



Leal, J., Murphy, J., Garriga, C., Delmestri, A., Rangan, A., Price, A., Carr, A., Prieto-Alhambra, D., & Judge, A. (2020). Costs of joint replacement in osteoarthritis: a study using the National Joint Registry and Clinical Practice Research Datalink datasets. *Arthritis Care and Research*, *74*(3), 392-402. https://doi.org/10.1002/acr.24470

Peer reviewed version

Link to published version (if available): 10.1002/acr.24470

Link to publication record in Explore Bristol Research PDF-document

This is the author accepted manuscript (AAM). The final published version (version of record) is available online via Wiley at https://doi.org/10.1002/acr.24470 . Please refer to any applicable terms of use of the publisher.

University of Bristol - Explore Bristol Research General rights

This document is made available in accordance with publisher policies. Please cite only the published version using the reference above. Full terms of use are available: http://www.bristol.ac.uk/red/research-policy/pure/user-guides/ebr-terms/

Running head: Costs of joint replacement in osteoarthritis

Title: Costs of joint replacement in osteoarthritis: a study using the National Joint Registry and Clinical Practice Research Datalink datasets

Authors: Jose Leal^{*1}, DPhil; Jacqueline Murphy^{*1,2}, MSc; Cesar Garriga³, PhD; Antonella Delmestri³, PhD; Amar Rangan^{3,4}, MBBS FRCS; Andrew Price³, BA MBB DPhil; Andrew Carr³, ChM FMedSci; Daniel Prieto-Alhambra^{3,5}, MD PhD; Andrew Judge^{3,6}, PhD

* Jose Leal and Jacqueline Murphy contributed equally to this paper

¹ Nuffield Department of Population Health, University of Oxford; ² Wolfson Institute of Preventive Medicine, Queen Mary University London; ³ Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford; ⁴ National Joint Registry for England, Wales, Northern Ireland and the Isle of Man; ⁵ NIHR Oxford Biomedical Research Centre, John Radcliffe Hospital Oxford; ⁶ Musculoskeletal Research Unit, University of Bristol.

Source of funding: This work was supported by the NIHR Health Services and Delivery Research programme (project number 14/46/02). AJ is supported by the NIHR Biomedical Research Centre at the University Hospitals Bristol NHS Foundation Trust and the University of Bristol. The views expressed in this publication are those of the authors and do not necessarily reflect those of the NHS, the National Institute for Health Research or the Department of Health and Social Care.

Address correspondence to: Dr Jose Leal; Nuffield Department of Population Health, University of Oxford, Old Road Campus, OX3 7LF, UK; email: <u>jose.leal@dph.ox.ac.uk</u>; telephone: 00 44 1865 289 263.

Word count: 3875 words; 4 Tables, 2 Figures.

Conflict of interest: Amar Rangan reports grants from DePuy Ltd outside the submitted work. Andrew Price reports consulting fees, speaking fees, and/or honoraria from Zimmer Biomet (more than \$10,000), outside the submitted work. Daniel Prieto-Alhambra received grants from: Amgen; UCB Biopharma; Servier; Astellas; Novartis, outside the submitted work. Andrew Judge has received consulting fees, speaking fees, and/or honoraria from Freshfields Bruckhaus Deringer and Anthera Pharmaceuticals, INC (more than \$10,000 each). All other authors declare no conflicts of interest.

Abstract:

Objectives: The aim of this study was to estimate the costs of primary hip and knee replacement in individuals with osteoarthritis up to 2 years post-surgery, compare costs before and after the surgery, and identify predictors of hospital costs.

Methods: Patients aged 18 years or over with primary planned hip or knee replacements and osteoarthritis in England between 2008 and 2016 were identified from the National Joint Registry and linked with Hospital Episode Statistics data containing inpatient episodes. Primary care data linked with hospital outpatient records were also used to identify patients aged 18 years or over with primary hip or knee replacements between 2008 and 2016. All healthcare resource use was valued using 2016/17 costs and non-parametric censoring methods were used to estimate total 1-year and 2-year costs.

Results: We identified 854,866 individuals undergoing hip or knee replacement. The mean censor-adjusted 1-year hospitalisation costs for hip and knee replacement were £7,827 (95% CI £7,813 to £7,842) and £7,805 (95% CI £7,790 to £7,818), respectively. Complications and revisions were associated with up to a three-fold increase in 1-year hospitalisation costs. The censor-adjusted 2-year costs were £9,258 (95 % CI £9,233 to £9,280) and £9,452 (95% CI £9,430 to £9,475) for hip and knee replacement. Adding primary and outpatient care, the mean total hip and knee replacement 2-year costs were £11,987 and £12,578, respectively.

Conclusions: There are significant costs following joint replacement. Revisions and complications accounted for considerable costs and there is a significant incentive to identify best approaches to reduce these.

Significance and innovations:

- Joint replacement in osteoarthritis is associated with considerable healthcare costs and variation across surgery procedures
- Revisions and complications were associated with up to a three-fold increase in 1-year hospitalisation costs
- Costs in the second year after joint replacement were higher compared to costs in the year prior to surgery

Introduction:

Knee and hip replacement improve significantly the quality of life of individuals with osteoarthritis and have been shown to be very cost-effective compared to no surgery[1, 2]. In the UK, there were 96,117 primary hip procedures and 106,334 primary knee procedures in 2017, of which 90% and 99% of hip and knee replacements, respectively, had osteoarthritis as the indication for surgery.[3]

There is limited evidence about the primary care and hospital costs of primary planned joint replacement in the subsequent years after surgery. It is important to have up-to-date and robust data of the costs of joint replacement and its drivers to inform decisions about changes in health service delivery and produce good practice guidelines[4]. Investment and disinvestment decisions regarding novel interventions in this area are driven by cost-effectiveness evidence [5, 6], where resource use and costs are a key input.

The primary aim of this study is to estimate the primary care and hospital costs of primary joint replacement up to 2 years post-surgery. We used data from the UK National Joint Registry linked with hospital data records in England and data from a large patient-level primary care dataset representative of the English population. Secondly, we contrast the resource use and costs by operation types. Finally, we report the main predictors of hospital costs following joint replacement.

Patients and Methods

Setting and data sources

We adopted an incidence-based approach[7] to estimate the primary and hospital care costs associated with hip and knee replacement. This approach estimated the costs of individuals

from joint replacement backwards and forwards to the earliest and latest observed follow up point, respectively.

Data from the UK National Joint Registry (NJR) were linked with Hospital Episode Statistics (HES), which contains records of all admitted patient care episodes undertaken in NHS trusts in England. NJR contains data on hip replacement surgeries from all hospitals in England. NJR includes 2 million patients since 2003, and currently covers 95% and 96% of primary hip and knee replacements, respectively[8].

Before personal data and sensitive personal data are recorded in NJR, express written patient consent is provided. With support under Section 251 of the NHS Act 2006, the ethics and confidentiality committee allows the NJR to collect patient data where consent is indicated as not recorded [Confidentiality Advisory Group (CAG) reference: PIAG 2-05(j)/2006]. This study did not require ethical approval because it analysed information previously collected in the course of normal care, and patients or service users were not be identifiable to the research team carrying out the analysis [Medical Sciences Inter-divisional Research Ethics Committee, University of Oxford; CAG reference: 16/CAG/0111].

Planned hip and knee replacements in the HES dataset were linked to Patient Reported Outcome Measures (PROMs), i.e. Oxford hip/knee score (OHS/OKS)[9, 10] and EQ5D-3L questionnaires[11], before surgery and 6 months after their surgeries.

The CPRD GOLD dataset contained data on patient consultations entered by the GP, medical history, referrals data, tests and all pharmaceutical prescriptions from GP electronic health records. Hip and knee replacement were identified using pre-defined Read codes (see Appendix 1). The CPRD GOLD dataset was linked to hospital outpatient records in HES and Office for National Statistics (ONS) mortality data.

6

Study participants

To estimate hospitalisation costs, we only included individuals, identified in the NJR-HES linked dataset, with a planned surgery for joint replacement between April 2008 and January 2017. Patients without a concordant date of replacement between NJR and HES databases were excluded from the analysis.

To estimate outpatient and primary care costs, we only included patients in the CPRD GOLD dataset with a first ever clinical or referral record of planned joint replacement occurring from 1 April 2008 until 31 December 2016.

Ascertainment of change in patient reported outcomes at 6 months

We estimated the absolute change in OHS/OKS and EQ5D index scores (6 months - baseline score) to obtain a measure of change associated with the surgery. The scores from the 12 questions in the OHS/OKS were summed to obtain the total score spanning from 0 (the worst possible score) to 48 (the best possible score). The EQ5D-3L responses were converted into EQ5D utility scores using the UK value set[12]. Higher positive values for OHS/OKS and EQ5D score changes between time points represented greater reduction in pain, improvement in function and quality of life self-reported by the patient.

Ascertainment of death, complications and revisions at 1 year

All-cause mortality was estimated at 1 year from the day of planned admission due to joint replacement and using the date of death from the ONS mortality database. We defined post-operative complications as one or more events happening up to 1 year after joint replacement: stroke (excluding transient ischaemic attack), respiratory infection, acute myocardial infarction, pulmonary embolism/deep vein thrombosis, urinary tract infection, wound disruption, surgical site infection, fracture after implantation, complication of prosthesis, neurovascular injury, acute renal failure and blood transfusion. A group of four orthopaedic

surgeons independently went through all the relevant ICD10 diagnosis and OPCS4 operation codes, and came to a consensus on the final list of codes for complications relevant to this study. This was further checked by a senior data manager who conducted additional searches based on the list of codes identified to ensure no potential relevant codes had been missed. (see Appendix 2). We also identified revisions occurring up to 1 year following joint replacement from revisions declared to the NJR registry by the surgeons[13] and revisions reported to HES using codes from Appendix 3.

Costs

Each finished consultant episode (FCE) in a hospital admission was assigned into a Healthcare Resource Group (HRG) via the 2016/17 Casemix Grouper Software (HRG4+)[14]. HRGs are standard groups of clinically similar treatments that consume a common set of healthcare resources. HRGs for each FCE were valued using NHS reference costs from 2016/17[15] and appropriate methodology[16] and summed to produce the total cost per hospital admission.

Primary care contacts and tests were costed using 2016/17 unit costs from national cost databases[17] (see Appendix 4 for full details of methodology). Pharmaceuticals were costed by matching each prescribed medication to a BNF code and valuing these using 2016/17 cost data from NHS Digital Prescription Cost Analysis.[18]

Total costs per patient were aggregated into monthly and annual amounts for the purposes of the analysis.

Statistical analysis

The NJR-HES database was censored on January 20th 2017, and complete follow-up was not available for all cases. Hence, we report total hospital inpatient costs for those patients with complete follow-up data at years 1 and 2 following joint replacement and for the whole

sample after adjusting for censoring using the methodology developed by Lin et al. [19]. Costs are reported as means together with their 95% confidence intervals (CIs), obtained from 1000 bootstrap estimates.

Predictors of hospitalisation costs of joint replacement were estimated using a generalised linear model (GLM). Based on our review of the literature, we examined the following predictors of costs in the year of the joint replacement: age; gender; EQ5D-3L/ Oxford Hip/Knee score before surgery and change at 6 months; complications and revision up to 1 year after surgery; multiple deprivation index; Charlson co-morbidity score up to surgery (see Appendix 5); BMI prior to surgery; type of joint replacement (partial, total and patellofemoral for knee; resurfacing or total for hip); surgical variables; ASA grade before surgery; thrombolysis agents used (LWMH, none, aspirin and other), type of anaesthesia (general, epidural, spinal and nerve block), death, and year of surgery.

We used t-test and Pearson Chi square test to evaluate the missingness for the potential predictors of costs (e.g. BMI, EQ5D/Oxford Hip/Knee scores before surgery and change at 6 months) in terms of age, gender, hospitalisation costs, length of stay, Charlson co-morbidity score and type of joint replacement. We also performed multiple imputation of the missing data using a chained model with 20 iterations regressed on non missing variables (see Appendix 6 for more details) to inform the prediction models.[20]

The choice of the GLM model family and link functions was informed by the modified Park test and the Box-Cox test, respectively.[21] We applied stepwise backward selection (at p<0.05) per 300 bootstrap samples to identify variables that were consistently selected for at least 50% of the analyses and inform the final models. A two-tailed t-test with alpha=0.01 (to account for the large sample size) was used to determine whether each coefficient was statistically significantly different from zero, and their selection as predictors of costs was

9

informed using Akaike's information criterion, mean square error and likelihood test. All analyses were performed using STATA version 15 (StataCorp, College Station, TX).

Results

Patient sample

Between April 1, 2008 and January 30, 2017, we identified 397,119 and 457,747 patients with osteoarthritis as having had a primary hip or knee replacement, respectively, in the NJR-HES linked dataset. Table 1 reports the baseline characteristics of the two cohorts. There were more women in the hip replacement cohort than the knee replacement cohort (57.0% vs 40.4%). Individuals undergoing hip replacement were slightly younger (69.1 years vs. 69.5 years) and with lower BMI (28.8 kg/m2 vs. 30.7 kg/m2, i.e. overweight vs. obese) compared to individuals undergoing knee replacement. Furthermore, the absolute change for Oxford and EQ5D scores were slightly lower in the hip replacement cohort (17.4 points vs. 18.2 points for OHS/OKS and 0.33 vs. 0.37 for EQ5D utilities). Osteoarthritis was the most common indication for joint replacement, with only 3.2% (hips) and 1.2% (knees) of cases having an indication other than osteoarthritis alone.

- TABLE 1 -

Patient outcomes and hospitalisation costs

The mean duration of follow up for the hip and knee replacement cohorts was 3.9 years (SD 2.5) (see Table 2). The mean difference between 6-months and preoperative OHS/OKS was 20.1 points (SD 10.2 points, n=202,761) and 15.3 points (SD 10.0 points, n=216,322) for hip and knee replacement, respectively.

The mean hospitalisation costs associated with index admission for hip replacement were $\pounds 6,208$ (median $\pounds 5,824$, SD $\pounds 969$) compared to $\pounds 6,122$ (median $\pounds 5,692$, SD $\pounds 967$) for knee replacement. Mean length of stay in the index admission was 4.8 (median 4, SD 3.8, IQR 3–6) and 4.8 (median 4, SD 3.5, IQR 3–5) days for hip and knee replacement, respectively.

Within one year of joint replacement, the mean hospitalisation costs were estimated at £7,817 (median £6,258, SD £4,618) and £7,784 (median £6,226, SD £4,520) for hip and knee replacement, respectively, of which the index admission accounted for 79.4% and 78.5% of the total. Hospitalisation costs and length of stay within one year were highly correlated for both types of joint replacement (Spearman correlation coefficient 0.84, p<0.001).

The three most common reasons for hospital readmission within the first year of joint replacement were similar in both cohorts: musculoskeletal (ICD-10 chapter 13: 32%-35% of readmission costs), injury (ICD-10 chapter 19: 21%), and circulatory system (ICD-10 chapter 9: 8%-9%) (see Appendix 7, Table 7.1). For hip replacement, 2,404 (0.7%) patients, with complete 1-year follow up, had a hip revision in the following year according to the NJR registry. We found 610 more 1-year revisions using HES giving a total of 3,014 (0.9%). For knee replacement, 1,769 (0.5%) patients, with complete 1-year follow up, had a knee revision in the following year according to the NJR registry. We found 610 more 1-year revisions using HES giving a total of 1,947 (0.5%).

For hip replacement, individuals undergoing metal-on-metal resurfacing had on average lower 1-year and 2-year costs and length of stay (at 2 years: mean £7,374 [SD 4246] and 5.6 [SD 7.8] days, n=6,643) compared to individuals undergoing total hip replacement (at 2 years: £9,321 [SD 6971] and 9.5 [SD 16.5] days, n=286,975) (see Appendix 7, table 7.2).

For knee replacement, individuals undergoing unicondylar joint replacement had on average lower 1-year and 2-year costs and length of stay (at 2 years: mean £8,198 [SD 5145] and 5.6

[SD 9.5] days, n=24,203] compared to individuals undergoing patellofemoral joint replacement (at 2 years: £9,209 [SD 6252] and 7.4 [SD 12.7] days, n=3,726] and total knee replacement (at 2 years: £9,548 [SD 7088] and 9.8 [SD 17.0] days, n=305,194) (see Appendix 7, table 7.3).

Adjusting for censoring, the mean 1-year costs were similar to the complete follow up analysis (including individuals who died in that year) at £7,827 (95% CI £7,813 to £7,842) and £7,805 (95% CI £7,790 to £7,818) for hip and knee replacement, respectively. For hip replacement, the mean costs in the first 2 years following joint replacement (2-year) adjusted for censoring were £9,258 (95 % CI £9,233 to £9,280) compared to £9,277 using only individuals with complete follow up (including those who died in that year, n = 293,618). For knee replacement, the costs in the first 2 years following joint replacement (2-year) adjusted for censoring were £9,452 (95%CI £9,430 to £9,475) and similar to £9,446 using only individuals with complete follow up (n=333,123). Table 7.4 (Appendix 7) reports hospital admissions, length of stay and costs during the first 2 years following joint replacement.

- TABLE 2 -

Predictors of hospitalisation costs in the first year following joint replacement

About 50% and 70% of patients had missing data for Oxford and EQ5D scores (before surgery and at 6 months), BMI or other variables to inform the prediction of hospitalisation costs for hip and knee replacement, respectively (see Appendix 7, Table 7.5). Following multiple imputation, the predictors of hospitalisation costs for hip and knee replacement are shown in Tables 3 and 4, respectively. A GLM model with gamma family and identity link function had the best fit.

Adjusting for all covariates, conventional total hip replacement was more expensive on average than metal-on-metal resurfacing (£451, p<0.001). Women had higher mean hospitalisation costs than men (£167, p<0.001), and older and more deprived individuals were associated with higher costs. Individuals with higher quality of life values (EQ5D and Oxford hip score) prior to surgery and reporting improvements at 6 months were associated with lower hospitalisation costs. There was strong evidence (p<0.01) that ceramic on ceramic, ceramic on metal and metal on ceramic bearing were associated with lower mean 1year hospitalisation costs than metal on polythene bearings (the most common bearing type in the cohort). Costs were also lower in recent years (-£31 per year, p<0.001), holding all else constant. Complications and revisions within the year were significantly associated with higher mean costs, with an additional £6,601 (1.9 fold increase, p<0.001) and £11,255 (2.5 fold increase, p<0.001) respectively and £17,857 together (3.4 fold increase). Holding all else constant, the complications associated with the highest increase in 1-year costs were blood transfusion (an additional £7,782), surgical site infection (£6,799), stroke (£6,791), fracture after implant (£6,585), and wound disruption (£6,209) (see Appendix 7, Table 7.6).

Adjusting for all covariates, total knee replacement was significantly associated with higher 1-year hospitalisation costs than unicondylar knee replacement (£404, p<0.001). Women had higher mean hospitalisation costs than men (£255, p<0.001) and costs increased with age (£31 per additional year, p<0.001) and higher deprivation. Individuals with higher quality of life values (EQ5D and Oxford knee score) at baseline and those reporting improvements at 6 months had lower hospitalisation costs. Higher deformity and lower range of flexion were also significantly associated with higher costs. Costs were also lower in recent years (-£14 per year, p<0.001), holding all else constant. Complications and revisions within the first year were significantly associated with higher costs, with an additional £6220 (1.8 fold increase, p<0.001) and £10,406 (2.3 fold increase, p<0.001), respectively, and £16,626 together (3.0

fold increase). Holding all else constant, the knee surgery complications associated with the highest increase in 1-year hospitalisation costs were fracture after implant (an additional £9,875), blood transfusion (£7,691), stroke (£6,749), wound disruption (£6,889) and urinary tract infection (£6,529) (see Appendix 7, table 7.6).

For completeness, Tables 7.7 and 7.9 (Appendix 7) report the predictors of 1-year hospitalisation costs for hip and knee replacement, respectively, using only the subgroups of individuals with no missing data (complete cases). The results were similar in terms of direction and magnitude of the associations between hospitalisation costs and covariates. The cohorts with complete data had lower mortality rates at one year and lower hospitalisation costs compared to cases with missing data (see Appendix 7, Tables 7.8 and 7.9).

- TABLE 3 -

- TABLE 4 -

Costs before and after joint replacement

Adding primary, outpatient and inpatient hospitalisation costs, the mean costs associated with hip replacement amounted to £9,295 in the year of surgery compared to £9,483 following knee replacement (Figure 1). Hospitalisation costs accounted for the highest proportion of the total 1-year cost for both hip and knee replacement (82-84%).

Using the annual number of UK joint replacements in 2017, the NHS primary and hospital costs were estimated at £899 million (n=96,717) and £1,008 million (n=106,334) in the year of the hip and knee replacement, respectively. In the second year after joint replacement, total costs were £2,692 for hip and £3,095 for knee replacement cohorts, with inpatient costs being the largest component (53% for both knee and hip).

Figure 2 reports the hospitalisation costs in the months before and after joint replacement. The annual hospitalisation costs in the year of joint replacement were £6,753 (95%CI: £6732 to £6774) and £6,563 (95%CI: £6544 to £6583) higher for hip and knee replacement, respectively, compared to that of the previous year. However, there was a decrease in hospitalisation costs in the 5 months prior to surgery reflecting lower hospital admissions leading up to the planned admission. Costs in the second year after joint replacement were £389 (95%CI: 370 to 407) and £349 (95%CI: 329 to 368) higher compared to costs in the year prior to surgery for knee and hip replacement, respectively.

A similar pattern was observed with primary care and outpatient costs (see Appendix 7, figures 7.1 and 7.2). However, outpatient costs in the second year after surgery were significantly lower than in the year preceding the surgery for both types of joint replacement (-£105 [95%CI: -£78 to -£133] and -£126 [95%CI: -£109 to -£143] for knee and hip, respectively). In contrast, primary care costs were lower in the second year after surgery for hip replacement (by -£53) but higher for knee replacement (by £37) compared to the year preceding surgery.

- FIGURE 1 -

- FIGURE 2 -

Discussion

In this study, we estimated the immediate- and medium-term (up to 2 years) hospital and primary care costs of joint replacement compared with costs in the year prior to surgery in a large representative sample of patients in England, and explored the main variables influencing these costs. We also identified revisions and complications within the first year of joint replacement as major drivers of hospitalisation costs accounting for up to a three-fold increase in costs.

Previous studies have examined the costs of joint replacement but consisted of smaller samples and without linkage to NJR data[22, 23] We were able to examine the hospitalisation costs of different types of joint replacement through their identification in the NJR dataset and linkage to hospital records. We found unicondylar knee replacement to have lower 1-year costs than total knee replacement and metal-on-metal resurfacing also had lower costs than conventional total hip replacement, even after adjusting for potential confounders. However, these cost differences could be offset with longer follow up than 2 years if revision rates are observed to be relatively higher with unicondylar and metal-on-metal resurfacing.

We assessed hospitalisation costs by month before and after surgery and identified a reduction in hospitalisation costs in the 5 months prior to surgery for both types of joint replacement, reflecting fewer hospitalisations leading up to the planned admission. Furthermore, primary care costs were slightly lower in the second year after surgery for hip replacement but slightly higher for knee replacement compared to the year preceding surgery, possibly reflecting differences in recovery times between the two procedures.

Overall, we also found the predictors of costs to be similar for hip and knee replacement. Consistent with previous work,[22] we found preoperative quality of life, as measured using Oxford scores and EQ5D, to be associated with hospitalisation costs; 1-year costs were higher for individuals with worse preoperative quality of life even after adjusting for other covariates. Also, 1-year costs were lower for individuals reporting larger improvements in quality of life at 6 months.

Knee and hip replacement costs are significant but these are very cost-effective procedures compared to no joint surgery in individuals with osteoarthritis[1, 2, 24-26]. There is then an

16

economic incentive to fund research aimed at identifying cost-effective ways of further improving the quality of life of patients with osteoarthritis following joint replacement and reducing the risk of revisions and complications.

A key advantage of this study is the use of the NJR dataset, which is the largest arthroplasty dataset in the world, linked to hospital care data and supplemented with a large primary care dataset. This means that the data are representative of the range of individuals with osteoarthritis undergoing joint replacement in England and generalisable for use in other similar health care systems. However, our study had some limitations. NJR data were obtained for individuals undergoing joint replacement with osteoarthritis as an indication for surgery. Hence, individuals without osteoarthritis as one of the indications were not available for analysis, e.g. rheumatoid arthritis or fractures. Furthermore, private joint replacements were not available in the hospital care dataset and we were not able to relate hospital readmissions to joint replacement. However, the majority of costs following joint replacement were associated with readmissions due to musculoskeletal and injury reasons (53-56% of all readmission costs). The study also lacked a control group and additional costs associated with joint replacement were estimated by comparing the costs in the year of replacement with those in the previous year. Another potential limitation of the analysis is the use of HRGs and reference costs as opposed to detailed micro-costing approaches to estimate hospitalisation costs. HRGs and reference costs are nationally representative but may lack the precision to capture changes in resource use across individuals within the same HRG. To mitigate these issues we followed best practice to ensure that all hospital contacts were captured and costed appropriately (16, 27). Finally, a large proportion of the cohort had missing data for one or more key covariates of the hospitalisation costs, in particular EQ5D/Oxford Hip score responses and BMI, which necessitated the use of missing data methods, specifically multiple imputation. A key assumption using multiple imputation was

that the missing data was missing at random; that is, the missingness can be adjusted for (i.e. explained) using the observed data. This assumption is always untestable but due to the large number of relevant covariates in our linked data we judged it to be reasonable in this case. For completeness, we also present the results of the analysis using complete cases in the supplementary information, which we found to be similar to the findings following multiple imputation.

In conclusion, our results show the impact of hip and knee replacement on primary and hospital care and its predictors in England. We highlight the differences in costs between the types of replacement and the significant impact of revisions and complications in individuals with osteoarthritis. Our results can be used as inputs in future work assessing the cost and cost-effectiveness of hip and knee replacement, and in particular to explore heterogeneity between patient subgroups. This will be useful to commissioners, providers and researchers interested in the prevention and management of osteoarthritis.

Acknowledgements

We thank the patients and staff of all the hospitals in England, Wales and Northern Ireland who have contributed data to the National Joint Registry. We are grateful to the Healthcare Quality Improvement Partnership (HQIP), the NJR Research Committee and staff at the NJR Centre for facilitating this work. The authors have conformed to the NJR's standard protocol for data access and publication. The views expressed represent those of the authors and do not necessarily reflect those of the National Joint Registry Steering Committee or the Healthcare Quality Improvement Partnership (HQIP) who do not vouch for how the information is presented. This study is based in part on data from the CPRD obtained under licence from the UK Medicines and Healthcare products Regulatory Agency. However, the interpretation and conclusions contained in this study are those of the author/s alone.

References

1 Dakin H, Gray A, Fitzpatrick R, MacLennan G, Murray D. Rationing of total knee replacement: a cost-effectiveness analysis on a large trial data set. BMJ Open 2012;2:e000332.

Fordham R, Skinner J, Wang X, Nolan J. The economic benefit of hip replacement: a
5-year follow-up of costs and outcomes in the Exeter Primary Outcomes Study. BMJ Open
2012;2:e000752.

3 National Joint Registry. 15th Annual Report 2018. Surgical data to 31 December
2017. [Internet. Accessed January, 1, 2020]. Available from: http://www.njrreports.org.uk

4 Luchinskaya DS, P. Stoye, G. UK health and social care spending. [Internet. Accessed January, 1, 2020]. Available from:

https://www.ifs.org.uk/uploads/publications/budgets/gb2017/gb2017ch5.pdf

5 National Institute for Health and Care Excellence. Total hip replacement and resurfacing arthroplasty for end-stage arthritis of the hip [TA304]. [Internet. Accessed January, 1, 2020]. Available from: https://www.nice.org.uk/guidance/ta304

6 National Institute for Health and Care Excellence. Guideline Scope. Hip, knee and shoulder joint replacement. [Internet. Accessed January, 1, 2020]. Available from: https://www.nice.org.uk/guidance/gid-ng10084/documents/draft-scope

7 Lipscomb J, Yabroff KR, Brown ML, Lawrence W, Barnett PG. Health care costing: data, methods, current applications. Med Care 2009;47:S1-6.

8 National Joint Registry. 14th Annual Report. Surgical data to 31 December 2016.
[Internet. Accessed January, 1, 2020]. Available from: http://www.njrreports.org.uk

20

9 Dawson J, Fitzpatrick R, Carr A, Murray D. Questionnaire on the perceptions of patients about total hip replacement. J Bone Joint Surg Br 1996;78:185-90.

10 Dawson J, Fitzpatrick R, Murray D, Carr A. Questionnaire on the perceptions of patients about total knee replacement. J Bone Joint Surg Br 1998;80:63-9.

11 EuroQol Group. EuroQol-a new facility for the measurement of health-related quality of life. Health Policy 1990;16:199-208.

Dolan P. Modeling valuations for EuroQol health states. Med Care 1997;35:1095-108.

13 National Joint Registry. Data collection forms - revision procedure for hip. 2014.[Internet. Accessed January, 1, 2020]. Available

from:http://www.njrcentre.org.uk/njrcentre/Portals/0/Documents/England/Data%20collection %20forms/MDSv6.0_H2_V004.pdf

14 NHS Digital. HRG 4+ 2016/17 Reference Costs Grouper. [Internet. Accessed January, 1, 2020]. Available from: https://digital.nhs.uk/services/national-casemixoffice/downloads-groupers-and-tools/grouper-and-tools-archive/costing-hrg4-2016-17reference-costs-grouper

 15 NHS Improvement. Reference Costs 2016/17. National schedule of reference costs 1.
 [Internet. Accessed January, 1, 2020]. Available from: https://improvement.nhs.uk/resources/reference-costs

Leal J, Manetti S, Buchanan J. The Impact of Hospital Costing Methods on Cost-Effectiveness Analysis: A Case Study. Pharmacoeconomics 2018;36:1263-72.

17 Curtis L, Burns A. Unit Costs of Health and Social Care 2017. [Internet. AccessedJanuary, 1, 2020]. Available from: https://doi.org/10.22024/UniKent/01.02/65559

21

18 NHS Digital. Prescription Cost Analysis. England 2017. [Internet. Accessed January,
1, 2020]. Available from: https://digital.nhs.uk/data-and-

information/publications/statistical/prescription-cost-analysis/prescription-cost-analysisengland-2017

19 Lin DY, Feuer EJ, Etzioni R, Wax Y. Estimating medical costs from incomplete follow-up data. Biometrics 1997;53:419-34.

20 Faria R, Gomes M, Epstein D, White IR. A guide to handling missing data in costeffectiveness analysis conducted within randomised controlled trials. Pharmacoeconomics 2014;32:1157-70.

21 Deb P, Norton EC. Modeling Health Care Expenditures and Use. Annu Rev Public Health 2018;39:489-505.

Eibich P, Dakin HA, Price AJ, Beard D, Arden NK, Gray AM. Associations between preoperative Oxford hip and knee scores and costs and quality of life of patients undergoing primary total joint replacement in the NHS England: an observational study. BMJ Open 2018;8:e019477.

Burn E, Edwards CJ, Murray DW, Silman A, Cooper C, Arden NK, et al. Trends and determinants of length of stay and hospital reimbursement following knee and hip replacement: evidence from linked primary care and NHS hospital records from 1997 to 2014. BMJ Open 2018;8:e019146.

Jenkins PJ, Clement ND, Hamilton DF, Gaston P, Patton JT, Howie CR. Predicting the cost-effectiveness of total hip and knee replacement: a health economic analysis. Bone Joint J 2013;95-B:115-21. 25 Ferket BS, Feldman Z, Zhou J, Oei EH, Bierma-Zeinstra SM, Mazumdar M. Impact of total knee replacement practice: cost effectiveness analysis of data from the Osteoarthritis Initiative. BMJ 2017;356:j1131.

26 Rasanen P, Paavolainen P, Sintonen H, Koivisto AM, Blom M, Ryynanen OP, et al. Effectiveness of hip or knee replacement surgery in terms of quality-adjusted life years and costs. Acta Orthop 2007;78:108-15.

27 National Institute for Health and Care Excellence. Guide to the methods of technology appraisal 2013. [Internet. Accessed January, 1, 2020]. Available from: https://www.nice.org.uk/process/pmg9/chapter/foreword.

TABLES

| | Hip replacement | Knee replacement |
|--|-----------------|------------------|
| N= | 397,119 | 457,747 |
| Age, mean (SD) | 69.1 (10.8) | 69.5 (9.5) |
| Female, % | 40.4% | 57.0% |
| White ethnicity, % ^a | 86.1% | 82.4% |
| Index of multiple deprivation, mean (SD) ^b | 18.0 (13.2) | 19.4 (14.0) |
| BMI, mean (SD) ^c | 28.8 (5.2) | 30.7 (5.4) |
| - Underweight (less than 18.5) | 0.7% | 0.2% |
| - Normal (18.5 to 25) | 19.4% | 9.7% |
| - Overweight (25 to 30) | 39.8% | 34.4% |
| - Class I obese (30 to 35) | 26.6% | 32.8% |
| - Class II obese (35 to 40) | 10.1% | 16.4% |
| - Class III obese (40 or more) | 3.4% | 6.7% |
| Oxford Hip/Knee Score before surgery, mean (SD) ^d | 17.4 (8.2) | 18.2 (7.8) |
| EQ5D-3L score before surgery, mean (SD) ^e | 0.33 (0.32) | 0.37 (0.32) |
| Location, % ^f | | |
| - Urban | 71.3% | 74.7% |
| - Town and fringe | 12.8% | 11.8% |
| - Village/isolated | 15.9% | 13.5% |
| Mean Charlson co-morbidity index, mean (SD) | 0.37 (0.75) | 0.4 (0.8) |
| - Median (interguartile range) | 0 (0-1) | 0 (0-1) |
| ASA grade, % | () | × , |
| - Fit and healthy (I) | 13.8% | 10.2% |
| - Mild disease not incapacitating (II) | 70.3% | 73.7% |
| - Incapacitating systemic disease (III) | 15.5% | 15.9% |
| - Life threatening disease or expected to die | 0.4% | 0.3% |
| within 24 hours (IV and V) | | |
| Indication | | |
| - Osteoarthritis | 96.8% | 98.8% |
| - Osteoarthritis and other | 3.2% | 1.2% |
| Operation type, n $(\%)^{g}$ | | |
| - Total joint replacement | 381,145 (98,1%) | 418.510 (92.4%) |
| - Partial joint replacement | - | 34,299 (7.8%) |
| - Patellofemoral joint replacement | - | 4,939 (1,1%) |
| - Metal-on-metal resurfacing | 7.271 (1.9%) | - |
| Implant type ^h | | |
| - Bicondylar | - | 92.0% |
| - Metal-on-Metal | 4.6% | - |
| - Non Metal-on-Metal | 95.4% | - |
| Anaesthesia ⁱ | | |
| - General | 38.9% | 35.4% |
| - Epidural | 4.6% | 4.6% |
| - Nerve block | 8.0% | 15.3% |
| - Spinal | 71.0% | 68.5% |
| Thromboprophylaxis for joint replacement | | |
| - None | 3.1% | 3.7% |
| - Aspirin only | 5.1% | 5.6% |
| - LMWH (with or without other) | 66.0% | 72.3% |
| - Other (no LMWH) | 25.8% | 18.4% |

Table 1. Patient characteristics of study cohorts at primary joint replacement

a 1.5% and 1.3% missing in hip and knee, respectively;

- b 1.1% and 1.0% missing in hip and knee, respectively;
- c 29.0% and 29.1% missing in hip and knee, respectively;
- d 41.2% and 45.3% missing in hip and knee, respectively;
- e 41.9% and 45.9% missing in hip and knee, respectively;
- f 0.3% missing in each cohort;
- g 2.2% missing in each cohort;
- h 1.3% missing in each cohort;
- i 0.5% missing in both cohorts.

| | Hip | Knee replacement |
|---|---------------|------------------|
| | replacement | |
| Follow-up time in years, mean (SD) | 3.9 (2.5) | 3.9 (2.5) |
| Mortality, n (%) | | |
| - Within 1 year ^a | 4,071 (1.2%) | 2,965 (0.8%) |
| Initial hospitalisation (index admission to | | |
| discharge) ^b | | |
| - Hospital length of stay, mean (SD) | 4.8 (3.8) | 4.8 (3.5) |
| - Hospitalisation costs, mean (SD) | £6,208 (£969) | £6,122 (£967) |
| Oxford Hip/Knee Score change at 6 months, | 20.1 (10.2) | 15.3 (10.0) |
| mean (SD) ^c | | |
| EQ5D-3L score change at 6 months, mean | 0.40 (0.34) | 0.29 (0.33) |
| (SD) ^d | | |
| Hospitalisation costs within 1 year of | | |
| replacement ^a | | |
| - Index hospitalisation, mean (SD) | £6,207 (£990) | £6,110 (£979) |
| - Emergency hospitalisations after discharge, | £648 (£2,880) | £606 (£2,730) |
| mean (SD) | | |
| - Planned hospitalisations after discharge, | £963 (£2,825) | £1,067 (£2,850) |
| mean (SD) | | |
| - Total, mean (SD) | £7,817 | £7,784 (£4,520) |
| | (£4,618) | |
| Total length of hospital stay within 1 year of | | |
| replacement ^a | | |
| - Index hospitalisation, mean (SD) | 4.9 (3.8) | 4.8 (3.5) |
| - Emergency hospitalisations after discharge, | 1.4 (7.4) | 1.4 (7.2) |
| mean (SD) | | |
| - Planned hospitalisations after discharge, | 0.9 (5.3) | 1.0 (5.5) |
| mean (SD) | | |
| - Total, mean (SD) | 7.3 (11.2) | 7.2 (11.2) |
| Hospitalisation costs within year 2 after joint | | |
| replacement ^e | | |
| - Emergency hospitalisations, mean (SD) | £524 (£2,598) | £549 (£2,692) |
| - Planned hospitalisations, mean (SD) | £908 (2841) | £1,090 (£3,020) |
| - Total costs, mean (SD) | £1,432 | £1,639 (£4,353) |
| | (£4,169) | |
| Total length of hospital stay within year 2 after | 1.9 (9.1) | 2.1 (9.5) |

Table 2. Patient outcomes and hospitalisation costs

joint replacement^e, mean (SD) a 344,721 and 394,118 individuals with complete follow up, including those who died in that year, in the hip and knee cohorts, respectively.

b 397,119 and 457,747 individuals in the hip and knee replacement cohorts respectively

c 202,761 and 216,322 individuals with pre-surgery and 6 months Oxford hip/knee scores in the hip and knee replacement cohorts respectively

d 187,636 and 201,077 individuals with pre-surgery and 6 months EQ5D scores in the hip and knee replacement cohorts respectively

e 293,618 and 333,123 individuals with complete follow up, including those who died within 2 years of hip and knee replacement, respectively.

| | Frequency | Mean additional | 95% CI | p>z |
|--|-----------|--------------------|------------------|---------|
| | | cost | | |
| Type of joint replacement | | | | |
| - Total hip replacement | 97.9% | Reference | | |
| - Metal-on-metal resurfacing | 2.1% | -£451 | -556 to -347 | p<0.001 |
| Age at replacement (centered at 69) | 69.1 | £28 | 27 to 30 | p<0.001 |
| Age at replacement squared | • • • • | £0.9 | 0.8 to 0.9 | p<0.001 |
| Sex | | | | P |
| - Male | 59.5% | Reference | | |
| - Female | 40.5% | £167 | 147 to 188 | p<0.001 |
| Charlson co-morbidity score | 0.36 | £380 | 362 to 399 | p<0.001 |
| BMI at hip replacement | 28.8 | -£4 | -6 to -1 | p=0.002 |
| EO5D score at baseline (.10) | 0.3 | -£105 | -113 to -96 | p<0.001 |
| EO5D score change at 6 months (.10) | 0.4 | -£97 | -104 to -89 | p<0.001 |
| Hip score at baseline | 17.4 | -£30 | -32 to -27 | p<0.001 |
| Hip score change at 6 months | 20.1 | -£17 | -19 to -14 | p<0.001 |
| Calendar year of replacement (centered | | -£31 | -35 to -26 | p<0.001 |
| at 2012) | | | | I |
| ASA grade | | | | |
| - Fit and healthy (I) | 13.9% | -£150 | -174 to -126 | p<0.001 |
| - Mild disease not incapacitating | 70.4% | Reference | | I |
| (II) | | | | |
| - Incapacitating systemic disease | 15.3% | £637 | 600 to 675 | p<0.001 |
| (III) | | | | I |
| - Life threatening disease or | 0.4% | £2,112 | 1,772 to 2,452 | p<0.001 |
| expected to die within 24 hours | | | | |
| (IV and V) | | | | |
| Head size | | | | |
| - 28mm or under | 42.2% | Reference | | |
| - 29 to 35mm | 31.4% | £45 | 22 to 69 | p<0.001 |
| - 36 to 42mm | 23.4% | £56 | 27 to 85 | p<0.001 |
| - 43 to 48mm | 1.4% | £29 | -72 to 129 | p=0.579 |
| - 49 to 52mm | 1.2% | £66 | -59 to 191 | p=0.300 |
| - 53mm and above | 0.4% | £226 | 60 to 392 | p=0.008 |
| Bearing surfaces | | | | • |
| - Metal on polyethylene (MoP) | 61.9% | Reference | | |
| - Metal on Metal (MoM) | 4.3% | -£29 | -105 to 47 | p=0.450 |
| - Ceramic on ceramic (CoC) | 16.9% | -£40 | -69 to -10 | p=0.009 |
| - Ceramic on polyethylene (CoP) | 16.6% | -£24 | -51 to 4 | p=0.094 |
| - Other (ceramic on metal or metal | 0.4% | -£194 | -324 to -64 | p=0.003 |
| on ceramic) | | | | |
| Surgeon volume of hip procedures (per | 97.4 | -£16 | -28 to -4 | p=0.007 |
| 100) | | | | • |
| Complications within 1 year | 6.0% | £6,601 | 6472 to 6731 | p<0.001 |
| Revision within 1 year | 0.9% | £11,255 | 10,800 to 11,709 | p<0.001 |
| Death | 1.0% | £4,682 | 4,374 to 4,991 | p<0.001 |
| Constant | | £8,600 | 8,500 to 8,700 | p<0.001 |

Table 3. Predictors of 1-year hospitalisation costs following hip replacement (n=330,765)

| | Frequency | Mean additional | 95% CI | p>z |
|---|-----------|-----------------|------------------|---------|
| | | cost | | |
| Type of joint replacement | | | | |
| - Total knee replacement | 92.5% | Reference | | p<0.001 |
| - Partial knee replacement | 7.4% | -£404 | -443 to -366 | p<0.001 |
| - Patellofemoral replacement | 0.1% | -£137 | -237 to -38 | p=0.007 |
| Age at replacement (centered at 69) | 69.5 | £31 | 30 to 32 | p<0.001 |
| Age at replacement squared | | £1.1 | 1.0 to 1.2 | p<0.001 |
| Sex | | | | 1 |
| - Male | 56.8% | Reference | | |
| - Female | 43.2% | £255 | 234 to 277 | p<0.001 |
| Charlson co-morbidity score | 0.39 | £364 | 348 to 380 | p<0.001 |
| Year of surgery (centered in 2012) | | -£14 | -19 to -10 | p<0.001 |
| IMD score (divided by 100) | 0.2 | -£276 | -350 to -203 | p<0.001 |
| EQ5D score at baseline (.10) | 0.4 | -£97 | -105 to -89 | p<0.001 |
| EQ5D score change at 6 months (.10) | 0.3 | -£94 | -101 to -87 | p<0.001 |
| Knee score at baseline | 18.2 | -£28 | -30 to -25 | p<0.001 |
| Knee score change at 6 months | 15.2 | -£10 | -12 to -8 | p<0.001 |
| ASA grade | | | | |
| - Mild disease not incapacitating (II) | 73.7% | Reference | | |
| - Fit and healthy (I) | 10.2% | -£153 | -184 to -121 | p<0.001 |
| - Incapacitating systemic disease (III) | 15.7% | £617 | 585 to 549 | p<0.001 |
| - Life threatening disease or expected | 0.3% | £1,605 | 1,346 to 1,863 | p<0.001 |
| to die within 24 hours (IV and V) | | | , , | 1 |
| Deformity | | | | |
| - Under 10 | 65.2% | Reference | | |
| - 10 to 30 | 33.7% | £61 | 38 to 85 | p<0.001 |
| - Over 30 | 1.1% | £507 | 396 to 618 | p<0.001 |
| Range of flexion | | | | 1 |
| - 91 to 110 | 45.3% | Reference | | |
| - under 70 | 2.1% | £93 | 15 to 171 | p=0.027 |
| - 70 to 90 | 19.7% | £56 | 26 to 86 | p<0.001 |
| - over 110 | 32.9% | -£15 | -41 to 11 | p=0.238 |
| Type of surgeon | | | | I |
| - Consultant | 78.5% | Reference | | |
| - Other | 21.5% | £54 | 29 to 78 | p<0.001 |
| Approach | | | | 1 |
| - Medial parapatellar | 93.0% | Reference | | |
| - Lateral parapatellar | 1.0% | £175 | 72 to 279 | p=0.001 |
| - Mid-Vastus | 3.1% | £30 | -26 to 87 | p=0.295 |
| - Sub-Vastus | 1.2% | £138 | 43 to 232 | p=0.004 |
| - Other | 1.7% | -£20 | -96 to 56 | p=0.603 |
| Type of fixation | | | | I |
| - Cemented | 95.0% | Reference | | |
| - Uncemented | 4.2% | -£71 | -119 to -22 | p=0.004 |
| - Hybrid | 0.7% | £54 | -67 to 175 | p=0.382 |
| General anaesthesia | 36.5% | £77 | 56 to 87 | p<0.001 |
| Complications within 1 year | 6.0% | £6,220 | 6,139 to 6.301 | p<0.001 |
| Revision within 1 year | 0.5% | £10,406 | 10,012 to 10,799 | p<0.001 |
| Death | 0.8% | £4,622 | 4,390 to 4.854 | p<0.001 |
| Constant | | £8,152 | 8,094 to 8,210 | p<0.001 |

Table 4. Predictors of 1-year hospitalisation costs following knee replacement (n=391,691)

Figure legends

Figure 1. Costs in the months before and after knee (A) and hip (B) replacement. Legend: *Complete cases, including those who died in that year

Figure 2. Hospitalisation costs in the months before and after joint replacement. Legend: *Complete cases, including those who died in that year