Risk factors associated with revision for prosthetic joint infection after hip replacement: a prospective observational cohort study

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Summary

Background The risk of prosthetic joint infection (PJI) is influenced by patient, surgical, and health-care factors. Existing evidence is based on short-term follow-up. It does not differentiate between factors associated with early onset caused by the primary intervention from those associated with later onset more likely to result from haematogenous spread. We aimed to assess the overall and time-specific associations of these factors with the risk of revision due to PJI after primary total hip replacement.

Methods We did a prospective observational cohort study analysing 623253 primary hip procedures performed between April 1, 2003, and Dec 31, 2013, in England and Wales and recorded the number of procedures revised because of PJI. We investigated the associations between risk factors and risk of revision for PJI across the overall follow-up period using Poisson multilevel models. We reinvestigated the associations by post-operative time periods (0–3 months, 3–6 months, 6–12 months, 12–24 months, >24 months) using piece-wise exponential multilevel models with period-specific effects. Data were obtained from the National Joint Registry linked to the Hospital Episode Statistics data.

Findings 2705 primary procedures were subsequently revised for an indication of PJI between 2003 and 2014, after a median (IQR) follow up of 4·6 years (2·6–7·0). Among the factors associated with an increased revision due to PJI there were male sex (1462 [1·2–2%] of 1 237 170 male-years vs 1243 [0·7%] of 1849 691 female-years; rate ratio [RR] 1·7 [95% CI 1·6–1·8]), younger age (739 [1·1%] of 68 000 person-years <60 years vs 242 [0·6%] of 387 049 person-years ≥80 years; 0·7 [0·6–0·8]), elevated body-mass index (BMI; 941 [1·8%] 517 278 person-years with a BMI ≥30 kg/m² vs 272 [0·9%] of 297 686 person-years with a BMI <25 kg/m²; 1·9 [1·7–2·2]), diabetes (245 [1·4%] 178 381 person-years with diabetes vs 2120 [1·0%] of 2 043 907 person-years without diabetes; 1·4 [1·2–1·5]), dementia (5 [10·1‰] of 497 person-years with dementia at 3 months vs 311 [2·6‰] of 120 850 person-years without dementia; 3·8 [2·7–5·2]), previous septic arthritis (22 [7·2‰] of 305 500 person-years with previous infection vs 2683 [0·9‰] of 308 386 person-years without previous infection; 6·7 [4·2–9·8]), fractured neck of femur (66 [1·5%] of 4 378 person-years operated for a fractured neck of femur vs 2639 [0·9%] of 3 043 483 person-years without a fractured neck of femur; 1·8 [1·4–2·3]), and use of ceramic rather than metal bearings was associated with a decreased risk of revision for PJI (94 [0·4%] of 239 512 person-years with ceramic-on-ceramic bearings vs 602 [0·5%] of 1114 239 person-years with metal-on-polyethylene bearings at ≥24 months; RR 0·6 [0·4–0·7]; and 82 [0·4‰] of 190 884 person-years with ceramic-on-polyethylene bearings vs metal-on-polyethylene bearings at ≥24 months; 0·7 [0·5–0·9]). Most of these factors had time-specific effects. The risk of revision for PJI was marginally or not influenced by the grade of the operating surgeon, the absence of a consultant surgeon during surgery, and the volume of procedures performed by hospital or surgeon.

Interpretation Several modifiable and non-modifiable factors are associated with the risk of revision for PJI after primary hip replacement. Identification of modifiable factors, use of targeted interventions, and beneficial modulation of some of these factors could be effective in reducing the incidence of PJI. It is important for clinicians to consider non-modifiable factors and factors that exhibit time-specific effects on the risk of PJI to counsel patients appropriately preoperatively.

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Introduction Hip replacement is a successful and cost-effective elective surgical intervention that is widely used to treat disabling joint pain, mainly caused by osteoarthritis. Some patients experience complications and one of the most severe is prosthetic joint infection (PJI), which is most commonly caused by coagulase-negative staphylococcus or Staphylococcus aureus. Although uncommon, PJI is devastating and leads to severe pain, poor function, reduced quality of life, and even death. The treatment...
Evidence before this study

Prosthetic joint infection (PJI) is a devastating complication after hip replacement. In a systematic review published in 2016, we searched MEDLINE, Embase, Web of Science, and The Cochrane Library databases from inception up to Sept 1, 2015, using a registered protocol (PROSPERO: CRD42015023485) to identify the role of patient characteristics on the risk of developing PJI. Our search strategy combined terms related to exposures (eg, “risk factor”, “body mass index”, “comorbidity”) with those related to outcomes (eg, “periprosthetic joint infection”, “prosthetic joint infection”, “deep prosthesis infection”, “deep infection”, “deep surgical site infection”). Longitudinal studies that reported on the associations of any patient factors with PJI after primary or revision total arthroplasty, who had at least 12 months of follow-up and who had a Newcastle-Ottawa Scale score of more than 5 were eligible. 512 508 hip replacements were pooled and showed that male sex, high body-mass index (BMI), steroid use, diabetes, rheumatoid arthritis, congestive heart failure, depression, and smoking and alcohol intake are each associated with an increased risk of PJI. The published literature was limited by short-term postoperative follow-up, variably adjusted data which did not enhance consistent comparison, substantial heterogeneity between contributing studies, and by not disentangling factors associated with early onset of PJI caused by the primary intervention from factors associated with later onset resulting from haematogenous spread. Older reviews had investigated the role of surgical intervention and health-care setting factors on the risk of revision for PJI but were also limited by the size of the studied samples, infected cases, short postoperative follow-up (≤12 months), and between study heterogeneity.

Repeating the search on March 19, 2018, we identified two registry studies and a meta-analysis published since our previous review. Registry studies from Denmark and New Zealand observed increased risk of PJI in men, older patients, those with a high BMI, and those with rheumatoid arthritis. The meta-analysis showed weak evidence of reduced risk of PJI for non-metallic bearing surfaces. The authors highlighted the need for larger studies with adjustment for confounders.

Added value of this study

This study investigated the overall and postoperative period-specific effects of patient, surgical, and health system factors on the risk of revision for PJI, with a single dataset of 623 053 primary hip replacements in which patients were followed up for up to 11 years. Considering patient characteristics, this work corroborates the previous findings of our review and identifies other factors such as younger age, chronic pulmonary disease, liver disease, and dementia that are associated with an increased risk of PJI. Surgical factors, including indication for the primary surgery, surgery type, the lateral surgical approach, and non-ceramic bearing surfaces, were associated with an increased risk of PJI. We identified no effects or only small effects for surgeon and hospital volume or surgeon grade. More importantly, we identified that these factors have a different effect according to the postoperative period considered, with comorbidities such as dementia influencing early revision for PJI and liver diseases influencing long-term revision. The effect of bearing surfaces also varied according to the period considered but factors, such as age or BMI, increased the risk during all postoperative periods.

Implications of all the available evidence

The risk of revision for PJI after primary hip replacement is multifactorial, mainly driven by patient and surgical level factors with time-varying effects. The modifiable factors identified in this study should be considered by clinicians in their practice to develop targeted interventions and propose beneficial modulation of some of these factors. Of equal importance is for clinicians to consider the non-modifiable factors and the factors that exhibit time-specific effects on the risk of PJI, to counsel patients appropriately preoperatively.
health-care setting factors with the risk of revision due to PJI in prospectively collected observational data of 623,253 primary total hip replacements performed in England and Wales.

Methods
Study design and participants
In this observational cohort study, we report analyses of data for England and Wales from the National Joint Registry (NJR) for England, Wales, Northern Ireland, and the Isle of Man between April 1, 2003, and Dec 31, 2014.

NJR data were linked to Hospital Episode Statistics and Patient Episode Database for Wales to obtain data on inpatient and day case admissions. Data from the Office for National Statistics were linked to obtain the date of death.

We included all patients who had a primary hip replacement between April 1, 2003, and Dec 31, 2013, in the study. Patient consent was obtained for data collection and linkage by the NJR. According to the National Health Service Health Research Authority, separate consent and ethical approval were not required for this study.

Procedures
We analysed primary hip replacements performed between April 1, 2003, and Dec 31, 2013, and revision procedures due to PJI that occurred after the primary replacement between April 1, 2003, and Dec 31, 2014. The reason for revision was recorded by clinicians at the time of the revision procedure and reflected a clinical judgment sufficient to lead the surgeon to perform an invasive procedure tailored to tackle a PJI. The diagnosis and treatment strategy for PJI was at the discretion of the surgeon and treating unit and was reflective of contemporary practice over the study period, with raised inflammatory markers, joint specific symptoms, sinuses, and positive microbiological cultures being common diagnostic features over that period.

Each patient who had a primary hip replacement was followed up for a minimum of 12 months until the end of the observation period (Dec 31, 2014) or until the date of revision for PJI, revision for another indication, or death. Revisions for PJI included debridement and implant retention with modular exchange, a single or a two-stage revision procedure.

We considered the patient characteristics age, sex, ethnicity, BMI, American Society of Anaesthesiologists (ASA) grade, and comorbidities. We obtained data for ethnicity and comorbidities from the Hospital Episode Statistics records. We used ICD-10 codes to classify comorbidities for which patients had been admitted to hospital in the 5 years preceding their primary operation (appendix).

We considered surgical factors such as indication for surgery, anaesthesia type, thromboprophylaxis regime, surgical approach, hip replacement type, bearing surface, use of bone graft, and occurrence of intraoperative complications.

We considered health system factors such as hospital type, funding stream, country, operating surgeon grade, consultant involvement, and volume of hip surgeries (categorised into quartiles) performed by the hospital, operating surgeon and surgeon in charge of the procedure in the preceding 12 months.

Statistical methods
We first investigated the associations between the risk factors and risk of revision for PJI across the overall follow-up period. We used Poisson multilevel models accounting for clustering at unit level (random intercept). Clustering at surgeon level was negligible and therefore ignored.

PJI management varies according to the time since the primary procedure and onset of infection. Early onset of PJI within 24 months of primary procedure is generally considered to result from the primary intervention. Later onset of PJI is more likely to be due to haematogenous spread. For patients with early post-operative or acute haematogenous PJI and a short duration of symptoms, debridement, modular exchange, and implant retention rather than full revision are appropriate. Therefore, we reinvestigated the associations over several at-risk postoperative periods: 0–3 months, 3–6 months, 6–12 months, 12–24 months, and more than 24 months. We split each patient’s at-risk period (time elapsed between their primary procedure and endpoint) according to the time spent in each of these periods and we assigned the revision for PJI status (revised for PJI or not) to the relevant period. We used a piece-wise exponential multilevel model with period-specific effects to assess these associations—ie, their rate ratios (RR) and 95% CIs across these time-periods. We did analyses by running MLwiN from Stata 14.1 (StataCorp LP, TX, USA) using Markov Chain Monte Carlo methods. To account for test multiplicity, we derived adjusted p values using Simes’ false discovery rate testing controlling procedure.

To be confident that 95% of the effects tested were not due to chance, we only discussed evidence of association for adjusted p value of 0·05 or lower.

We did the analyses on the overall sample for all exposures except for ethnicity and comorbidities, which we investigated in the 495,456 patients operated on in England with a record of hospital admission in HES but not in PEDW, and no evidence of residency outside England (appendix). We adjusted the regressions for age, sex, ASA grade, and BMI. BMI is an important risk factor for PJI but has substantial missing data in the NJR (47%), partly because it was not included as a variable in the early data collection forms. We used a multiple imputation strategy to impute BMI, assuming that data were missing at random, using a Gaussian normal regression imputation model with the factors age, sex, and ASA used as covariates, and the log of the observed count as the dependent variable (Appendix).
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and combined regression estimates by Rubin’s rules. Unadjusted and adjusted models without BMI are available on request. To avoid overadjustment, we did not adjust models investigating the effect of comorbidities for ASA grade, a proxy indicator of comorbid profile.

Role of the funding source

The National Institute for Health Research had no role in study design, data collection analysis, interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

623 253 primary hip procedures were done in 460 different surgical units with a median (IQR) of 1050 (460–1940) per unit. Baseline study sample characteristics are presented in figure 1 and the table.

Figure 1: Description of the sample

HES=Hospital Episode Statistics for England. PEDW=Patient Episode Database for Wales. *Only data for England and Wales were considered; data collection for Northern Ireland started Feb 2, 2013, and primary revision procedures could not be considered due to their limited number and restricted follow-up. Data collection for the Isle of Man started on July 1, 2015, after the endpoint of this study and were not considered. †As recorded in HES for the 5 years preceding the primary hip replacement.

623 253 primary hip replacements performed in England and Wales from the National Joint Registry* (sample used to analyse all factors except comorbidities and ethnicity)

2705 revised for a prosthetic joint infection (6133 person-years)

16785 revised for another indication (54 335 person-years)

495 456 surgeries done in England linked with HES (sample used to analyse comorbidities and ethnicity)

68 450 deceased (277 390 person-years)

535 333 followed-up until endpoint (Dec 31, 2014; 2 748 404 person-years)

127 797 excluded from analyses including comorbidities and ethnicity

86 503 surgeries done in England not linked with HES or PEDW

35 854 surgeries done in Wales linked with PEDW

50 177 surgeries done in Wales not linked with PEDW

423 with evidence of residency outside of England

2705 revised for a prosthetic joint infection (6133 person-years)

16785 revised for another indication (54 335 person-years)

495 456 surgeries done in England linked with HES (sample used to analyse comorbidities and ethnicity)

68 450 deceased (277 390 person-years)

535 333 followed-up until endpoint (Dec 31, 2014; 2 748 404 person-years)

2705 revised for a prosthetic joint infection (6133 person-years)

16785 revised for another indication (54 335 person-years)

495 456 surgeries done in England linked with HES (sample used to analyse comorbidities and ethnicity)

68 450 deceased (277 390 person-years)

535 333 followed-up until endpoint (Dec 31, 2014; 2 748 404 person-years)

and for patients younger than 60 years. However, this reduced risk was only observed after the first 6 months (appendix). BMI of 30 kg/m² or higher was associated with an increased risk compared with BMI of less than 25 kg/m². Patients with an ASA grade of 2 or higher were at greater risk than healthy patients (table). This was particularly evident during the first 6 months (appendix).

Patients with a pre-existing history of chronic pulmonary disease, diabetes, liver disease, congestive heart failure, or connective tissue and rheumatologic diseases had a higher risk than did those without pre-existing history of these diseases (figure 2). Patients with diabetes or dementia were at increased risk of early revision for PJI (figure 3). Patients with liver disease were only at high risk beyond 24 months. No time-specific effect was observed for other comorbidities (appendix).

The risk varied according to the indication for the primary procedure. Patients operated on for osteoarthritis were less likely to be revised for PJI than those without osteoarthritis. Patients operated on for a fractured neck of femur, avascular necrosis (figure 2), or history of previous infection of the operated joint were at increased risk (table; appendix). A fractured neck of the femur was only associated with an increased risk of early revision for PJI (figure 3).

Operations done via a posterior surgical approach had the lowest risk of revision for PJI compared with other surgical approaches (figure 2). The surgical approach did not influence the early risk of revision for PJI (figure 3), but from 3 months onwards patients who had undergone a lateral approach were at higher risk (appendix).

Patients who had a primary hip resurfacing were at lower risk of revision for PJI (figure 2), but this lower risk was not evident in the first 3 postoperative months (figure 3). In the early postoperative period, patients who
### Patients, n Person-years Cases, n Incidence per 1000 person-years (95% CI)

#### Sex
- **Female**: 372256 1849691 1243 0.67 (0.64-0.71)
- **Male**: 250997 1237170 1462 1.18 (1.12-1.24)

#### Age, years
- **<60**: 131803 688000 739 1.07 (1.00-1.15)
- **60-69**: 191128 97963 942 0.96 (0.90-1.03)
- **70-79**: 210307 103380 782 0.76 (0.70-0.81)
- **≥80**: 89335 387049 242 0.63 (0.55-0.71)

#### Ethnicity
- **White**: 469129 2256675 2308 1.02 (0.98-1.07)
- **Black African origin**: 2855 13145 12 0.91 (0.47-1.59)
- **South Asian**: 1605 7223 6 0.83 (0.30-1.81)
- **Other and mixed**: 3235 14405 14 0.97 (0.53-1.63)
- **Unclear**: 18612 96431 25 0.26 (0.17-0.38)

#### Body mass index, kg/m²
- **<25**: 71584 297686 272 0.91 (0.81-1.03)
- **25-29.9**: 132037 552826 580 1.04 (0.96-1.13)
- **≥30**: 125856 512278 941 1.82 (1.70-1.94)
- **Missing**: 297276 1174072 912 0.53 (0.50-0.57)

#### American Society of Anaesthesiologists grade
- **1**: 114367 467059 482 0.73 (0.67-0.80)
- **2**: 418335 2056022 1772 0.87 (0.83-0.91)
- **3-5**: 90551 393780 451 1.15 (1.04-1.26)

#### Chronic pulmonary disease
- **No**: 433003 2127270 2064 0.97 (0.93-1.01)
- **Yes**: 62453 260615 301 1.15 (1.03-1.29)
- **Unavailable***: 127797 669972 340 0.49 (0.44-0.54)

#### Diabetes
- **No**: 452557 2209507 2120 0.96 (0.92-1.00)
- **Yes**: 42399 178381 245 1.37 (1.21-1.56)
- **Unavailable***: 127797 669972 340 0.49 (0.44-0.54)

#### Dementia
- **No**: 493382 2381198 2355 0.99 (0.95-1.03)
- **Yes**: 2074 6690 10 1.49 (0.72-2.75)
- **Unavailable***: 127797 669972 340 0.49 (0.44-0.54)

#### Liver disease
- **No**: 491430 2327883 2327 0.98 (0.94-1.02)
- **Yes**: 4026 15005 38 2.53 (1.79-3.48)
- **Unavailable***: 127797 669972 340 0.49 (0.44-0.54)

#### Congestive heart failure
- **No**: 484748 2346960 2307 0.98 (0.94-1.02)
- **Yes**: 10708 40928 58 1.42 (1.08-1.83)
- **Unavailable***: 127797 669972 340 0.49 (0.44-0.54)

#### Connective tissue and rheumatic disease
- **No**: 473594 2292733 2251 0.98 (0.94-1.02)
- **Yes**: 21862 95156 114 1.20 (0.99-1.44)
- **Unavailable***: 127797 669972 340 0.49 (0.44-0.54)

(Continued from previous column)

#### Cancer
- **No**: 473046 2289171 2262 0.98 (0.94-1.03)
- **Yes**: 18511 77688 85 1.09 (0.87-1.35)
- **Unavailable***: 127797 669972 340 0.49 (0.44-0.54)

#### Cerebrovascular disease
- **No**: 485508 2348220 2329 0.99 (0.95-1.03)
- **Yes**: 9948 39668 36 0.91 (0.64-1.26)
- **Unavailable***: 127797 669972 340 0.49 (0.44-0.54)

#### Myocardial infarction
- **No**: 481922 2330894 2305 0.90 (0.95-1.03)
- **Yes**: 13534 56959 60 1.05 (0.80-1.36)
- **Unavailable***: 127797 669972 340 0.49 (0.44-0.54)

#### Paraplegia and hemiplegia
- **No**: 493415 2379416 2351 0.99 (0.95-1.03)
- **Yes**: 2041 8472 14 1.65 (0.90-2.77)
- **Unavailable***: 127797 669972 340 0.49 (0.44-0.54)

#### Peptic ulcer disease
- **No**: 488994 2358642 2333 0.99 (0.95-1.03)
- **Yes**: 6462 29247 32 1.09 (0.75-1.54)
- **Unavailable***: 127797 669972 340 0.49 (0.44-0.54)

#### Peripheral vascular disease
- **No**: 485720 2349624 2318 0.99 (0.95-1.03)
- **Yes**: 9716 38265 47 1.23 (0.90-1.63)
- **Unavailable***: 127797 669972 340 0.49 (0.44-0.54)

#### Renal disease
- **No**: 479616 2337545 2311 0.99 (0.95-1.03)
- **Yes**: 15840 50343 54 1.07 (0.81-1.40)
- **Unavailable***: 127797 669972 340 0.49 (0.44-0.54)

#### Osteoarthritis
- **No**: 43632 189279 249 1.32 (1.16-1.49)
- **Yes**: 579580 2897582 2456 0.85 (0.81-0.88)

#### Fractured neck of femur
- **No**: 610593 3043483 2639 0.87 (0.83-0.90)
- **Yes**: 12560 43378 66 1.52 (1.18-1.94)

#### Previous hip infection
- **No**: 622597 3083806 2683 0.87 (0.84-0.90)
- **Yes**: 656 3055 22 7.20 (4.51-10.90)

#### Avascular necrosis
- **No**: 607308 3007214 2507 0.86 (0.83-0.90)
- **Yes**: 15945 79647 108 1.36 (1.11-1.64)

#### Dysplasia or congenital dislocation
- **No**: 613710 3038936 2677 0.88 (0.85-0.92)
- **Yes**: 9543 48825 28 0.57 (0.38-0.83)

(Table continues in next column)
had undergone an un cemented, hybrid, or reverse hybrid total hip replacement (THR other, figure 3B) were at higher risk than those with cemented implants but from 3 to 24 months, they were at lower or similar risk higher risk than those with cemented implants but from (appendix). Further analysis showed a higher early risk of revision in patients with hybrid implant THR (RR3mth 1·7, CI 1·2–2·3) than in those with reverse hybrid implants (0·9, 0·4–2·0).
The risk of revision for PJI was also influenced by the type of bearing surfaces and this varied according to the time period. In the early postoperative period, no differences were observed (figure 3). Between 3 and 24 months, metal-on-metal THRs had a lower or similar risk than did metal-on-polyethylene THRs; beyond 24 months, the risk was higher for metal-on-metal (appendix). When the model was further adjusted for the type of surgery (resurfacing and THR cemented or not) the higher revision risk for PJI in the metal-on-metal group was identified earlier, from 12 months postoperation onwards (RR12–24mth 1·8, 95% CI 1·3–2·3; RR >24mth 2·2, 1·8–2·6). Ceramic-on-ceramic and ceramic-on-polyethylene surfaces were associated with a lower risk of long-term revision (from 12 months for ceramic-on-ceramic and 24 months for ceramic-on-polyethylene postoperation onwards) than metal-on-polyethylene bearings, which

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### A. Patient factors
- Sex male *(female)*
- Age 60–69 years *(<60)*
- Age 70–79 years *(<60)*
- Age ≥80 *(<60)*
- BMI 25–29·9 (≥30)
- BMI ≥30 *(<25)*
- ASA 2 *(1)*
- ASA 3–5 *(1)*
- Chronic pulmonary disease *
- Diabetes *
- Dementia *
- Liver disease *
- Congestive heart failure *
- Connective tissue-rheumatic disease *
- Cancer non-metastatic *
- Cancer metastatic *
- Cerebrovascular disease *
- Myocardial infarction *
- Paraplegia or hemiplegia *
- Peptic ulcer disease *
- Peripheral vascular disease *
- Renal disease *

### B. Surgery factors
- Osteoarthritis *
- Fractured neck of femur *(<60)*
- Avascular necrosis *
- Dysplasia or congenital dislocation *
- Inflammatory arthropathy *
- Lateral surgical approach *(posterior)*
- Other surgical approach *(posterior)*
- Resurfacing *(THR cemented)*
- THR uncemented *(THR cemented)*
- THR other *(THR cemented)*
- Bearing MoM *(MoP)*
- Bearing CoP *(MoP)*
- Bearing CoC *(MoP)*
- Bearing MoM *(MoP)*
- Bearing undetermined *(MoP)*
- General anaesthesia *
- Nerve block anaesthesia *
- Epidural anaesthesia *
- Spinal anaesthesia *
- Non-chemical thromboprophylaxis (chemical)
- Acetabulum bone graft *
- Femur bone graft *
- Intraoperative event *

### C. Health system factors
- Place of surgery Wales *(England)*
- Independent funding *(NHS)*
- Unknown funding *(NHS)*
- Grade operating surgeon other *(consultant)*
- Assisting consultant *(operating consultant)*
- No consultant *(operating consultant)*
- Operating surgeon volume 28–63 (≥28)
- Operating surgeon volume 63–114 *(≥28)*
- Operating surgeon volume >114 *(≥28)*
- In charge surgeon volume 42–84 (≥41)
- In charge surgeon volume 84–148 *(≥41)*
- In charge surgeon volume >148 *(≥41)*
- Hospital surgeon volume 143–256 (≥143)
- Hospital surgeon volume 256–406 *(≥143)*
- Hospital surgeon volume >406 *(≥143)*

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Figure 2: Risk factors of revision for prosthetic joint infection for the overall postoperative period, 2003–13
Reference category in parentheses. BMI=body-mass index. ASA=American Society of Anaesthesiologists. THR=total hip replacement. MoM=metal-on-metal. MoP=metal-on-polyethylene. CoP=ceramic-on-polyethylene. CoC=ceramic-on-ceramic. CoM=metal-on-ceramic. *Adjusted p value <0·05 (details in the appendix alongside the rate ratios and 95% CIs).
also had a higher risk of long-term revision for PJI (appendix).

Little or no difference in the risk of revision for PJI was found for the choice of anaesthetic technique, thromboprophylaxis regime, use of acetabular bone graft, or experience of intraoperative complication (figures 2, 3; appendix) Patients who received a femoral bone graft during the primary procedure were at higher risk of PJI with no evidence of a postoperative period-specific effect (figure 3; appendix).

The risk of revision for PJI was not different between Wales and England nor between the funding sources of the primary procedure (figure 2).

Revision for PJI was not influenced by the grade of the operating surgeon and the presence or absence of a consultant surgeon during surgery (figure 2).

Operating surgeons who had performed over 63 procedures in the 12 months preceding the primary surgery were weakly associated with a lower risk of
revision for PJI than surgeons with a lower volume (figure 2). This pattern was inconsistent between time-periods and did not influence the early risk of revision for PJI (figure 3; appendix). The volume of all hip procedures done by the surgeon in charge of the surgery did not affect the risk of revision (figure 2). The risk of revision for PJI was higher in the first 3 months after primary surgery in hospitals that had performed over 255 hip procedures in the 12 months preceding the primary surgery than with hospitals with a small volume of activity (figure 3). No specific difference in the rate ratios were found beyond this period or for units with lower volumes of hip procedures (appendix).

Discussion

At the patient level, men, younger patients, and those with high BMI or high ASA grades had an increased risk of revision for PJI. Comorbidities that increased the risk of revision for PJI included chronic pulmonary disease, diabetes, dementia, liver disease, congestive heart failure, and connective tissue or rheumatic diseases. These comorbidities and elevated BMI can potentially be optimised before surgery. A targeted preoperative intervention for male patients with high BMI and specific comorbidities seems particularly relevant.

At the surgical level, patients undergoing THR for fractured neck of femur or avascular necrosis were at higher risk of revision for PJI. Patients with a fracture are different to those who have conditions such as osteoarthritis, generally being older with a higher risk of mortality. Conditions that cause avascular necrosis, such as steroid use or irradiation, cause immunosuppression and also predispose towards PJI. The markedly higher risk in those with historical infection of the hip is novel, though unsurprising, and might be due to quiescent bacteria or other immune conditions that predispose to PJI. Lateral surgical approach and use of femoral bone graft also increased the risk. The increased risk with the lateral surgical approach is a novel finding that we postulate is due to increased tissue damage and bleeding caused by violating the abductor mechanism. Previous studies have suggested that the lateral approach is associated with more bleeding, worse patient related outcomes, and higher mortality. Approximately one third of hip replacements undertaken in England and Wales in 2016, still utilised this approach—although its use is declining. Early revision for PJI was higher in those receiving uncemented than cemented implants independent of bearing surface. At later time points, the risk was lower for uncemented THRs and resurfacings. This might reflect an initial protective effect of antibiotic impregnated bone cement. Long-term risk was higher in metal-on-metal bearings, possibly due to the soft tissue destruction associated with these implants, and was lower in bearings that included ceramic heads, which is concordant with a report from the Medicare population in the USA. In this Medicare population, ceramic bearings were used in younger and healthier patients. Our study adjusted for age and health status, which should mitigate the effects of any selection bias. A meta-analysis also showed weak evidence of reduced risk of PJI for ceramic bearing surfaces.

Factors at the health-care system level appear to be less important with no marked sustained associations across the time periods studied.

Consistent with previous studies, we observed higher risk in men and patients with high BMI. Contrary to previous findings, younger patients were at higher risk, which could reflect the increased follow up in our study. Older patients could be at lower risk due to a propensity to non-operative management of PJI in this group. Smoking has previously been identified as a risk factor and although we did not have information on smoking habit, the surrogate comorbidity of chronic pulmonary disease was associated with increased risk. Evidence of an association between alcohol intake and increased risk has been inconsistent. We observed higher risk in patients with liver disease, but this might represent several pathologies. Our study corroborates the previous findings of increased risk in patients with diabetes, rheumatoid arthritis, and congestive heart failure. We have shown for the first time that dementia is associated with an increased risk of early revision for PJI, which might reflect the high prevalence of other comorbidities in these patients.

The current study has several strengths. To our knowledge, this is the largest and most comprehensive investigation of several patient, surgical, and health-care related factors and their risk for revision for PJI of the hip. We used a large-scale cohort design comprising more participants (n=623 253) than those of the most up-to-date review on the topic (n=512 508 hip and knee replacements). Other strengths include the longer term follow-up of the cohort (median 4-6 years) and cutting-edge statistical analyses, which include the assessment of the effects of these potential risk factors at time-specific periods.

Our study has some limitations. Although prospectively collected, our data is observational and we can only draw inferences on the nature and magnitude of the associations but cannot establish causation. In the UK, no national gold standards have been agreed upon that are available to orthopaedic surgeons to diagnose PJI. As such, the reported indication of PJI in the NJR might vary between units but is reflective of contemporary practice with raised inflammatory markers, joint specific symptoms, sinuses, and positive microbiological cultures being used to diagnose PJI. The PJI diagnosis reflects a clinical judgment sufficient to lead the surgeon to conduct a very severe and invasive procedure tailored to tackle a PJI. Issues relating to under-reporting of revision for PJI, and thus potentially lower incidence estimates, are acknowledged. Linkage of the NJR data to microbiology data could reduce any misdiagnoses of PJI.
but has proven to be of limited generalisability with 12% NJR linkage achievable.26
The associations we have identified might vary with different causative pathogens, but unfortunately we do not have the data to explore this. Our findings should be considered as conservative estimates of the risk factors with the strongest effects. The investigations of the effect of comorbidities were limited to a subset of NJR patients linked to HES. This subset had higher ASA grades and therefore higher rate of revision for PJI than those excluded from these investigations, but they did not differ in terms of age, sex, BMI, or surgical characteristics, suggesting little evidence of differential selection bias. All other factors were investigated on the entire sample.

We have done appropriate modelling to adjust for known relevant confounders but residual confounding is still possible. We had no specific data on confounders, such as smoking and alcohol consumption, but have surrogate markers, such as chronic pulmonary disease and liver disease. BMI was not collected in the early years of the registry necessitating imputation of the data as with a previous study on this dataset.27 Competing risk due to revision for another cause or death, which in combination affected 55% of the primary hip replacements in the dataset during the period of observation, could not be accounted for in the modelling strategy. This was a pragmatic decision because we chose a strategy focusing on time-specific effects while accounting for the clustering nature of the data to disentangle the effect associated with surgical factors (likely to be more marked in the short-term to mid-term follow-up period) from those associated with health-risk behaviour (likely to be more marked in the mid-term to long-term follow-up period). This strategy was optimal because evidence supports non-proportional hazard rates. Finally, it was not possible to investigate any ethnic disparities in terms of revision for PJI due to the insufficient number of ethnic minority patients revised for PJI.

Preventive strategies for PJI largely focus on hygiene, use of protective equipment, management of care equipment and occupational exposure, and safe care of linens, the environment, and waste.28 Combinations of systemic antibiotics, antibiotic-impregnated cement, and conventional operating theatre ventilation are considered cost effective for preventing PJI.29 Identification of patient factors associated with increased need for revision for PJI can further guide the development of interventions and help target the provision of appropriate preventative care.

Using the largest longitudinal sample of primary hip replacements, we have shown several modifiable and non-modifiable factors to be associated with the risk of revision for a PJI after a primary hip replacement. For patients about to have hip replacement, identification of modifiable factors, use of targeted interventions, and beneficial modulation of some of these factors could be effective in reducing the incidence of PJI. It is important for clinicians to consider the non-modifiable factors, and the factors that exhibit time-specific effects on the risk of PJI, to counsel patients appropriately preoperatively.

Contributors
All authors designed the study. The data were extracted by Northgate (Hemel Hempstead, UK). EL, MRW, ADB, SKK, and AWB performed the literature search. EL performed the data analysis. All authors interpreted data, drafted, and reviewed the final manuscript. All authors approved the submitted manuscript. EL had full access to all the data and AWB is the guarantor.

Declaration of interests
MP is Medical Director of the National Joint Registry and a member of the Programme Steering Committee for the National Institute for Health Research programme grant for applied research. We declare no competing interests.

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References


