

**Does regional anaesthesia reduce complications following total hip and knee replacement compared with general anaesthesia? An analysis from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man**

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**Does regional anaesthesia reduce complications following total hip and knee replacement compared with general anaesthesia? An analysis from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man**

**Abstract**

**Background**

Regional anaesthesia is increasingly used in enhanced recovery programmes following total hip replacement (THR) and total knee replacement (TKR). However debate remains about its potential benefit over general anaesthesia given complications following surgery are rare. We assessed the risk of complications in THR and TKR patients receiving regional anaesthesia compared with general anaesthesia using the world's largest joint replacement registry.

**Methods**

We studied the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man linked to English hospital inpatient episodes for 779,491 patients undergoing THR and TKR. Patients received either regional anaesthesia (n=544,620, 70%) or general anaesthesia (n=234,871, 30%). Outcomes assessed at 90 days included length of stay, readmissions, and complications. Regression models were adjusted for patient and surgical factors to determine the effect of anaesthesia on outcomes.

**Results**

Length of stay was reduced with regional anaesthesia compared with general anaesthesia (THR=-0.49 days, 95% confidence interval (CI)=-0.51 to -0.47 days,  $p<0.001$ ; TKR=-0.47 days, CI=-0.49 to -0.45 days,  $p<0.001$ ). Regional anaesthesia also had a reduced risk of

readmission (THR odds ratio (OR)=0.93, CI=0.90-0.96; TKA OR=0.91, CI=0.89-0.93); any complication (THR OR=0.88, CI=0.85-0.91; TKA OR=0.90, CI=0.87-0.93); urinary tract infection (THR OR=0.85, CI=0.77-0.94; TKR OR=0.87, CI=0.79-0.96); and surgical site infection (THR OR=0.87, CI=0.80-0.95; TKR OR=0.84, CI=0.78-0.89). Anaesthesia type did not affect the risk of revision surgery or mortality.

## **Conclusions**

Regional anaesthesia was associated with reduced length of stay, readmissions, and complications following THR and TKR when compared with general anaesthesia. We recommend regional anaesthesia should be considered the reference-standard for patients undergoing THR and TKR.

## **Key words**

Anaesthesia; Hip Replacement; Knee Replacement; Outcome research; Orthopaedic Surgery

## Introduction

Total hip replacement (THR) and total knee replacement (TKR) are commonly performed and effective interventions for treating arthritis.[1] Predictions suggest that the number of these procedures will continue to increase worldwide.[2, 3] Being high volume elective surgical procedures, THR and TKR lend themselves well to standardising best practice for improving patient outcomes, and were the main drivers of enhanced recovery protocols in musculoskeletal care. Through a Department of Health led programme an “enhanced recovery” patient pathway for THR and TKR was introduced across all English hospitals from 2009.[4, 5]. Enhanced recovery is a complex intervention that focuses on quality improvement in key areas of the patient care pathway – this includes changes that can reduce the risk of complications and speed up patients’ recovery time. There is a need for clarity on its core components, and how they are exerting their effect.[6, 7].

Both THR and TKR can be performed under either general anaesthesia or regional anaesthesia, however there is uncertainty about which method of anaesthesia leads to better outcomes.[8] The advent of enhanced recovery has led to an increase in the use of regional anaesthesia for THR and TKR.[9, 10] A systematic review of 29 studies involving 10,488 patients undergoing THR or TKR showed that regional anaesthesia was associated with a lower length of stay compared with general anaesthesia; however both techniques were equally effective with a similar risk of adverse events.[11] The authors concluded that there was limited evidence to suggest that regional anaesthesia was associated with better perioperative outcomes. By contrast, observational studies have suggested advantages of regional anaesthesia over general anaesthesia following THR and TKR in terms of mortality, complications, and blood loss, in addition to length of stay.[12-15]

The absolute risk of complications following THR and TKR is rare,[16] therefore randomised controlled trials comparing anesthetic types would need very large numbers for assessing serious adverse events such as mortality and cardiorespiratory complications, and may not be feasible. Observational studies have been criticised given these involved relatively small cohorts (under 20,000 patients); they are limited by the information available; do not report relevant outcomes, particularly patient reported outcomes;[11] and some only report morbidity during the hospital admission, thus not capturing post-discharge events.[12] There is therefore the need to examine the effects of regional anaesthesia over general anaesthesia in terms of morbidity and mortality following THR and TKR in a large patient cohort with sufficiently granular data, in order to overcome these limitations.

The study aim was to assess the risk of complications following THR and TKR in patients receiving regional anaesthesia compared with general anaesthesia using data from the world's largest mandated national arthroplasty registry. We also assessed temporal trends in anaesthesia use.

## Methods

### Study design and data source

A retrospective analysis of prospectively collected observational data was performed using data from the National Joint Registry (NJR) for England, Wales, Northern Ireland and the Isle of Man. Data capture commenced in April 2003 and contains over 2 million primary THR and TKR procedures, capturing approximately 95% of all such procedures.[16] Patients consent for their details to be recorded within the NJR and data linkage to be performed, with 92% providing consent.[16] Operating teams complete data capture forms after performing THR and TKR, which are entered onto the NJR database. Independent validation studies have reported that data completion and accuracy are excellent for procedures within the NJR.[17, 18]

Primary operations from the NJR were subsequently linked with Hospital Episode Statistics (HES) data, which contains records of all hospital inpatient episodes undertaken in National Health Service trusts in England (125 million each year). HES uses International Classification of Diseases 10<sup>th</sup> revision (ICD-10) to record diagnoses and the Office of Population Censuses and Surveys version 4 (OPCS-4) procedures to record diseases, complications, interventions and procedures from secondary care (Appendix 1). The NJR dataset was also linked with the Office for National Statistics (ONS) database, which provides data on all-cause mortality.

### Exclusion criteria

All patients undergoing primary THR or TKR for osteoarthritis recorded in the NJR were eligible for inclusion up until February 2017. Exclusions were made as follows: (1) patients

with metal-on-metal THR bearings, or partial knee replacements; (2) received anaesthesia not defined by the exposure group (below); (3) procedure performed as an emergency; and (4) no linkage to HES data (i.e. surgery prior to 2008). There were 779,491 patients included for analysis (Figure 1).

## **Exposure**

The NJR collects data on the type of anaesthesia used for each procedure. Patients were grouped as having either regional anaesthesia (spinal anaesthesia +/- sedation +/- nerve block: n=544,620, 70%) or general anaesthesia (+/- nerve block: n=234,871, 30%). The proportion receiving each anaesthesia type was similar for THA (69.8% regional vs. 30.2% general) and TKA (69.9% regional vs. 30.1% general). These groups were chosen to reflect enhanced recovery protocols compared with standard anaesthesia techniques.

## **Covariates**

For each procedure data were available on patient demographics and the type of surgery. This included age, sex, body mass index (BMI), area-level deprivation using the index of multiple deprivation (IMD: based on patient residential postcode and rural/urban indicator),[19] American Society of Anesthesiologists (ASA) grade,[20] Charlson comorbidity score,[21] unit type (public or private), mechanical and chemical venous thromboembolism (VTE) prophylaxis, surgeon grade, surgical approach (including whether minimally invasive technique), and components implanted (fixation, use of bone graft, and for THRs information on the bearing surface and femoral head size).

## **Outcomes**



Outcomes of interest were length of stay, and complications within 90 days of surgery, which is consistent with the recommended period for reporting morbidity following these procedures.[16, 22-24] The latter included readmission, revision surgery (removal, exchange, or addition of an implant), re-operations (excluding revision), and mortality, in addition to specific complications like stroke, infection (chest, urine, and surgical site), wound disruption, myocardial infarction, VTE, acute renal failure, blood transfusion, major haemorrhage (intracranial and gastrointestinal), and anaemia. Validated generic and joint specific patient reported outcome measures (PROMs) (preoperative and at 6 months postoperatively) were also assessed. These included the EQ5D,[25] the Oxford Hip Score (OHS) and the Oxford Knee Score (OKS).[26-28] The Oxford Scores are both scored from 0 (worst) to 48 (best), whilst a score of 1 is the best outcome with the EQ5D.

#### **Statistical analysis**

The effect of anaesthesia type on outcomes following surgery was assessed using linear regression (for length of stay, EQ5D, OHS and OKS) and logistic regression (for complications). Analyses were performed separately for THRs and TKRs. For each outcome, models were adjusted for all patient and surgical factors, apart from BMI, given BMI is frequently missing in the NJR.[16] Patient and surgical factors adjusted for were age, sex, ASA grade, Charlson grade, year of primary surgery (as a binary variable: 2008-2012 versus 2013-2017), unit type, deprivation status, chemical and mechanical VTE prophylaxis, surgeon grade, surgical approach, minimally invasive surgery, and implant fixation. In the THR analyses, adjustment was also made for bearing material and femoral head size. Models predicting the postoperative EQ5D, OHS, and OKS were also adjusted for the respective preoperative score.

157 We performed the following sensitivity analyses: (1) regression models were adjusted for all  
158 patient and surgical factors, including BMI; (2) tested for evidence of an interaction between  
159 year of surgery and type of anaesthesia on outcomes using a likelihood ratio test; (3) assessed  
160 outcomes in (a) general anaesthesia only vs. general anaesthesia with a nerve block, and in  
161 (b) spinal anaesthesia only vs. spinal anaesthesia with a nerve block. All statistical analyses  
162 were performed with Stata (version 14.2).

## Results

Of 779,491 patients studied, 353,387 underwent THR and 426,104 underwent TKR (Table 1).

### *Length of stay*

Following THR, mean (standard deviation) length of stay after regional anaesthesia was 4.6 days (3.4 days) compared with 5.2 days (4.0 days) following general anaesthesia (Table 2). Following TKR, mean (standard deviation) length of stay after regional anaesthesia was 4.7 days (3.5 days) compared with 5.2 days (3.9 days) following general anaesthesia. Regional anaesthesia was associated with a significantly reduced length of stay compared with general anaesthesia following THR (coefficient = -0.49 days, 95% confidence interval (CI)=-0.51 to -0.47 days,  $p<0.001$ ) and following TKR (coefficient = -0.47 days, CI= -0.49 to -0.45 days,  $p<0.001$ ) (Table 3).

For the whole cohort, the length of stay decreased between 2008 to 2017: for THR mean 6.3 days to 3.4 days, and for TKR mean 6.1 days to 3.5 days. This decrease in length of stay over time was consistent across both the anaesthesia groups. However length of stay was always lower for the regional anaesthesia group compared with general anaesthesia for every calendar year from 2008 to 2017.

### *General complications*

In both THR and TKR patients, regional anaesthesia was associated with a significantly reduced risk of readmission (THR odds ratio (OR)=0.93, CI=0.90-0.96; TKR OR=0.91, CI=0.89-0.93) and any complication (THR OR=0.88, CI=0.85-0.91; TKR OR=0.90, CI=0.87-0.93). In TKR only, regional anaesthesia was associated with a reduced risk of

reoperation compared with general anaesthesia (OR=0.79, CI=0.68-0.92, p=0.002). In both THR and TKR patients, the risk of revision surgery or mortality was not related to anaesthesia type (Table 3).

### *Specific complications*

In THR patients, compared with general anaesthesia, regional anaesthesia was associated with a significantly reduced risk of the following: any VTE (OR=0.85, CI=0.77-0.93, p=0.001), pulmonary embolism (OR=0.77, CI=0.67-0.88, p<0.001), urinary tract infection (OR=0.85, CI=0.77-0.94, p=0.003), surgical site infection (OR=0.87, CI=0.80-0.95, p=0.001), acute renal failure (OR=0.78, CI=0.68-0.89, p<0.001), blood transfusion (OR=0.62, CI=0.48-0.80, p<0.001), and anaemia (OR=0.85, CI=0.79-0.92, p<0.001). There was no difference in the risk of all other complications between anaesthesia groups in THRs, including chest infection (Table 3).

In TKR patients, compared with general anaesthesia, regional anaesthesia was associated with a significantly reduced risk of the following: urinary tract infection (OR=0.87, CI=0.79-0.96, p=0.007), surgical site infection (OR=0.84, CI=0.78-0.89, p<0.001), and anaemia (OR=0.89, CI=0.83-0.95, p=0.001). There was no difference in the risk of all other complications between anaesthetic groups in TKRs, including chest infection, VTE, acute renal failure, and blood transfusion (Table 3).

The relative distribution of the specific complications between regional and general anaesthetic groups was similar following both THR and TKR (Table 2).

## **PROMs**

Postoperative EQ5D scores were significantly higher in patients having regional anaesthesia compared with general anaesthesia (THR coefficient=0.021, CI=0.018-0.023,  $p<0.001$  and TKR coefficient=0.019, CI=0.017-0.022,  $p<0.001$ ). Postoperative OHS and OKS were significantly higher in patients having regional anaesthesia compared with general anaesthesia (THR coefficient=0.79, CI=0.70-0.88,  $p<0.001$  and TKR coefficient=0.80, CI=0.71-0.88,  $p<0.001$ ). None of the differences observed in postoperative PROMs reached clinical significance (OHS=5 points; OKS=4 points).[26, 29]

All regression models were repeated for the sensitivity analysis, which produced similar findings to those of the main analysis (Appendix 2).

## **Temporal Trends in anaesthesia use**

Overall the proportion of patients receiving regional anaesthesia was 69.8% in THR and 69.9% in TKR. From 2008 to 2016 there has been a steady increase in the use of regional anaesthesia following both THR (from 57.1% to 76.8%) (Figure 2) and TKR (from 57.2% to 77.8%). This change was associated with a concomitant steady decline in the use of general anaesthesia.

## **Sensitivity analysis: Variation of anaesthesia use over time**

Given the variation of anaesthesia use over time, we also examined for interactions between year of surgery and type of anaesthesia on outcomes. This analysis would establish whether the effect of regional anaesthesia on outcomes was the same in earlier versus later years of surgery.

For THR, the only evidence of a significant interaction with year of surgery was for surgical site infection ( $p=0.0292$ ). Stratified analyses showed there was only an effect of regional anaesthesia reducing the risk of surgical site infection for the later years (2013-17) compared with earlier years ( $OR=0.80$ ,  $CI=0.17-0.90$ ,  $p<0.001$ ).

For TKR, there was evidence of interactions with year of surgery for the following outcomes: readmission ( $p=0.0016$ ), respiratory tract infection ( $p=0.0074$ ), major haemorrhage ( $p=0.0245$ ) and anaemia ( $p=0.0034$ ). For readmission, the effect of regional anaesthetic was weaker in 2008-12 ( $OR=0.94$ ,  $CI=0.91-0.96$ ,  $p<0.001$ ), compared to 2013-17 ( $OR=0.88$ ,  $CI=0.86-0.91$ ,  $p<0.001$ ). There was only evidence of a significant effect in later years (i.e. 2013-17) for major haemorrhage ( $OR=0.70$ ,  $CI=0.55-0.90$ ,  $p=0.004$ ) and anaemia ( $OR=0.79$ ,  $CI=0.72-0.88$ ,  $p<0.001$ ). There was an increased risk of respiratory tract infection for regional anaesthesia but only in 2008-12 ( $OR=1.20$ ,  $CI=1.04-1.37$ ,  $p=0.011$ ).

#### ***Sensitivity analysis: Addition of a nerve block***

Compared to general anaesthesia only, the addition of a nerve block had a reduced risk of readmission in both THR ( $OR=0.92$ ,  $CI=0.87-0.97$ ,  $p=0.004$ ) and TKR ( $OR=0.95$ ,  $CI=0.92-0.99$ ,  $p=0.013$ ) (Appendix 3). In TKR only, general anaesthesia with a nerve block was also associated with a reduced risk of surgical site infection ( $OR=0.80$ ,  $CI=0.70-0.90$ ,  $p<0.001$ ) and improved EQ5D score though the later did not reach clinical significance (Appendix 3).

Compared to spinal anaesthesia only, the addition of a nerve block was associated with an increased length of stay for TKR only, though this may not reach clinical significance (coefficient=0.12 days; Appendix 3).

## Discussion

This is the largest study assessing the risk of complications following THR and TKR in patients receiving regional anaesthesia compared with general anaesthesia. We observed that regional anaesthesia was associated with a reduced length of stay, and a reduced risk of readmissions and complications following THR and TKR when compared with general anaesthesia.

Regional anaesthesia was associated with a reduced length of stay (approximately half a day) compared with general anaesthesia following both THR and TKR. This is consistent with the findings of a systematic review of 29 studies, which reported the overall reduction in length of stay observed with regional anaesthesia was 0.40 days.[11] Furthermore a large cohort study reported fewer patients receiving regional anaesthesia had a prolonged length of stay (above 75<sup>th</sup> percentile) compared with general anaesthesia.[12] Given that over 200,000 joint replacements are recorded annually on the NJR[16] and the significant costs associated with hospital admissions,[30] the decrease in length of stay alone which was associated with regional anaesthesia has the potential for substantial healthcare savings.

The reduced risk of readmissions and complications following THR and TKR that we observed with regional anaesthesia would also provide further healthcare savings as noted previously,[12] in addition to the obvious benefits of reduced patient morbidity. A systematic review reported no difference between the risk of complications when using regional or general anaesthesia.[11] However this review included 19 trials, which means the power to detect differences in relatively rare secondary outcomes was low. Observational studies have shown regional anaesthesia has been associated with a lower risk of complications, including surgical site infection, blood transfusion, and VTE[12-15] We found similar results with

regional anaesthesia reducing the risk of surgical site infection, urinary tract infection, and anaemia in both THR and TKR patients, and reducing the risk of VTE, acute renal failure, and blood transfusion in THR patients only. Although it is acknowledged that the absolute risk of complications in each anaesthetic group were low (Table 2) and the difference in these risks between the anaesthetic groups were also low, these are important findings as many of these complications have substantial burdens for the patient and healthcare systems. For example surgical site infection, which is nationally reported in England[31] and very costly to treat (medical treatment alone per case is £3,696 / \$4,657).[30] Some of the differences in complication risk between THR and TKR we observed are likely to reflect how the procedures are performed, for example with blood transfusion given TKR is performed with a tourniquet so there is less blood loss compared with THR.

We did not find that regional anaesthesia reduced mortality, which is consistent with the findings from a recent systematic review.[15] Although some studies have observed the contrary,[12, 32] it has recently been shown that any potential effect of anaesthesia on mortality wanes with time.[33] We observed no clinically significant differences in generic and joint specific PROMs between anaesthesia types, therefore suggesting that patients gain no clinically meaningful benefit in these domains in relation to anaesthetic at six-months postoperatively.

In more recent years nerve blocks have been frequently used as an adjunct anaesthesia technique in patients receiving THR and TKR. However currently there is still a lack of evidence to establish whether nerve blocks provide any clinical benefit over not administering one [34]. Our sensitivity analysis assessing the addition of a nerve block with spinal anaesthesia suggested that with the outcomes available for assessment there was no



significant clinical benefit of having a nerve block (compared with not having one); however there was a suggestion that nerve blocks were associated with an increased length of stay for TKR patients. Following general anaesthesia, the addition of a nerve block reduced the risk of readmission following both THR and TKR, and reduced the risk of surgical site infection following TKR. On the basis of our data, nerve blocks may be beneficial in patients undergoing general anaesthesia, but they may not provide any additional benefit in patients undergoing spinal anaesthesia. It is therefore recommended that further studies assess the benefit of adding a nerve block to both general anaesthesia and spinal anaesthesia in THR and TKR patients, which specifically assess early postoperative pain scores and other relevant outcome measures.

There has been a steady increase in regional anaesthesia use for joint replacement since 2008, with 77% of patients now receiving regional anaesthesia. These observations were identical in the hip and knee cohorts, and likely reflect changes in clinical practice during this time. Between 2009 and 2011 the Department of Health in England introduced the Enhanced Recovery Partnership Programme, which promotes the use of regional anaesthesia.[5] More recently there have been attempts to perform THR and TKR as daycase surgery, with regional anaesthesia used in these cases in a number of countries given it is considered an important factor in reducing hospital stay and morbidity.[35] Our observations support the notion that regional anaesthesia has a number of advantages for patients undergoing THR and TKR in terms of length of stay, readmissions and complications. Given these findings, we recommend that all anaesthetists involved in joint replacement surgery should be capable of performing regional anaesthesia, as it is recognised to be more technically demanding and time consuming than general anaesthesia which has contributed to some of the resistance for using regional anaesthesia in certain regions.[12, 36]

338

339 Using a nationwide cohort from the world's largest joint replacement registry helps increase  
340 the external validity and generalisability of our findings. However this study has recognised  
341 limitations. Using observational data means causality cannot be inferred. Registry data does  
342 not include information regarding why the anaesthetic method was selected (regional versus  
343 general), the specific anaesthetic administered (technique, drugs, dose etc), the specific  
344 perioperative protocols used (including enhanced recovery), and the discharge destination.  
345 Although we have adjusted our data for numerous patient and surgical factors, it is  
346 recognised these factors, and other important variables not recorded in routinely collected  
347 datasets (e.g. the need for invasive intraoperative monitoring), may influence our findings  
348 with respect to the differences in complications and length of stay between the two  
349 anaesthetic groups. In addition, although we have adjusted for numerous important patient  
350 and surgical factors, using observational data means we cannot definitively exclude that  
351 changes in surgical practice over time were responsible for the better findings in the regional  
352 anaesthesia group, rather than the effect of the anaesthesia technique itself. However we did  
353 perform sensitivity analyses assessing for interactions between year of surgery and type of  
354 anaesthesia on outcomes, which supported our main findings and suggested that some of the  
355 findings in favour of using regional anaesthesia were only significant in more recent years  
356 (2013-17) so were a reflection of modern clinical practice. Missing BMI data is a limitation  
357 of NJR based studies.[22, 37, 38] We observed that the BMI distribution was balanced  
358 between the anaesthesia groups, and analysis of the subgroup of patients with BMI data  
359 available did not alter the findings from the regression models (Appendix 2). Although  
360 PROMs were available at 6 months, it is recognised that we had no early patient reported  
361 outcomes available regarding pain and nausea like those collected in trials.[8, 10] Finally, we  
362 had to exclude a number of cases from the NJR without HES data linkage (prior to 2008),

however it is suspected these early procedures would be less of a reflection of current clinical practice.

## **Conclusions**

Regional anaesthesia was associated with a reduced length of stay, and a reduced risk of readmissions and complications following THR and TKR when compared with general anaesthesia. We recommend that regional anaesthesia should be considered the reference-standard anaesthetic technique for patients undergoing THR and TKR.

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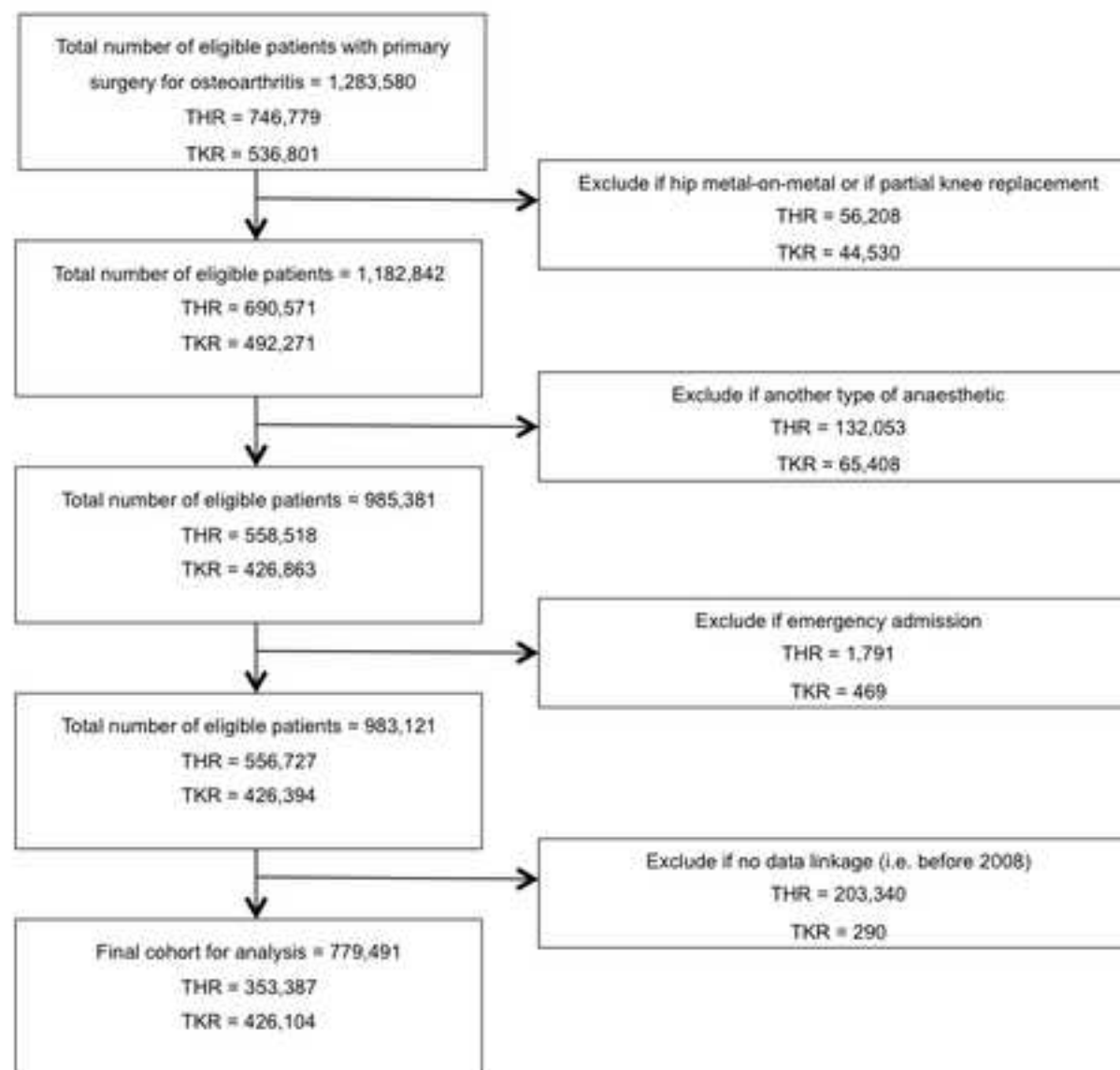
## **Figure Legends**

### **Figure 1** Study selection criteria

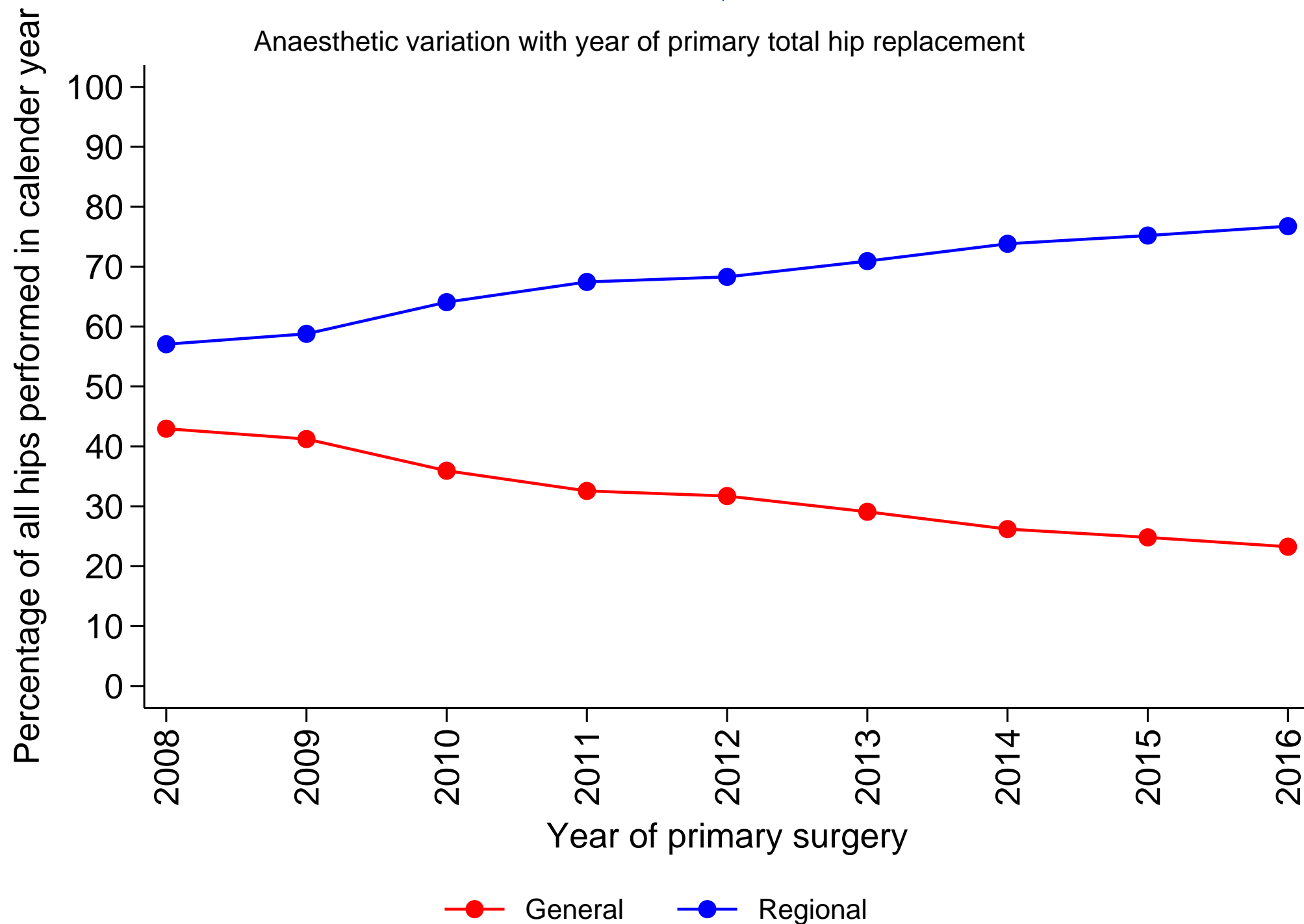
THR = total hip replacement; TKR = total knee replacement

### **Figure 2** Temporal trends in anaesthesia use following total hip replacement

Almost identical findings seen following total knee replacement.



## Anaesthetic variation with year of primary total hip replacement



**Table 1** Patient and surgical factors in primary total hip and knee replacement

	<b>All primary THR (n=353,387) (100%)</b>	<b>General anaesthetic (n=106,782) (30.2%)</b>	<b>Regional anaesthetic (n=246,605) (69.8%)</b>		<b>All primary TKRs (n=426,104) (100%)</b>	<b>General anaesthetic (n=128,089) (30.1%)</b>	<b>Regional anaesthetic (n=298,015) (69.9%)</b>
<i>Covariate</i>							
<b>Sex</b>							
Female vs. male	214,913 (60.8)	66,229 (62.0)	148,684 (60.3)		244,265 (57.3)	76,886 (60.0)	167,379 (56.2)
<b>Age at primary (yr)</b>							
Mean (SD)	69.6 (10.5)	68.5 (11.1)	70.0 (10.2)		70.2 (9.2)	69.4 (9.4)	70.6 (9.0)
<b>BMI (kg/m<sup>2</sup>) *</b>							
Mean (SD)	28.9 (5.2)	29.1 (5.4)	28.9 (5.2)		31.1 (5.5)	31.2 (5.6)	31.0 (5.4)
<b>Deprivation status</b>							
Most deprived 20%	42,437 (12.0)	13,620 (12.8)	28,817 (11.7)		64,052 (15.0)	19,800 (15.5)	44,252 (14.9)
More deprived 20-40%	59,477 (16.8)	18,696 (17.5)	40,781 (16.5)		78,398 (18.4)	24,203 (18.9)	54,195 (18.2)
Middle point	77,430 (21.9)	23,314 (21.8)	54,116 (21.9)		92,816 (21.8)	27,993 (21.9)	64,823 (21.8)
Less deprived 20-40%	86,346 (24.4)	24,887 (23.3)	61,459 (24.9)		97,049 (22.8)	28,038 (21.9)	69,011 (23.2)
Least deprived 20%	84,228 (23.8)	24,569 (23.0)	59,659 (24.2)		89,890 (21.1)	26,153 (20.4)	63,737 (21.4)
Missing	3,469 (1.0)	1,696 (1.6)	1,773 (0.72)		3,899 (0.92)	1,902 (1.5)	1,997 (0.67)
<b>Primary year</b>							
2008-2012	159,404 (45.1)	57,010 (53.4)	102,394 (41.5)		198,678 (46.6)	71,379 (55.7)	127,299 (42.7)
2013-2017	193,983 (54.9)	49,772 (46.6)	144,211 (58.5)		227,426 (53.4)	56,710 (44.3)	170,716 (57.3)
<b>Unit</b>							
NHS vs. independent	269,664 (76.3)	85,498 (80.1)	184,166 (74.7)		326,690 (76.7)	103,188 (80.6)	223,502 (75.0)
<b>Primary ASA grade</b>							
1	44,162 (12.5)	13,734 (12.9)	30,428 (12.3)		37,213 (8.7)	11,965 (9.3)	25,248 (8.5)
2	250,641 (70.9)	75,393 (70.6)	175,248 (71.1)		314,979 (73.9)	94,397 (73.7)	220,582 (74.0)
3 or above	58,584 (16.6)	17,655 (16.5)	40,929 (16.6)		73,912 (17.4)	21,727 (17.0)	52,185 (17.5)
<b>Charlson group</b>							
None	259,179 (73.3)	80,287 (75.2)	178,892 (72.5)		297,106 (69.7)	91,848 (71.7)	205,258 (68.9)
Mild	65,699 (18.6)	18,864 (17.7)	46,835 (19.0)		92,408 (21.7)	26,652 (20.8)	65,756 (22.1)
Moderate	19,235 (5.4)	5,216 (4.9)	14,019 (5.7)		25,313 (5.9)	6,689 (5.2)	18,624 (6.3)
Severe	9,274 (2.6)	2,415 (2.3)	6,859 (2.8)		11,277 (2.7)	2,900 (2.3)	8,377 (2.8)
<b>VTE – chemical</b>							
LMWH (+/-other)	233,080 (66.0)	73,862 (69.2)	159,218 (64.6)		309,130 (72.6)	93,304 (72.8)	215,826 (72.4)
Aspirin only	17,796 (5.0)	6,212 (5.8)	11,584 (4.7)		22,874 (5.4)	8,664 (6.8)	14,210 (4.8)
Other	93,185 (26.4)	22,653 (21.2)	70,532 (28.6)		79,122 (18.6)	19,204 (15.0)	59,918 (20.1)
None	9,326 (2.6)	4,055 (3.8)	5,271 (2.1)		14,978 (3.5)	6,917 (5.4)	8,061 (2.7)
<b>VTE – mechanical</b>							
Any vs. none	333,840 (94.5)	100,276 (93.9)	233,564 (94.7)		402,751 (94.5)	120,993 (94.5)	281,758 (94.5)
<b>Surgeon grade</b>							

Consultant vs. <i>other</i>	284,891 (80.6)	86,549 (81.1)	198,342 (80.4)		333,305 (78.2)	100,731 (78.6)	232,574 (78.0)
<b>THR surgical approach</b> Posterior vs. <i>other</i>	216,787 (61.4)	65,491 (61.3)	151,296 (61.4)		NA	NA	NA
<b>TKR surgical approach</b> Medial parapatellar vs. <i>other</i>	NA	NA	NA		399,552 (93.8)	119,678 (93.4)	279,874 (93.9)
<b>Cup fixation</b> Cemented	137,768 (39.0)	40,346 (37.8)	97,422 (39.5)		NA	NA	NA
Uncemented	211,989 (60.0)	64,875 (60.8)	147,114 (59.7)				
Missing	3,630 (1.0)	1,561 (1.5)	2,069 (0.84)				
<b>Stem fixation</b> Cemented	194,900 (55.2)	56,385 (52.8)	138,515 (56.2)		NA	NA	NA
Uncemented	153,083 (43.3)	48,336 (45.3)	104,747 (42.5)				
Missing	5,404 (1.5)	2,061 (1.9)	3,343 (1.4)				
<b>Femoral head size (mm)</b> 28 or less	146,631 (41.5)	43,720 (40.9)	102,911 (41.7)		NA	NA	NA
32	119,213 (33.7)	34,690 (32.5)	84,523 (34.3)				
36 or above	79,836 (22.6)	25,142 (23.6)	54,694 (22.2)				
Missing	7,707 (2.2)	3,230 (3.0)	4,477 (1.8)				
<b>Bearing surface</b> MoP	221,139 (62.6)	63,843 (59.8)	157,296 (63.8)		NA	NA	NA
CoC	56,245 (15.9)	20,357 (19.1)	35,888 (14.6)				
CoP	64,908 (18.4)	18,027 (16.9)	46,881 (19.0)				
Other	1,033 (0.29)	353 (0.33)	680 (0.28)				
Missing	10,062 (2.9)	4,202 (3.9)	5,860 (2.4)				
<b>TKR fixation</b> Cemented	NA	NA	NA		411,370 (96.5)	123,228 (96.2)	288,142 (96.7)
Uncemented					12,751 (3.0)	4,247 (3.3)	8,504 (2.9)
Hybrid					1,983 (0.47)	614 (0.48)	1,369 (0.46)
<b>Minimally invasive surgery</b>	12,186 (3.5)	3,601 (3.4)	8,585 (3.5)		9,334 (2.2)	3,436 (2.7)	5,898 (2.0)
<b>Bone graft (femoral)</b>	2,226 (0.63)	591 (0.55)	1,635 (0.66)		4,021 (0.94)	1,307 (1.0)	2,714 (0.91)
<b>Bone graft (acetabular)</b>	12,521 (3.5)	4,141 (3.9)	8,380 (3.4)		NA	NA	NA
<b>Bone graft (tibia)</b>	NA	NA	NA		1,668 (0.39)	537 (0.42)	1,131 (0.38)

ASA = American Society of Anesthesiologists; BMI = body mass index; CoC = ceramic-on-ceramic; CoP = ceramic-on-polyethylene; LMWH = low molecular weight heparin; MoP = metal-on-polyethylene; NHS =

National Health Service; NA = not applicable; SD = standard deviation; THR = total hip replacement; TKR = total knee replacement; VTE = venous thromboembolism.

Values in brackets are percentages unless otherwise indicated.

\* Missing BMI data for 96,777 hips and 119,760 knees

**Table 2** Outcomes after primary total hip and knee replacement by anaesthetic type

	<b>All primary THR (n=353,387) (100%)</b>	<b>General anaesthetic (n=106,782) (30.2%)</b>	<b>Regional anaesthetic (n=246,605) (69.8%)</b>		<b>All primary TKRs (n=426,104) (100%)</b>	<b>General anaesthetic (n=128,089) (30.1%)</b>	<b>Regional anaesthetic (n=298,015) (69.9%)</b>
<b>Length of stay in days</b>							
Mean (SD)	4.75 (3.62)	5.15 (4.04)	4.58 (3.41)		4.84 (3.65)	5.24 (3.91)	4.67 (3.51)
<b>Readmissions within 90 days</b>	41,441 (11.7)	12,953 (12.1)	28,488 (11.6)		58,477 (13.7)	18,361 (14.3)	40,116 (13.5)
<b>Any complication within 90 days</b>	14,547 (4.1)	4,697 (4.4)	9,850 (4.0)		17,364 (4.1)	5,440 (4.3)	11,924 (4.0)
<b>Revision at 90 days</b>	1,355 (0.38)	438 (0.41)	917 (0.37)		387 (0.09)	111 (0.09)	276 (0.09)
<b>Reoperations within 90 days (not including revision)</b>	706 (0.20)	231 (0.22)	475 (0.19)		803 (0.19)	278 (0.22)	525 (0.18)
<b>Mortality at 90 days</b>	1,038 (0.29)	312 (0.29)	726 (0.29)		679 (0.16)	190 (0.15)	489 (0.16)
<b>Specific complications within 90 days</b>							
VTE (DVT &/or PE)	2,043 (0.58)	718 (0.67)	1,325 (0.54)		2,757 (0.65)	871 (0.68)	1,886 (0.63)
DVT only	1,102 (0.31)	380 (0.36)	722 (0.29)		1,449 (0.34)	459 (0.36)	990 (0.33)
PE only	1,001 (0.28)	360 (0.34)	641 (0.26)		1,396 (0.33)	444 (0.35)	952 (0.32)
Urinary tract infection	1,712 (0.48)	544 (0.51)	1,168 (0.47)		1,902 (0.45)	580 (0.45)	1,322 (0.44)
Surgical site infection	2,639 (0.75)	886 (0.83)	1,753 (0.71)		4,378 (1.0)	1,503 (1.2)	2,875 (0.96)
Acute renal failure	1,063 (0.30)	332 (0.31)	731 (0.30)		1,406 (0.33)	379 (0.30)	1,027 (0.34)
Blood transfusion	258 (0.07)	106 (0.10)	152 (0.06)		192 (0.05)	58 (0.05)	134 (0.04)
Anaemia	3,224 (0.91)	1,043 (0.98)	2,181 (0.88)		3,614 (0.85)	1,115 (0.87)	2,499 (0.84)
Respiratory tract infection	2,089 (0.60)	594 (0.56)	1,495 (0.61)		2,316 (0.54)	615 (0.48)	1,701 (0.57)
Myocardial infarction	460 (0.13)	139 (0.13)	321 (0.13)		572 (0.13)	162 (0.13)	410 (0.14)
Stroke	368 (0.10)	111 (0.10)	257 (0.10)		481 (0.11)	146 (0.11)	335 (0.11)
Major haemorrhage	478 (0.14)	145 (0.14)	333 (0.14)		643 (0.15)	207 (0.16)	436 (0.15)
Wound disruption	546 (0.15)	164 (0.15)	382 (0.15)		1,187 (0.28)	377 (0.29)	810 (0.27)
<b>EQ5D at 6 months *</b>							
Mean (SD)	0.77 (0.26)	0.74 (0.27)	0.77 (0.25)		0.71 (0.26)	0.69 (0.28)	0.72 (0.26))
<b>OHS or OKS at 6 months *</b>							
Median (IQR)	41 (34-46)	41 (33-45)	42 (35-46)		36 (28-42)	35 (27-42)	37 (29-43)

DVT = deep vein thrombosis; IQR = interquartile range; OHS = Oxford Hip Score; OKS = Oxford Knee Score; PE = pulmonary embolism; SD = standard deviation; THR = total hip replacement; TKR = total knee replacement; VTE = venous thromboembolism.

Values in brackets are percentages unless otherwise indicated.

\* Missing data for stated number of hips: EQ5D (n=170,324); OHS (n=169,851)

\* Missing data for stated number of knees: EQ5D (n=205,848); OKS (n=205,754)

**Table 3** Regression analysis for the effect of anaesthetic type on outcomes following total hip and knee replacement

Outcome of interest	THR adjustment for all variables excluding BMI (n=342,268)	TKR adjustment for all variables excluding BMI (n=422,205)
<b>Length of stay</b>	Coefficient = -0.49 (-0.51 to -0.47)  <b>p&lt;0.001</b>  Based on 342,246 hips	Coefficient = -0.47 (-0.49 to -0.45)  <b>p&lt;0.001</b>  Based on 422,179 knees
<b>Readmissions within 90 days</b>	OR = 0.93 (0.90-0.96)  <b>p&lt;0.001</b>	OR = 0.91 (0.89-0.93)  <b>p&lt;0.001</b>
<b>Any complication within 90 days</b>	OR = 0.88 (0.85-0.91)  <b>p&lt;0.001</b>	OR = 0.90 (0.87-0.93)  <b>p&lt;0.001</b>
<b>Revision at 90 days</b>	OR = 1.01 (0.88-1.17)  p=0.849	OR = 0.99 (0.79-1.23)  p=0.899
<b>Reoperations within 90 days</b>	OR = 0.86 (0.73-1.01)  p=0.062	OR = 0.79 (0.68-0.92)  <b>p=0.002</b>
<b>Mortality at 90 days</b>	OR = 0.91 (0.77-1.08)  p=0.300	OR = 1.01 (0.86-1.20)  p=0.865
<b>Specific complications within 90 days</b>		
VTE (DVT &/or PE)	OR = 0.85 (0.77-0.93)  <b>p=0.001</b>	OR = 0.96 (0.89-1.05)  p=0.370
DVT only	OR = 0.93 (0.82-1.06)  p=0.257	OR = 0.98 (0.88-1.10)  p=0.760
PE only	OR = 0.77 (0.67-0.88)	OR = 0.93 (0.83-1.05)



	<b>p&lt;0.001</b>	p=0.236
Urinary tract infection	OR = 0.85 (0.77-0.94) <b>p=0.003</b>	OR = 0.87 (0.79-0.96) <b>p=0.007</b>
Surgical site infection	OR = 0.87 (0.80-0.95) <b>p=0.001</b>	OR = 0.84 (0.78-0.89) <b>p&lt;0.001</b>
Acute renal failure	OR = 0.78 (0.68-0.89) <b>p&lt;0.001</b>	OR = 0.93 (0.82-1.04) p=0.208
Blood transfusion	OR = 0.62 (0.48-0.80) <b>p&lt;0.001</b>	OR = 0.96 (0.70-1.31) p=0.780
Anaemia	OR = 0.85 (0.79-0.92) <b>p&lt;0.001</b>	OR = 0.89 (0.83-0.95) <b>p=0.001</b>
Respiratory tract infection	OR = 0.99 (0.90-1.09) p=0.808	OR = 1.05 (0.96-1.16) p=0.278
Myocardial infarction	OR = 0.90 (0.73-1.10) p=0.293	OR = 0.93 (0.77-1.11) p=0.409
Stroke	OR = 0.92 (0.74-1.16) p=0.500	OR = 0.88 (0.72-1.07) p=0.203
Major haemorrhage	OR = 0.94 (0.77-1.15) p=0.531	OR = 0.86 (0.73-1.02) p=0.075
Wound disruption	OR = 0.94 (0.78-1.14) p=0.550	OR = 0.91 (0.80-1.03) p=0.124
<b>EQ5D at 6 months</b>	Coefficient = 0.021 (0.018 to 0.023) <b>p&lt;0.001</b> Based on 170,173 hips	Coefficient = 0.019 (0.017 to 0.022) <b>p&lt;0.001</b> Based on 208,894 knees
<b>OHS or OKS at 6 months</b>	Coefficient = 0.79 (0.70 to 0.88)	Coefficient = 0.80 (0.71 to 0.88)

	<p><b>p&lt;0.001</b></p> <p>Based on 176,776 hips</p>	<p><b>p&lt;0.001</b></p> <p>Based on 216,474 knees</p>
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BMI = body mass index; DVT = deep vein thrombosis; OHS = Oxford Hip Score; OKS = Oxford Knee Score; PE = pulmonary VTE = venous thromboembolism

Numbers in brackets represent the 95% confidence intervals.

Odds ratios below 1 represent a reduced risk of the specified outcome in the regional anaesthetic group.

Statistically significant p-values (p<0.05) are in **bold**

**Appendix 1** Codes for outcomes of interest**Deep vein thrombosis (ICD 10)**

- I80.1 Phlebitis and thrombophlebitis of femoral vein
- I80.2 Phlebitis and thrombophlebitis of other deep vessels of lower extremities
- I80.3 Phlebitis and thrombophlebitis of lower extremities, unspecified

**Pulmonary embolism (ICD 10)**

- I26.0 Pulmonary embolism with mention of acute cor pulmonale
- I26.9 Pulmonary embolism without mention of acute cor pulmonale

**Reoperation hip (OPCS4)**

- W801 Z756 Open debridement and irrigation of joint - Acetabulum
- W801 Z761 Open debridement and irrigation of joint - Head of femur
- W801 Z843 Open debridement and irrigation of joint - Hip joint
- W801 Z902 Open debridement and irrigation of joint - Hip NEC
- W802 Z756 Open debridement of joint NEC - Acetabulum
- W802 Z761 Open debridement of joint NEC - Head of femur
- W802 Z843 Open debridement of joint NEC - Hip joint
- W802 Z902 Open debridement of joint NEC - Hip NEC
- W803 Z756 Open irrigation of joint NEC - Acetabulum
- W803 Z761 Open irrigation of joint NEC - Head of femur
- W803 Z843 Open irrigation of joint NEC - Hip joint
- W803 Z902 Open irrigation of joint NEC - Hip NEC
- W808 Z756 Other specified debridement and irrigation of joint - Acetabulum
- W808 Z761 Other specified debridement and irrigation of joint - Head of femur
- W808 Z843 Other specified debridement and irrigation of joint - Hip joint
- W808 Z902 Other specified debridement and irrigation of joint - Hip NEC
- W809 Z756 Unspecified debridement and irrigation of joint - Acetabulum
- W809 Z761 Unspecified debridement and irrigation of joint - Head of femur
- W809 Z843 Unspecified debridement and irrigation of joint - Hip joint
- W809 Z902 Unspecified debridement and irrigation of joint - Hip NEC

**Reoperation knee (OPCS4)**

- W852 Endoscopic irrigation of knee joint
- W801 Z765 Open debridement and irrigation of joint - Lower end of femur NEC
- W801 Z774 Open debridement and irrigation of joint - Upper end of tibia NEC
- W801 Z787 Open debridement and irrigation of joint - Patella
- W801 Z844 Open debridement and irrigation of joint - Patellofemoral joint
- W801 Z845 Open debridement and irrigation of joint - Tibiofemoral joint
- W801 Z846 Open debridement and irrigation of joint - Knee joint
- W802 Z765 Open debridement of joint NEC - Lower end of femur NEC
- W802 Z774 Open debridement of joint NEC - Upper end of tibia NEC
- W802 Z787 Open debridement of joint NEC - Patella
- W802 Z844 Open debridement of joint NEC - Patellofemoral joint
- W802 Z845 Open debridement of joint NEC - Tibiofemoral joint
- W802 Z846 Open debridement of joint NEC - Knee joint
- W803 Z765 Open irrigation of joint NEC - Lower end of femur NEC
- W803 Z744 Open irrigation of joint NEC - Upper end of tibia NEC
- W803 Z787 Open irrigation of joint NEC - Patella

W803	Z844	Open irrigation of joint NEC - Patellofemoral joint
W803	Z845	Open irrigation of joint NEC - Tibiofemoral joint
W803	Z846	Open irrigation of joint NEC - Knee joint
W808	Z765	Other specified debridement and irrigation of joint - Lower end of femur NEC
W808	Z774	Other specified debridement and irrigation of joint - Upper end of tibia NEC
W808	Z787	Other specified debridement and irrigation of joint - Patella
W808	Z844	Other specified debridement and irrigation of joint - Patellofemoral joint
W808	Z845	Other specified debridement and irrigation of joint - Tibiofemoral joint
W808	Z846	Other specified debridement and irrigation of joint - Knee joint
W809	Z765	Unspecified debridement and irrigation of joint - Lower end of femur NEC
W809	Z774	Unspecified debridement and irrigation of joint - Upper end of tibia NEC
W809	Z787	Unspecified debridement and irrigation of joint - Patella
W809	Z844	Unspecified debridement and irrigation of joint - Patellofemoral joint
W809	Z845	Unspecified debridement and irrigation of joint - Tibiofemoral joint
W809	Z846	Unspecified debridement and irrigation of joint - Knee joint

#### **Blood transfusion (ICD 10 and OPCS 4)**

X33.2 Intravenous blood transfusion of packed cells  
X33.3 Intravenous blood transfusion of platelets  
X33.8 Other specified other blood transfusion  
X33.9 Unspecified other blood transfusion  
X33.1 Intra-arterial blood transfusion  
X33.7 Autologous transfusion of red blood cells

X331	Intra-arterial blood transfusion
X332	Intravenous blood transfusion of packed cells
X333	Intravenous blood transfusion of platelets
X337	Autologous transfusion of red blood cells
X338	Other specified blood transfusion
X339	Other unspecified blood transfusion
X341	Transfusion of coagulation factor
X342	Transfusion of plasma NEC
X343	Transfusion of serum NEC
X344	Transfusion of blood expander

#### **Major bleeding (ICD 10)**

K25.0 Gastric ulcer : acute with haemorrhage†  
K25.1 Gastric ulcer : acute with perforation  
K25.2 Gastric ulcer : acute with both haemorrhage and perforation  
K25.3 Gastric ulcer : acute without haemorrhage or perforation  
K25.4 Gastric ulcer : chronic or unspecified with haemorrhage  
K25.5 Gastric ulcer : chronic or unspecified with perforation  
K25.6 Gastric ulcer : chronic or unspecified with both haemorrhage and perforation  
K25.7 Gastric ulcer : chronic without haemorrhage or perforation  
K25.9 Gastric ulcer : unspecified as acute or chronic, without haemorrhage or perforation  
K26.0 Duodenal ulcer : acute with haemorrhage  
K26.1 Duodenal ulcer : acute with perforation  
K26.2 Duodenal ulcer : acute with both haemorrhage and perforation  
K26.3 Duodenal ulcer : acute without haemorrhage or perforation  
K26.4 Duodenal ulcer : chronic or unspecified with haemorrhage

- K26.5 Duodenal ulcer : chronic or unspecified with perforation
- K26.6 Duodenal ulcer : chronic or unspecified with both haemorrhage and perforation
- K26.7 Duodenal ulcer : chronic without haemorrhage or perforation
- K26.9 Duodenal ulcer : unspecified as acute or chronic, without haemorrhage or perforation
- K27.0 Peptic ulcer, site unspecified : acute with haemorrhage
- K27.1 Peptic ulcer, site unspecified : acute with perforation
- K27.2 Peptic ulcer, site unspecified : acute with both haemorrhage and perforation
- K27.3 Peptic ulcer, site unspecified : acute without haemorrhage or perforation
- K27.4 Peptic ulcer, site unspecified : chronic or unspecified with haemorrhage
- K27.5 Peptic ulcer, site unspecified : chronic or unspecified with perforation
- K27.6 Peptic ulcer, site unspecified : chronic or unspecified with both haemorrhage and perforation
- K27.7 Peptic ulcer, site unspecified : chronic without haemorrhage or perforation
- K27.9 Peptic ulcer, site unspecified : unspecified as acute or chronic, without haemorrhage or perforation
- K28.0 Gastrojejunal ulcer : acute with haemorrhage
- K28.1 Gastrojejunal ulcer : acute with perforation
- K28.2 Gastrojejunal ulcer : acute with both haemorrhage and perforation
- K28.3 Gastrojejunal ulcer : acute without haemorrhage or perforation
- K28.4 Gastrojejunal ulcer : chronic or unspecified with haemorrhage
- K28.5 Gastrojejunal ulcer : chronic or unspecified with perforation
- K28.6 Gastrojejunal ulcer : chronic or unspecified with both haemorrhage and perforation
- K28.7 Gastrojejunal ulcer : chronic without haemorrhage or perforation
- K28.9 Gastrojejunal ulcer : unspecified as acute or chronic, without haemorrhage or perforation
  
- I60.X Subarachnoid haemorrhage
- I61.0 Intracerebral haemorrhage in hemisphere, subcortical
- I61.1 Intracerebral haemorrhage in hemisphere, cortical
- I61.2 Intracerebral haemorrhage in hemisphere, unspecified
- I61.3 Intracerebral haemorrhage in brain stem
- I61.4 Intracerebral haemorrhage in cerebellum
- I61.5 Intracerebral haemorrhage, intraventricular
- I61.6 Intracerebral haemorrhage, multiple localized
- I61.8 Other intracerebral haemorrhage
- I61.9 Intracerebral haemorrhage, unspecified

### **Anaemia (ICD 10)**

- D46.0 Refractory anaemia without ring sideroblasts, so stated
- D46.1 Refractory anaemia with ring sideroblasts
- D46.2 Refractory anaemia with excess of blasts [RAEB]
- D46.4 Refractory anaemia, unspecified
- D46.5 Refractory anaemia with multi-lineage dysplasia
- D46.7 Other myelodysplastic syndromes
- D46.9 Myelodysplastic syndrome, unspecified
- D50.0 Iron deficiency anaemia secondary to blood loss (chronic)
- D50.8 Other iron deficiency anaemias
- D50.9 Iron deficiency anaemia, unspecified
- D51.0 Vitamin B12 deficiency anaemia due to intrinsic factor deficiency
- D51.1 Vitamin B12 deficiency anaemia due to selective vitamin B12 malabsorption with proteinuria
- D51.2 Transcobalamin II deficiency
- D51.3 Other dietary vitamin B12 deficiency anaemia
- D51.8 Other vitamin B12 deficiency anaemias

- D51.9 Vitamin B12 deficiency anaemia, unspecified
- D52.0 Dietary folate deficiency anaemia
- D52.1 Drug-induced folate deficiency anaemia
- D52.8 Other folate deficiency anaemias
- D52.9 Folate deficiency anaemia, unspecified
- D53.0 Protein deficiency anaemia
- D53.1 Other megaloblastic anaemias, not elsewhere classified
- D53.2 Scorbutic anaemia
- D53.8 Other specified nutritional anaemias
- D53.9 Nutritional anaemia, unspecified
- D59.0 Drug-induced autoimmune haemolytic anaemia
- D59.1 Other autoimmune haemolytic anaemias
- D59.2 Drug-induced nonautoimmune haemolytic anaemia
- D59.3 Haemolytic-uraemic syndrome
- D59.4 Other nonautoimmune haemolytic anaemias
- D59.6 Haemoglobinuria due to haemolysis from other external causes
- D59.8 Other acquired haemolytic anaemias
- D59.9 Acquired haemolytic anaemia, unspecified
- D61.0 Constitutional aplastic anaemia
- D61.1 Drug-induced aplastic anaemia
- D61.2 Aplastic anaemia due to other external agents
- D61.3 Idiopathic aplastic anaemia
- D61.8 Other specified aplastic anaemias
- D61.9 Aplastic anaemia, unspecified
- D62 Acute posthaemorrhagic anaemia
- D63.0 Anaemia in neoplastic disease (C00-D48)
- D63.8 Anaemia in other chronic diseases classified elsewhere
- D64.1 Secondary sideroblastic anaemia due to disease
- D64.2 Secondary sideroblastic anaemia due to drugs and toxins
- D64.3 Other sideroblastic anaemias
- D64.8 Other specified anaemias
- D64.9 Anaemia, unspecified
- O99.0 Anaemia complicating pregnancy, childbirth and the puerperium
- P61.2 Anaemia of prematurity
- P61.4 Other congenital anaemias, not elsewhere classified

### **Wound disruption and surgical site infection (ICD 10)**

- T84.5 Infection and inflammatory reaction due to internal joint prosthesis
- T81.3 Disruption of operation wound, not elsewhere classified
- T81.4 Infection following a procedure, not elsewhere classified

### **Myocardial infarction (ICD 10)**

- I21.0 Acute transmural myocardial infarction of anterior wall
- I21.1 Acute transmural myocardial infarction of inferior wall
- I21.2 Acute transmural myocardial infarction of other sites
- I21.3 Acute transmural myocardial infarction of unspecified site
- I21.4 Acute subendocardial myocardial infarction
- I21.9 Acute myocardial infarction, unspecified
- I22.0 Subsequent myocardial infarction of anterior wall
- I22.1 Subsequent myocardial infarction of inferior wall

- I22.8 Subsequent myocardial infarction of other sites
- I22.9 Subsequent myocardial infarction of unspecified site

### **Acute renal failure (ICD 10)**

- N17.0 Acute renal failure with tubular necrosis
- N17.1 Acute renal failure with acute cortical necrosis
- N17.2 Acute renal failure with medullary necrosis
- N17.8 Other acute renal failure
- N17.9 Acute renal failure, unspecified

### **Urinary tract infection (ICD 10)**

- N30.0 Acute cystitis. Excluding irradiation cystitis and trigonitis
- N39.0 Urinary tract infection, site not specified

### **Respiratory tract infection (ICD 10)**

- J12.X Viral pneumonia, not elsewhere classified: bronchopneumonia due to viruses other than influenza viruses
- J13 Pneumonia due to *Streptococcus pneumoniae*
- J14 Pneumonia due to *Haemophilus influenzae*
- J15.X Bacterial pneumonia, not elsewhere classified: bronchopneumonia due to bacteria other than *S. pneumoniae* and *H. influenzae*
- J18.0 Bronchopneumonia, unspecified. Excluding bronchiolitis
- J18.1 Lobar pneumonia, unspecified
- J18.2 Hypostatic pneumonia, unspecified
- J18.8 Other pneumonia, organism unspecified
- J18.9 Pneumonia, Unspecified
- J22 Unspecified acute lower respiratory infection
- J44.0 Chronic obstructive pulmonary disease with acute lower respiratory infection. Excluding with influenza
- J44.1 Chronic obstructive pulmonary disease with acute exacerbation, unspecified
- J69.0 Pneumonitis due to food and vomit. Excluding Mendelson syndrome
- J69.1 Pneumonitis due to oils and essences
- J69.8 Pneumonitis due to other solids and liquids. Pneumonitis due to aspiration of blood
- J85.1 Abscess of lung with pneumonia. Excluding with pneumonia due to specified organism

### **Stroke (ICD 10)**

- I60.X Subarachnoid haemorrhage
- I61.0 Intracerebral haemorrhage in hemisphere, subcortical
- I61.1 Intracerebral haemorrhage in hemisphere, cortical
- I61.2 Intracerebral haemorrhage in hemisphere, unspecified
- I61.3 Intracerebral haemorrhage in brain stem
- I61.4 Intracerebral haemorrhage in cerebellum
- I61.5 Intracerebral haemorrhage, intraventricular
- I61.6 Intracerebral haemorrhage, multiple localized
- I61.8 Other intracerebral haemorrhage
- I61.9 Intracerebral haemorrhage, unspecified
- I63.0 Cerebral infarction due to thrombosis of precerebral arteries
- I63.1 Cerebral infarction due to embolism of precerebral arteries
- I63.2 Cerebral infarction due to unspecified occlusion or stenosis of precerebral arteries
- I63.3 Cerebral infarction due to thrombosis of cerebral arteries

- I63.4 Cerebral infarction due to embolism of cerebral arteries
- I63.5 Cerebral infarction due to unspecified occlusion or stenosis of cerebral arteries
- I63.6 Cerebral infarction due to cerebral venous thrombosis, nonpyogenic
- I63.8 Other cerebral infarction
- I63.9 Cerebral infarction, unspecified
- I64.X Stroke, not specified as haemorrhage or infarction



**Appendix 2** Sensitivity analysis for total hip and knee replacements: univariable regression models and multivariable models adjusted for all variables including body mass index

<b>Outcome of interest</b>	<b>THR univariable analysis (n=353,387)</b>	<b>THR adjustment for all variables* including BMI (n=249,848)</b>	<b>TKR univariable analysis (n=426,104)</b>	<b>TKR adjustment for all variables* including BMI (n=304,538)</b>
<b>Length of stay</b>	Coefficient = -0.56 (-0.59 to -0.54) <b>p&lt;0.001</b> Based on 353,365 hips	Coefficient = -0.39 (-0.42 to -0.36) <b>p&lt;0.001</b> Based on 249,832 hips	Coefficient = -0.57 (-0.59 to -0.55) <b>p&lt;0.001</b> Based on 426,078 knees	Coefficient = -0.37 (-0.40 to -0.34) <b>p&lt;0.001</b> Based on 304,520 knees
<b>Readmissions within 90 days</b>	OR = 0.95 (0.93-0.97) <b>p&lt;0.001</b>	OR = 0.93 (0.90-0.96) <b>p&lt;0.001</b>	OR = 0.93 (0.91-0.95) <b>p&lt;0.001</b>	OR = 0.91 (0.89-0.93) <b>p&lt;0.001</b>
<b>Any complication within 90 days</b>	OR = 0.90 (0.87-0.94) <b>p&lt;0.001</b>	OR = 0.88 (0.84-0.92) <b>p&lt;0.001</b>	OR = 0.94 (0.91-0.97) <b>p&lt;0.001</b>	OR = 0.90 (0.87-0.94) <b>p&lt;0.001</b>
<b>Revision at 90 days</b>	OR = 0.91 (0.81-1.02) p=0.091	OR = 1.01 (0.88-1.17) p=0.849	OR = 1.07 (0.86-1.33) p=0.554	OR = 1.01 (0.77-1.31) p=0.970
<b>Reoperations within 90 days</b>	OR = 0.89 (0.76-1.04) p=0.147	OR = 0.82 (0.68-0.99) <b>p=0.042</b>	OR = 0.81 (0.70-0.94) <b>p=0.005</b>	OR = 0.73 (0.61-0.87) <b>p&lt;0.001</b>
<b>Mortality at 90 days</b>	OR = 1.01 (0.88-1.15)	OR = 0.91 (0.77-1.08)	OR = 1.11 (0.94-1.31)	OR = 1.09 (0.88-1.35)

	p=0.911	p=0.300	p=0.237	p=0.449
<b>Specific complications within 90 days</b>				
VTE (DVT &/or PE)	OR = 0.80 (0.73-0.87) <b>p&lt;0.001</b>	OR = 0.84 (0.75-0.94) <b>p=0.002</b>	OR = 0.93 (0.86-1.01) p=0.078	OR = 0.97 (0.87-1.07) p=0.508
DVT only	OR = 0.82 (0.73-0.93) <b>p=0.002</b>	OR = 0.90 (0.76-1.05) p=0.180	OR = 0.93 (0.83-1.04) p=0.179	OR = 1.02 (0.89-1.18) p=0.750
PE only	OR = 0.77 (0.68-0.88) <b>p&lt;0.001</b>	OR = 0.78 (0.66-0.91) <b>p=0.002</b>	OR = 0.92 (0.82-1.03) p=0.155	OR = 0.91 (0.79-1.04) p=0.164
Urinary tract infection	OR = 0.93 (0.84-1.03) p=0.159	OR = 0.88 (0.77-1.00) p=0.052	OR = 0.98 (0.89-1.08) p=0.679	OR = 0.89 (0.79-1.00) p=0.055
Surgical site infection	OR = 0.86 (0.79-0.93) <b>p&lt;0.001</b>	OR = 0.82 (0.74-0.90) <b>p&lt;0.001</b>	OR = 0.82 (0.77-0.87) <b>p&lt;0.001</b>	OR = 0.83 (0.77-0.90) <b>p&lt;0.001</b>
Acute renal failure	OR = 0.95 (0.84-1.09) p=0.470	OR = 0.85 (0.72-0.99) <b>p=0.045</b>	OR = 1.17 (1.04-1.31) <b>p=0.011</b>	OR = 0.95 (0.82-1.10) p=0.495
Blood transfusion	OR = 0.62 (0.48-0.80) <b>p&lt;0.001</b>	OR = 0.57 (0.42-0.77) <b>p&lt;0.001</b>	OR = 0.99 (0.73-1.35) p=0.964	OR = 0.91 (0.62-1.32) p=0.621

Anaemia	OR = 0.90 (0.84-0.97) <b>p=0.008</b>	OR = 0.84 (0.77-0.92) <b>p&lt;0.001</b>	OR = 0.96 (0.90-1.03) p=0.297	OR = 0.90 (0.82-0.98) <b>p=0.017</b>
Respiratory tract infection	OR = 1.09 (0.99-1.20) p=0.075	OR = 0.99 (0.88-1.11) p=0.861	OR = 1.19 (1.08-1.31) <b>p&lt;0.001</b>	OR = 1.05 (0.94-1.18) p=0.390
Myocardial infarction	OR = 1.00 (0.82-1.22) p=1.00	OR = 0.92 (0.72-1.18) p=0.508	OR = 1.09 (0.91-1.31) p=0.364	OR = 0.79 (0.63-0.97) <b>p=0.028</b>
Stroke	OR = 1.00 (0.80-1.25) p=0.982	OR = 1.01 (0.76-1.33) p=0.970	OR = 0.99 (0.81-1.20) p=0.889	OR = 0.89 (0.70-1.14) p=0.366
Major haemorrhage	OR = 0.99 (0.82-1.21) p=0.955	OR = 1.04 (0.82-1.33) p=0.738	OR = 0.91 (0.77-1.07) p=0.238	OR = 0.87 (0.71-1.07) p=0.192
Wound disruption	OR = 1.01 (0.84-1.21) p=0.927	OR = 1.01 (0.81-1.27) p=0.906	OR = 0.92 (0.82-1.04) p=0.201	OR = 0.87 (0.75-1.01) p=0.060
<b>EQ5D at 6 months</b>	Coefficient = 0.024 (0.021 to 0.026) <b>p&lt;0.001</b> Based on 175,224 hips	Coefficient = 0.023 (0.020 to 0.026) <b>p&lt;0.001</b> Based on 127,258 hips	Coefficient = 0.025 (0.023 to 0.027) <b>p&lt;0.001</b> Based on 210,816 knees	Coefficient = 0.018 (0.016 to 0.021) <b>p&lt;0.001</b> Based on 154,704 knees
<b>OHS or OKS at 6 months</b>	Coefficient = 0.89 (0.80 to 0.98)	Coefficient = 0.85 (0.75 to 0.96)	Coefficient = 1.02 (0.93 to 1.10)	Coefficient = 0.80 (0.70 to 0.90)

	<b>p&lt;0.001</b> Based on 182,031 hips	<b>p&lt;0.001</b> Based on 132,167 hips	<b>p&lt;0.001</b> Based on 218,558 knees	<b>p&lt;0.001</b> Based on 160,333 knees
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BMI = body mass index; DVT = deep vein thrombosis; OHS = Oxford Hip Score; OKS = Oxford Knee Score; PE = pulmonary VTE = venous thromboembolism

Numbers in brackets represent the 95% confidence intervals.

Odds ratios below 1 represent a reduced risk of the specified outcome in the regional anaesthetic group.

Statistically significant p-values (p<0.05) are in **bold**

**Appendix 3** Sensitivity analysis for total hip and knee replacements to assess the effect of using a nerve block on outcomes: multivariable models adjusted for all variables excluding body mass index

<b>Outcome of interest</b>	<b>THR: GA alone (reference group) vs. GA with nerve block (n=102,206)</b>	<b>THR: SA alone (reference group) vs. SA with nerve block (n=246,605)</b>	<b>TKR: GA alone (reference group) vs. GA with nerve block (n=124,523)</b>	<b>TKR: SA alone (reference group) vs. SA with nerve block (n=298,015)</b>
<b>Length of stay</b>	Coefficient = -0.03 (-0.09 to 0.04)  p=0.375  Based on 97,498 hips	Coefficient = -0.05 (-0.11 to 0.004)  p=0.071  Based on 240,365 hips	Coefficient = 0.03 (-0.02 to 0.07)  p=0.299  Based on 122,658 knees	Coefficient = 0.12 (0.08 to 0.15)  <b>p&lt;0.001</b>  Based on 296,002 knees
<b>Readmissions within 90 days</b>	OR = 0.92 (0.87-0.97)  <b>p=0.004</b>	OR = 0.97 (0.91-1.03)  p=0.269	OR = 0.95 (0.92-0.99)  <b>p=0.013</b>	OR = 0.97 (0.94-1.01)  p=0.088
<b>Any complication within 90 days</b>	OR = 0.92 (0.84-1.01)  p=0.068	OR = 0.98 (0.89-1.07)  p=0.624	OR = 0.94 (0.89-1.01)  p=0.073	OR = 1.04 (0.98-1.10)  p=0.187
<b>Revision at 90 days</b>	OR = 1.03 (0.78-1.36)  p=0.841	OR = 0.97 (0.71-1.32)  p=0.827	OR = 1.08 (0.69-1.70)  p=0.739	OR = 1.23 (0.86-1.76)  p=0.267
<b>Reoperations within 90 days</b>	OR = 1.09 (0.76-1.56)  p=0.642	OR = 1.05 (0.70-1.57)  p=0.826	OR = 0.99 (0.75-1.31)  p=0.930	OR = 0.94 (0.71-1.25)  p=0.686
<b>Mortality at 90</b>	OR = 0.90	OR = 0.70	OR = 0.90	OR = 0.88

<b>days</b>	(0.64-1.24) p=0.511	(0.48-1.03) p=0.067	(0.64-1.26) p=0.537	(0.66-1.18) p=0.400
<b>Specific complications within 90 days</b>				
VTE (DVT &/or PE)	OR = 0.82 (0.65-1.03) p=0.081	OR = 0.87 (0.67-1.12) p=0.284	OR = 1.04 (0.89-1.22) p=0.610	OR = 1.01 (0.88-1.16) p=0.889
DVT only	OR = 0.84 (0.62-1.15) p=0.282	OR = 0.77 (0.54-1.11) p=0.161	OR = 0.94 (0.75-1.16) p=0.561	OR = 1.00 (0.82-1.22) p=0.998
PE only	OR = 0.84 (0.61-1.15) p=0.280	OR = 1.04 (0.73-1.46) p=0.839	OR = 1.12 (0.90-1.39) p=0.313	OR = 1.00 (0.82-1.22) p=0.995
Urinary tract infection	OR = 1.03 (0.80-1.31) p=0.826	OR = 0.98 (0.75-1.29) p=0.912	OR = 1.10 (0.91-1.32) p=0.347	OR = 1.16 (0.99-1.37) p=0.075
Surgical site infection	OR = 0.87 (0.71-1.07) p=0.186	OR = 1.01 (0.82-1.25) p=0.897	OR = 0.80 (0.70-0.90) <b>p&lt;0.001</b>	OR = 0.93 (0.82-1.04) p=0.209
Acute renal failure	OR = 1.15 (0.84-1.58) p=0.384	OR = 0.98 (0.69-1.38) p=0.895	OR = 0.77 (0.59-1.01) p=0.051	OR = 0.93 (0.75-1.14) p=0.464
Blood transfusion	OR = 0.58 (0.31-1.10)	OR = 1.35 (0.73-2.52)	OR = 0.79 (0.42-1.48)	OR = 1.01 (0.60-1.71)

	p=0.098	p=0.338	p=0.463	p=0.972
Anaemia	OR = 1.05 (0.88-1.24) p=0.611	OR = 0.93 (0.76-1.13) p=0.477	OR = 1.04 (0.91-1.20) p=0.569	OR = 1.05 (0.93-1.19) p=0.437
Respiratory tract infection	OR = 0.97 (0.76-1.23) p=0.777	OR = 0.88 (0.69-1.12) p=0.303	OR = 0.91 (0.75-1.11) p=0.352	OR = 1.15 (0.99-1.33) p=0.062
Myocardial infarction	OR = 0.73 (0.42-1.26) p=0.254	OR = 1.17 (0.72-1.89) p=0.523	OR = 0.86 (0.59-1.26) p=0.441	OR = 1.11 (0.82-1.50) p=0.495
Stroke	OR = 0.71 (0.39-1.31) p=0.278	OR = 1.12 (0.66-1.89) p=0.684	OR = 0.94 (0.63-1.39) p=0.745	OR = 0.93 (0.65-1.31) p=0.669
Major haemorrhage	OR = 0.69 (0.41-1.17) p=0.169	OR = 1.24 (0.80-1.92) p=0.340	OR = 0.94 (0.68-1.30) p=0.711	OR = 0.86 (0.63-1.18) p=0.357
Wound disruption	OR = 0.90 (0.57-1.41) p=0.645	OR = 0.80 (0.48-1.32) p=0.378	OR = 1.00 (0.78-1.27) p=0.987	OR = 1.04 (0.84-1.28) p=0.745
<b>EQ5D at 6 months</b>	Coefficient = -0.002 (-0.01 to 0.004) p=0.567 Based on 47,152 hips	Coefficient = 0.001 (-0.005 to 0.007) p=0.804 Based on 121,120 hips	Coefficient = 0.010 (0.002 to 0.012) <b>p=0.004</b> Based on 58,837 knees	Coefficient = -0.005 (-0.01 to -0.001) <b>p=0.022</b> Based on 148,595 knees

<b>OHS or OKS at 6 months</b>	Coefficient = -0.11 (-0.33 to 0.11)  p=0.331  Based on 49,056  hips	Coefficient = 0.01 (-0.20 to 0.21)  p=0.962  Based on 125,755  hips	Coefficient = 0.49 (-0.13 to 1.11)  p=0.122  Based on 47,552  knees	Coefficient = 0.46 (-0.08 to 1.00)  p=0.095  Based on 111,098  knees
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BMI = body mass index; DVT = deep vein thrombosis; GA = general anaesthesia; OHS = Oxford Hip Score; OKS = Oxford Knee Score; PE = pulmonary; SA = spinal anaesthesia; VTE = venous thromboembolism

Numbers in brackets represent the 95% confidence intervals.

Odds ratios below 1 represent a reduced risk of the specified outcome in the anaesthesia with nerve block group (compared with the anaesthesia alone group).

Statistically significant p-values ( $p < 0.05$ ) are in **bold**



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