–30 orthopaedic practitioners and/or unit managers will be recruited. Purposive sampling via sampling matrix will recruit participants with different experiences of a range of follow-up pathways while reflecting NHS trust type, geographical area (urban, rural); socioeconomic area (low/high socioeconomic status) and diverse ethnicity. Some selection criteria are likely to be nested (eg, hospital type, geographical area) and care will be taken to ensure that all viewpoints are represented.

Data collection

Semistructured, telephone interviews following a topic guide refined from the literature review and expert opinion (clinician coapplicants/advisors and PPI members). The researcher will probe pertinent initial responses and expand on issues raised. Interviews will be recorded and transcribed verbatim.

Data analysis

The guiding approach will be framework analysis.[25] Data analysis will comprise five stages: (1) data familiarisation;

(2) identifying the thematic framework; (3) indexing; (4) charting and (5) mapping and interpreting. The process of familiarisation enables the researcher to identify emerging themes or issues in the data. Little is known about why NHS trusts have chosen to either withdraw follow-up care or change the way it is delivered. The evidence generated from the literature review and input from our clinical coapplicants will be used to help identify and refine the thematic framework. Themes are flexible and can be modified in the light of new data, and a process of constant comparison will be undertaken across themes and cases.

WP3

As previous work conducted by members of our team has identified considerable heterogeneity in current follow-up pathways,[6] our cost-effectiveness analysis will compare the relative costs and quality-adjusted life years associated with having follow-up compared with not having follow-up. A third hypothetical scenario of a virtual follow-up will be considered.

Comparators

Both the findings from our systematic review and the prospective cohort will inform the criteria to be used to identify patients as having or not having follow-up. The 7-year reference point for a follow-up currently suggested by BHS and BOA guidelines is likely to be incorporated. Patients having an orthopaedic outpatient appointment around the reference point(s) following a primary arthroplasty will be used to group patients in the CPRD–HES–PROMS data set into the follow-up and no follow-up groups. Joint-specific revision procedures will be identified by OPCS-4 codes as reported in the Admitted Patient Care data set within HES, with corresponding linked records to primary care and PROMS.

Model structure

To identify the most appropriate modelling approach for the question and data at hand, we will conduct a series of preliminary analysis to determine if a cohort-level or patient-level decision analytic model should be employed. Previous models examining the long-term cost-effectiveness of hip and knee replacements have used cohort Markov models.[26 27] Analyses will include associations between patients' characteristics and revision rates, health utilities and costs and whether the risk for revision depends on the time patients stay unrevised after their primary. Regardless of the chosen model type, the key health state or event will be revision arthroplasty, with death and complications also considered. The model will be designed to cover patients' lifetime and analysed from an NHS and Personal Social Services perspective, with discounting of costs and outcomes as per current guide to the methods of technology appraisal.[28]

Model inputs

WP2 data sets will be used to quantify primary and hospital healthcare resource use for comparator groups of follow-up care models through estimation of NHS costs and health-related quality of life (HRQoL). The economic model will simulate long-term costs and quality adjusted life years (QALYs) associated with each care model. Primary care costs will include consultations, and hospital costs will be derived by grouping hospital episodes into Health Resource Groups, a set of casemix groupings utilising similar levels of healthcare resources. Panel data regression analysis[29–31] will be used to estimate hospital costs conditional on patient characteristics and comorbidities. QALYs and transition probabilities will be derived from the linked data sets and published literature as needed. The hypothetical costs of virtual follow-up will be based on similar virtual clinic alternatives previously studied and NHS X-ray-associated costs.

Analysis

Cost-effectiveness analyses will be performed separately for relevant patient subgroups based on gender, age and other potential covariates for which data may be available. As with all economic models, a number of assumptions will be made, and their plausibility and potential impact discussed, relating to model structure and input parameters for transition probabilities, health utilities and costs, including the cost of periprosthetic fractures if no reference is found for these in the literature. Sensitivity analyses will be conducted to explore the uncertainty associated with key assumptions and model parameters and the implications of using different estimates discussed.

WP4: Delphi-consensus process

This WP will use the collective evidence from WP1–3 to inform a consensus process to determine appropriate follow-up care pathways for hip and knee arthroplasty.

Evidence gathered from WP1–3 will feed into a consensus panel workshop. We intend to use methods employed by the National Institute for Health and Care Excellence (NICE) in both the technology assessment committees and Guideline Development Groups. The expert stakeholders invited to attend will have a special interest in patient follow-up after hip or knee replacement surgery. Participants will include patients, orthopaedic surgeons, arthroplasty practitioners, NHS managers and commissioners, manufacturers and representatives of the major orthopaedic bodies (including BOA, BHS and BASK). The purpose of this exercise is to consider the evidence and obtain agreement for future care pathways, supported by the evidence of their effectiveness and cost-effectiveness, to be recommended and adopted across the NHS. Following the NICE consensus model all participants will receive summaries of the main research findings in advance. There will be presentations from the work-stream leaders to outline the evidence for consideration.

Robert *et al*[7] demonstrate that decommissioning is often about more than the 'evidence' and that withdrawal of previously available services is often seen as being driven by the wrong kind of evidence, based on cost data and

political priorities and not on what patients and service users value.[7] It is a complex issue, perhaps as contentious as NICE decisions when they do not fund an effective intervention because it exceeds the threshold. However, NICE investment decisions are made with the explicit understanding that, with no increase in the budget, there must be some displacement of other healthcare technologies.[32] We plan to make use of the recommendations for engagement and the use of evidence outlined in Robert *et al* to ensure the results of this work are understood and considered as a genuine attempt to use the best evidence available to ensure that the NHS gets value for money and that patients remain safe.

Patient and public involvement

Members of the NIHR Leeds BRC, Oxford and Bristol PPI groups are involved in UK SAFE. The PPI co-applicant is a member of the study steering committee and contributes across all WPs. Two independent PPI advisors sit on the Independent Advisory Group. Specific areas where lay involvement will be pivotal include the interpretation of results of the systematic review, the expert panel discussion and consensus process, study oversight (steering group), preparation of patient material and study results and contribution to reports and newsletters for patients and NHS staff.

ETHICS AND DISSEMINATION

All studies will be conducted in accordance with the principles of Good Clinical Practice, and the UK Policy Framework for Health and Social Care Research, 2018. Favourable ethical opinion has been obtained for WP2a (RO-HES) (220520) and WP2B (220316) from the National Research Ethics Committee. Following advice from the Confidentiality Advisory Group (17/CAG/0122), data controllers for the data sets used in WP2a (RO–HES)—NHS Digital and The Phoenix Partnership—confirmed that Section 251 support was not required as no identifiable data was flowing into or out of these parties. Application for approval of WP2a (RO–HES) from the Independent Group Advising on the Release of Data (IGARD) at NHS Digital is in progress (DARS-NIC-147997). Section 251 support (17/CAG/0030) and NHS Digital approval (DARS-NIC-172121-G0Z1H-v0.11) have been obtained for WP2a (NJR-HES-PROMS). ISAC (11_050MnA2R2) approval has been obtained for WP2a (CPRD–HES).

At the end of the project, outputs will be disseminated nationally in the form of an executive summary statement of the agreed pathway/s through appropriate NHS Networks, NICE, the NHS England Elective Orthopaedics Sub-committee, the NHS Institute for Innovation and Improvement and professional societies, including BHS, BOA, BASK, Arthroplasty Care Practitioners Association and the NJR. Dissemination will be key to developing a culture of 'finding the best way of doing something and doing it everywhere' to significantly reduce wastage of clinical resources and optimise NHS spend. We will put forward the consensus statement to each society's AGM for adoption as a resolution. Internationally, dissemination platforms are in place through the International Society of Arthroplasty Registers (ISAR) and the European Federation of National Associations of Orthopaedics and Traumatology. A lay summary of the project will be produced for study participants. Findings will also be presented at relevant orthopaedic and methodological conferences, such as the BOA and the Exploiting Existing Data for Health Research conference. The chief investigator and co-applicants will be named as authors on main publications, and an appropriate first author agreed through discussion. Other key individuals will be included as authors or contributors as appropriate, at the discretion of the Senior Management Group. Any disputes relating to authorship will be resolved by the Steering Committee.

The Chair and Independent members of the Steering Committee will be acknowledged, but will not qualify for full authorship, in order to maintain their independence. Individual collaborators must not publish data concerning their participants' which are directly relevant to the questions posed in the study until the main results of the study have been published.

CONCLUSION

This research will deliver the first research-supported, best-for-patient, joint-specific, cost-effective recommendations for follow-up pathways, providing a gold standard for clinical excellence and follow-up advice for patients, surgeons, purchasers and the NHS as a whole. Value is not limited to the UK, but has substantial global impact potential.

The impact of this work will be to reduce the burden on patients and the NHS in terms of outpatient visits and clinical tests that do not add benefit, while optimising detection of potential problems. From an NHS perspective, this work will provide managers with economic and clinical information on arthroplasty follow-up to inform service planning and delivery, and the role of arthroplasty practitioners in this service, with the potential to reduce geographical disparity through NHS trusts modelling their service provision on a national evidence-based guideline; provide orthopaedic surgeons with guidance on follow-up, including patient and economic considerations of factors involved; produce arthroplasty follow-up guidelines for adoption by the relevant specialist societies and information for their members. From a patient perspective, this work will help to inform patients about follow-up practice, empower them to make choices about future healthcare relating to their joint arthroplasty and provide reassurance that their follow-up pathway is appropriate

The outputs of this project, in terms of evidence-based support for timing of follow-up and identification of the most cost-effective follow-up model, fit directly within the

NHS framework for improving outcomes from elective procedures. Rationalising current diversity of follow-up practices should enable substantial savings for the NHS. We envisage outputs to be readily applicable to the wider NHS, not only hip and knee but also other joint replacements. With the committed support of key national and international organisations already in place, we anticipate that these guidelines will be positively received and that implementation will be widespread.

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Supplementary file II: STROBE checklist

STROBE. Strengthening the reporting of observational studies in epidemiology. Available at: https://www.strobe-statement.org/.

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5,6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6,7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8,9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8,9
		(*b*) Describe any methods used to examine subgroups and interactions	11
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, explain how loss to follow-up was addressed	n/a
		(*e*) Describe any sensitivity analyses	11
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9,10
		(b) Give reasons for non-participation at each stage	10
		(c) Consider use of a flow diagram	

Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	Supp File 3: Tables A&B 10
Outcome data	15*	Report numbers of outcome events or summary measures over time	10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	13-17
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	18	Summarise key results with reference to study objectives	18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	20
Generalisability	21	Discuss the generalisability (external validity) of the study results	20
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	21

*Give information separately for exposed and unexposed groups.

Supplementary Data

Table A. Descriptive statistics for the CPRD GOLD-HES linked datasets

Descriptor	No. of records (17,047)
Year of primary	
1995-1999	1386 (8.1%)
2000-2004	4990 (29.3%)
2005-2009	7554 (44.3%)
2010-2011	3117 (18.3%)
Age at primary	68.4 (SD 10.5)
Sex	
Female	10530 (61.8%)
Male	6517 (38.2%)
Body mass index	
Underweight	145 (1.2%)
Normal	3455 (28.0%)
Overweight	4979 (40.4%)
Obese Class I (Moderately obese)	2633 (21.4%)
Obese Class II and higher	1112 (9.0%)
Index of Multiple Deprivation (IMD) quintiles	
Least deprived	4259 (25.0%)
2	4223 (24.8%)
3	3742 (22.0%)
4	2858 (16.8%)
Most deprived	1954 (11.5%)
Region	
East Midlands	678 (4.0%)
East of England	1986 (11.7%)
London	1253 (7.4%)
North East	408 (2.4%)
North West	2348 (13.8%)
South Central	2608 (15.3%)
South East Coast	2043 (12.0%)
South West	2643 (15.5%)
West Midlands	2329 (13.7%)
Yorkshire & The Humber	751 (4.4%)
Smoker	
Ex-smoker	4455 (32.3%)
Non-smoker	7591 (55.1%)
Current	1737 (12.6%)
Alcohol	
Previous alcohol consumer	280 (2.5%)

No	1806 (16.4%)
Yes	8935 (81.1%)
Diagnosis	
Recorded diagnosis of hip OA	6345 (37.2%)
Hip Fracture prior primary surgery	375 (2.2%)
Fracture in pelvis, proximal/humerus, wrist/forearm, spine or rib	557 (3.3%)
Comorbidities	
Asthma	1427 (8.4%)
Malabsorption	44 (0.3%)
Inflammatory bowel disease	117 (0.7%)
Hypertension	5142 (30.2%)
Hyperlipidaemia	1808 (10.6%)
Ischaemic heart disease	1348 (7.9%)
Myocardial infarction	336 (2.0%)
Stroke/cerebrovascular disease	512 (3.0%)
Chronic pulmonary disease	501 (2.9%)
Chronic kidney failure	1053 (6.2%)
Cancer	1385 (8.1%)
Diabetes	1192 (7.0%)
Drugs which can affect fracture risk (intake prior to primary surgery)	
Calcium and vitamin D supplements	1374 (8.1%)
Bisphosphonates	1281 (7.5%)
Selective oestrogen receptor modulators	41 (0.2%)
Oral glucocorticosteroid therapy	2995 (17.6%)
Drugs prior to primary surgery	
Proton pump inhibitors	6140 (36.0%)
Anti-arrhythmics	1550 (9.1%)
Anticonvulsants	711 (4.2%)
Antidepressants	5327 (31.3%)
Anti-Parkinson drugs	183 (1.1%)
Statins	4527 (26.6%)
Thiazide diuretics	7259 (42.6%)
Anxiolytics	3031 (17.8%)
Painkillers/anti-inflammatory drugs	
NSAIDs	14398 (84.5%)
NSAID cox	2332 (13.7%)
Paracetamol	13737 (80.6%)
Partial Opiates	12552 (73.6%)
Total Opiates	6419 (37.7%)
Injected Steroids	2875 (16.9%)

DDDs (daily defined dose) 1-year prior surgery	
Calcium and vitamin D supplements	
No dose	15673 (91.9%)
<120 DDD	329 (1.9%)
>=120 to 340 DDD	527 (3.1%)
>340 DDD	218 (1.3%)
Dose missing	300 (1.8%)
Bisphosphonates	
No dose	15766 (92.5%)
<140 DDD	290 (1.7%)
>=140 to 340 DDD	455 (2.7%)
>340 DDD	271 (1.6%)
Dose missing	265 (1.6%)
Selective oestrogen receptor modulators	
No dose	17006 (99.8%)
<280 DDD	8 (0.1%)
>=280 to 390 DDD	12 (0.1%)
>390 DDD	9 (0.1%)
Dose missing	12 (0.1%)
Oral glucocorticosteroid therapy	
No dose	14052 (82.4%)
<30 DDD	344 (2.0%)
>=30 to 280 DDD	456 (2.7%)
>280 DDD	325 (1.9%)
Dose missing	1870 (11.0%)
Proton pump inhibitors (no dose)	
No dose	10907 (64.0%)
<85 DDD	1262 (7.4%)
>=85 to 365 DDD	2296 (13.5%)
>365 DDD	727 (4.3%)
Dose missing	1855 (10.9%)
Anti-arrhythmics (no dose)	
No dose	15497 (90.9%)
<170 DDD	155 (0.9%)
>=170 to 365 DDD	245 (1.4%)
>365 DDD	130 (0.8%)
Dose missing	1020 (6.0%)
Anticonvulsants	
No dose	16336 (95.8%)
<85 DDD	141 (0.8%)
>=85 to 365 DDD	166 (1.0%)
>365 DDD	96 (0.6%)

Dose missing	308 (1.8%)
Antidepressants	
No dose	11720 (68.8%)
<85 DDD	858 (5.0%)
>=85 to 365 DDD	1343 (7.9%)
>365 DDD	496 (2.9%)
Dose missing	2630 (15.4%)
Drugs for Parkinson's disease	
No dose	16864 (98.9%)
<200 DDD	29 (0.2%)
>=200 to 600 DDD	50 (0.3%)
>600 DDD	17 (0.1%)
Dose missing	87 (0.5%)
Statins	
No dose	12520 (73.4%)
<280 DDD	1107 (6.5%)
>=280 to 370 DDD	1832 (10.8%)
>370 DDD	1028 (6.0%)
Dose missing	560 (3.3%)
Thiazide diuretics	
No dose	9788 (57.4%)
<225 DDD	1576 (9.3%)
>=225 to 390 DDD	2276 (13.4%)
>390 DDD	1401 (8.2%)
Dose missing	2006 (11.8%)
Anxiolytics	
No dose	14016 (82.2%)
<30 DDD	358 (2.1%)
>=30 to 350 DDD	559 (3.3%)
>350 DDD	263 (1.5%)
Dose missing	1851 (10.9%)
NSAIDs	
No dose	2649 (15.5%)
<60 DDD	2130 (12.5%)
>=60 to 300 DDD	4758 (27.9%)
>300 DDD	2538 (14.9%)
Dose missing	4972 (29.2%)
NSAID cox	
No dose	14715 (86.3%)
<60 DDD	346 (2.0%)
>=60 to 280 DDD	569 (3.3%)
>280 DDD	260 (1.5%)
Dose missing	1157 (6.8%)

Paracetamol	
No dose	3310 (19.4%)
<40 DDD	2683 (15.7%)
>=40 to 200 DDD	5502 (32.3%)
>200 DDD	2738 (16.1%)
Dose missing	2814 (16.5%)
Opioids mix	
No dose	4495 (26.4%)
<30 DDD	2036 (11.9%)
>=30 to 180 DDD	4300 (25.2%)
>180 DDD	2252 (13.2%)
Dose missing	3964 (23.3%)
Opioids total	
No dose	10628 (62.4%)
<200 DDD	1085 (6.4%)
>=200 to 600 DDD	2617 (15.4%)
>600 DDD	1018 (6.0%)
Dose missing	1699 (10.0%)
Injected Steroids	
No dose	14172 (83.1%)
<55 DDD	511 (3.0%)
>=55 DDD	187 (1.1%)
Dose missing	2177 (12.8%)

Key: NSAID, non-steroidal anti-inflammatory drug; DDD, daily defined dose;

Missing data: body mass index 4723 (27.7%), deprivation index 11 (0.1%), smoking 3264 (19.1%) and drinking 6026 (35.3%).

Table B. Descriptive statistics for the NJR-HES-PROMs linked dataset

Descriptor	No. of records (142,275)
Year of primary	
2008	23226 (16.3%)
2009	32930 (39.5%)
2010	40913 (68.2%)
2011	45206 (100.0%)
Age at primary hip replacement	70.0 (SD 10.1)
Sex	
Female	88019 (61.9%)
Male	54256 (38.1%)
Body mass index (mean, SD)	28.7 (SD 5.2)
Index of Multiple Deprivation (IMD) quintiles	
Least deprived	33555 (23.9%)
2	34791 (24.7%)
3	25620 (18.2%)
4	23745 (16.9%)
Most deprived	22970 (16.3%)
Rurality, at primary	
Urban >=10,000	100818 (71.0%)
Town and fringe	18532 (13.0%)
Village/isolated	22720 (16.0%)
Ethnicity	
White	125991 (96.4%)
Non-white	4676 (3.6%)
Number comorbidities at primary	
None	111172 (78.1%)
Mild	24930 (17.5%)
Moderate	4540 (3.2%)
Severe	1633 (1.2%)
ASA grade	
P1 - Fit and healthy	18755 (13.2%)
P2 - Mild disease not incapacitating	102121 (71.8%)
P3 - P5	21399 (15.0%)
Minimally invasive	
No	136683 (96.1%)
Yes	5592 (3.9%)
Surgical volume per consultant (per annum)	
<=10 operations	4910 (3.5%)
11-50	43017 (30.2%)
51-75	27348 (19.2%)
76-100	20264 (14.2%)

101-150	24336 (17.1%)
>150	22400 (15.7%)
Surgeon experience	
<8 training years	31082 (21.9%)
Consultant (≥8 training years)	111193 (78.2%)
Surgical approach (hip)	
Other	65239 (45.9%)
Posterior	77036 (54.2%)
Primary graft femur	
No	141496 (99.5%)
Yes	779 (0.6%)
Primary cup fixation	
Cementless	82556 (59.2%)
Cemented	56886 (40.8%)
Primary stem fixation	
Uncemented	62760 (45.7%)
Cemented THR stem	74645 (54.3%)
Primary graft cup	
No	137051 (96.3%)
Yes	5224 (3.7%)
Bearing surface	
MoP	88311 (66.1%)
CoC	27092 (20.3%)
CoP	17036 (12.8%)
CoM - MoC	1203 (0.9%)
Head size (in mm)	
≤28	73306 (54.0%)
32	32098 (23.7%)
36-42	29662 (21.9%)
≥44	612 (0.5%)
Type of mechanical thromboprophylaxis	
None	13531 (9.5%)
Any	128744 (90.5%)
Type of chemical thromboprophylaxis	
None	7966 (5.6%)
Aspirin only	11280 (7.9%)
LMWH (+/-Other)	98076 (68.9%)
Other (no LMWH)	24953 (17.5%)
Unit type	
Public hospital	115425 (81.1%)
Independent sector - hospital	19311 (13.6%)
Independent sector - treatment centre	7539 (5.3%)

OHS, baseline score (0 to 48, poor to good) (before primary hip replacement)	17.3 (SD 8.2)
EQ-5D, Anxiety Depression (before primary hip replacement)	
I am not anxious or depressed	49186 (58.4%)
I am moderately anxious or depressed	29203 (34.7%)
I am extremely anxious or depressed	3568 (4.2%)

Key: OHS, Oxford Hip Score; MoP, metal on polyethylene; CoP, Ceramic on polyethylene; CoC, Ceramic on ceramic; CoM, ceramic on metal; LMWH, low molecular weight heparin.

Missing data: body mass index 54,506 (38.3%), deprivation index 1594 (1.1%), rurality 205 (0.1%), ethnicity 11,608 (8.2%), primary cup fixation 2833 (2.0%), primary stem fixation 4870 (3.4%), bearing surface 8633 (6.1%), head size 6597 (4.6%).
Missing data for PROMS - baseline OHS 61,478 (43.2%) and EQ5D anxiety/depression 58042 (40.8%).

Table C. Cox regression model identifying risk factors of revision after 5 years of primary total hip replacement for osteoarthritis (hospital data): Subgroup analysis of metal-on-polyethylene and ceramic-on-polyethylene bearing surfaces.

Risk factors (reference category)	**Patients undergoing THR with MoP or CoP bearing surface(N=112,609)**	
	Crude analysis Hazard ratio [95% CI]; P-value	**Adjusted analysis Hazard ratio [95% CI]; P-value**
Age at primary THR (continuous variable)	0.98 [0.97-0.99]; **P=0.003**	0.98 [0.97-0.99]; **P<0.01**
Sex (Women)		
Men	1.21 [1.00-1.48]; **P=0.052**	1.28 [1.05-1.57]; **P=0.016**
Comorbidities		
Mild diabetes (without end organ damage - include ketoacidosis and coma)	6.74 [0.92-49.25]; P=0.06	7.73 [1.05-56.73]; **P=0.044**
Mild liver disease	0.72 [0.48-1.07]; P=0.11	0.64 [0.43-0.95]; **P=0.028**
Bearing surface (MoP)		
CoP	0.93 [0.71-1.21]; P=0.57	0.79 [0.60-1.04]; P=0.094
Head size (≤28 mm)		
32 mm	1.36 [1.07-1.71]; **P=0.01**	1.41 [1.11-1.79]; **P=0.005**
36-42 mm	1.15 [0.84-1.58]; P=0.39	1.16 [0.84-1.61]; P=0.36
≥44 mm	6.15 [2.73-13.84]; **P<0.01**	5.71 [2.52-12.92]; **P<0.01**
OHS, 6-month score (0 to 9 points, worst scores)		
(10 to 14 points)	0.65 [0.50-0.85]; **P=0.001**	0.63 [0.48-0.82]; **P=0.001**
(15 to 18 points)	0.65 [0.50-0.85]; **P=0.001**	0.62 [0.47-0.80]; **P<0.01**
(19 to 23 points)	0.39 [0.28-0.55]; **P<0.01**	0.36 [0.26-0.52]; **P<0.01**
(24 to 48 points)	0.34 [0.25-0.48]; **P<0.01**	0.31 [0.22-0.43]; **P<0.01**

Key: THR, total hip replacement; MoP, metal-on-polyethylene; CoC, ceramic-on-ceramic; CoP, ceramic-on-polyethylene; CoM - MoC, ceramic-on-metal; CI, confidence interval.