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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

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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.

Cover letter

Submission type: New

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Title: **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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All of the aforementioned authors have actively participated in the study, and the work has not been submitted elsewhere for consideration for publication.

IRB approval: With support under Section 251 of the NHS Act 2006, the Ethics and Confidentiality Committee (ECC), (now the Health Research Authority Confidentiality Advisory Group) allows the NJR to collect patient data where consent is indicated as 'Not Recorded'.

Consent for publication: Before Personal Data and Sensitive Personal Data is recorded, express written patient consent is provided. The NJR records patient consent as either 'Yes', 'No', or 'Not Recorded'.

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

Competing interests: GSM has received personal fees for undertaking medicolegal work for Leigh Day. CG has no relevant conflicts of interest. AR holds non-commercial research grants from NIHR, ORUK & H2020; his department has received educational and research grants from DePuy Ltd. AJ has received consultancy fees from Freshfields Bruckhaus Deringer, and has held advisory board positions (which involved receipt of fees) from Anthera Pharmaceuticals, INC.

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Authors' Contributions: All authors conceived and designed the study. GM, CG and AJ analysed the data. All authors interpreted data and wrote, edited and approved the final report. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. AJ is the guarantor for this study and had final responsibility for manuscript submission.

13th January 2020

Response to reviewer comments for Manuscript # JOA-D-19-01646

"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"

Many thanks for reviewing our work. We appreciate all the comments received and feel that these have helped improve our paper. All responses to the reviewer comments below are provided in **bold text**, and we have cited both page number and line number for any changes made in the manuscript. As requested we have only submitted a clean copy of the main text document.

Reviewer #1: This is a retrospective analysis on a large population-based registry which intends to compare general vs regional anesthesia for joint replacement surgery in terms of multiple outcomes.
No specific comments to address.

The study is well designed since it addresses most of relevant outcomes and potential confounders. Furthermore, the decision to combine multiple databases in order to detect as many outcomes as possible is a great effort that adds valuable information. In addition, the manuscript is clear, well-written and organized thus making the paper very enjoyable to read.
No specific comments to address.

My only concern is in regards to the effect of the historic trend in the use of anesthetic techniques on the current results since the proportion of general anesthesia was greater during the first years of observation.

Within the materials and methods section, authors state that the year of surgery was included for adjustment for the statistical analysis and then, in the discussion section, they acknowledge that the study can not exclude the possibility that the changes in practice are responsible for the differences found between anesthetic techniques. This topic deserves a more detailed description of the adjustment made during statistical analysis, further discussion and a modification in the conclusion statement, if needed.
We thank the reviewer for this useful comment. In the analyses we had adjusted for year as a confounding variable in the multivariable regression models, with year as a binary variable (2008-12 versus 2013-17). To help address the reviewers comment, we have now conducted further analyses, using likelihood ratio tests to test for evidence of an interaction between anaesthetic techniques with year of surgery, for each of the study outcomes. We have now explained these extra details in our statistical analysis section of the revised manuscript (lines 156-7 and lines 154-6). These analyses allow us to address the question of whether the effect of regional anaesthesia on outcomes is the same in earlier versus later years of surgery. The results of the extra analyses have been presented (lines 248-269) and it has also been discussed further in the paper (lines 374-8).

In summary, very interesting paper, well written, and it contributes to currently available knowledge. Must be published if authors are able to explain the effect of that possible shortcoming.

Thank you.

Reviewer #2: The authors performed a retrospective review of the large UK Registry to compare outcomes of TKR and THR performed under regional versus general anesthesia and found a statistically significant decrease in length of stay as well as certain complications. Overall, this is a well-written, relevant study that provides good evidence for the benefits of regional anesthesia. I do have a few questions and issues that I would like the authors to address.
Specific comments addressed in turn below

TITLE AND ABSTRACT: The nomenclature for the Registry that was studied is slightly confusing, at least to this non-European reviewer. In Line 15, it is listed as the "UK National Joint Registry," yet from the title (as well as Lines 87-88) it would appear that Scotland is not included. Also, Line 15 mentions "English hospital inpatient episodes": does the registry also include data from hospitals in Wales, Northern Ireland, etc.?
We thank the reviewer for highlighting this point, and apologise for the confusion. The National Joint Registry is based on data from England, Wales, Northern Ireland and the Isle of Man. Therefore the title and the text in the methods is correct, but we have now corrected the abstract (line 15) to reflect this, given data from Scotland is not included in the NJR. Linkage to determine outcomes following joint replacement is only permitted with hospital inpatient episodes that occur in England via the Hospital Episode Statistics data, as linkage to the NJR is currently not available for the small proportion of joint replacements recorded in the NJR which are performed in Wales, Northern Ireland and the Isle of Man.

INTRODUCTION:
Lines 45-53: The wording here, regarding the impetus for using joint replacement surgery as the impetus for "enhanced recovery" protocols, seems a bit awkward. Perhaps replace "focus of enhanced recovery" with "main drivers of enhanced recovery protocols," and replace "active ingredients" with "components."
These changes have now been made as suggested (line 51 and line 57).

METHODS:
Lines 115-6: It is implied that the "regional anesthesia" all received a spinal, possibly with the addition of a peripheral nerve block. Did any of the general anesthesia patients receive nerve blocks as well? Is it possible to tease out whether or not adding a peripheral block provided any significant additional benefits to the patients in either group?
Yes some of the general anaesthesia patients did receive a nerve block and we have adjusted the wording in the methods accordingly (line 122).

We have conducted a sensitivity analysis re-running the analyses for all outcomes for: a) spinal only vs spinal + nerve block in just the spinal cohort, and then general only vs general + nerve block in just the general anaesthesia cohort. We have added this to the statistical analysis section (lines 166-8) and also included the results of this analysis (lines 271-80, and Appendix 3) and discussed them appropriately (lines 327-342).

RESULTS:
Lines 161-8: While it is reported that regional anesthesia decreased by approximately half a day (for both THR and TKR), the overall LOS of 4-5 days seems a bit long. Did the length

of stay decrease over time during the years that were studied? And has the relative degree of reduction in LOS from using regional anesthesia changed over time?
This is a European based healthcare system, and given how these are designed (relative to USA systems) the length of stay is generally longer in European based studies. Furthermore we are presenting a large nationwide sample which is thus representative of practice across the nation over a 10-year period. Mean length of stay decreased from 6.1 days in 2008 to 3.5 days in 2017 for TKR and for THR from 6.3 days to 3.4 days. The decrease was consistent across both general and spinal groups, with LOS always lower for the regional group across all years of the study. We have now added this information to the results section (lines 188-192).

Lines 182-9: It is noted that regional anesthesia was associated with a decrease in overall complications, as well as a number of specific complications. However, did regional anesthesia result in a change in the relative distribution of specific complications (or, at least, a difference in which complications were most common)? Such a difference could also have implications for enhanced recovery protocols.
Table 2 shows the relative distribution of the specific complications in each anaesthetic group for hips, and also for knees.

In hips, the 5 commonest complications (in order) with regional anaesthesia were: anaemia, surgical site infection, respiratory tract infection, VTE, and urinary tract infection.
In hips, the 5 commonest complications (in order) with general anaesthesia were: anaemia, surgical site infection, VTE, respiratory tract infection, and urinary tract infection.

In knees, the 5 commonest complications (in order) with regional anaesthesia were: surgical site infection, anaemia, VTE, respiratory tract infection, and urinary tract infection.
In knees, the 5 commonest complications (in order) with general anaesthesia were: surgical site infection, anaemia, VTE, respiratory tract infection, and urinary tract infection.

Therefore, the relative distribution of the specific complications between regional and general anaesthetic groups was similar following both THR and TKR (Table 2). We have added such a statement to the Results to highlight this (lines 220-1).

Finally, while the use of the word "secular" in Lines 212 and 261 is technically correct (in the "economic" sense), it may be confusing to some readers who associate the term with its "non-religious" definition. Perhaps use "steady" or "persistent" instead.
These changes have now been made as suggested (lines 243, 245, and 344).

Reviewer #3: The authors have submitted a nice paper. A few questions/concerns:

1. I recommend eliminating the comment about the “world’s largest joint registry” (line 12). The AJRR now contains more patient records (over 1.5 million) thus making it the largest national registry in the world.
As stated in the methods of the initial paper the NJR “..contains over 2 million primary THR and TKR procedures..”. This can be confirmed on their website and in the latest

16th annual report on page 36, Figure 3.1, which confirms there are 2,293,452 primary THRs and TKRs combined which are recorded within the registry (available at: https://reports.njrcentre.org.uk/Portals/0/PDFdownloads/NJR%2016th%20Annual%20Report%202019.pdf). Data from the Australian joint Registry suggests 1,492,892 such procedures have been performed (https://aoanjrr.sahmri.com/documents/10180/668596/Lay+Summary+of+Hip+and+Knee+Replacement/9a0ce4fc-c157-0c7f-8850-a43027d2e044). Therefore we have left in the statement about the NJR being the worlds largest joint registry as we believe it is still valid.

2. Why is "smoking" listed as a key word (lines 38-39)?
We apologise for this mistake and have removed this key word.

3. For the exposure section (lines 114-117) the authors report the overall breakdown of general versus regional (30/70). How does that breakdown for THA vs TKA? I would think the percentage of patients receiving general alone is higher for THA compared to TKA. Please include this breakdown.
This breakdown was included in the first row of Table 1. For THA the split is 30.2% general vs. 69.8% regional. For TKA the split is 30.1% general vs. 69.9% regional. Therefore the split between anaesthetic types is almost identical between THA and TKA. For clarity we have added a sentence in the Methods to highlight the split by joint type (lines 122-4).

4. Please clarify the categories. Would a patient with general anesthesia and a nerve block fall into the "general" cohort? Line 114-117 suggests that the two categories are really spinal versus general anesthesia and the presence of nerve block does not matter (i.e. the only requirement to be in the regional category is presence of spinal). If I am correct, than isn't the category "regional" misleading as many patients who received a nerve block (which is a regional anesthesia technique) would end up in the general category? Please clarify.
We have now clarified the definition of the exposure group in the Methods in response to this and a previous reviewer comment (lines 121-2). The further analyses performed (see response to comment 5 below) confirmed that very few patients were in the general anaesthetic + nerve block group (4.5% for THR and 7.5% for TKR). Furthermore, although nerve block as a regional technique, they still had a general anaesthetic which is the main type of anaesthesia they received so we feel they cannot be classed as completely having "regional" anaesthesia. Therefore we consider it is still appropriate to keep the terminology of the exposure group as general vs. regional anaesthesia, and in addition our subanalysis below and in the revised manuscript highlights the effect of addition of a nerve block to both general and spinal alone, which helps clarify this issue.

5. Do the authors have the numbers available to compare multiple groups (spinal alone, spinal + nerve block, general alone, general + nerve block)? Breaking this into two categories seems to be an over simplification.
We have now performed this additional work as a sensitivity analysis in response to this and a previous reviewer comment (line 122 and 166-8 in the Methods, lines 271-80 in the Results, lines 327-342 in the Discussion, and Appendix 3). Please see also our specific response to reviewer 2's comment above.

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 anesthesia 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 10th 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.

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

Using a nationwide cohort from the world's largest joint replacement registry helps increase the external validity and generalisibility of our findings. However this study has recognised limitations. Using observational data means causality cannot be inferred. Registry data does not include information regarding why the anaesthetic method was selected (regional versus general), the specific anaesthetic administered (technique, drugs, dose etc), the specific perioperative protocols used (including enhanced recovery), and the discharge destination. Although we have adjusted our data for numerous patient and surgical factors, it is recognised these factors, and other important variables not recorded in routinely collected datasets (e.g. the need for invasive intraoperative monitoring), may influence our findings with respect to the differences in complications and length of stay between the two anaesthetic groups. In addition, although we have adjusted for numerous important patient and surgical factors, using observational data means we cannot definitively exclude that changes in surgical practice over time were responsible for the better findings in the regional anesthesia group, rather than the effect of the anaesthesia technique itself. However we did perform sensitivity analyses assessing for interactions between year of surgery and type of anaesthesia on outcomes, which supported our main findings and suggested that some of the findings in favour of using regional anaesthesia were only significant in more recent years (2013-17) so were a reflection of modern clinical practice. Missing BMI data is a limitation of NJR based studies.[22, 37, 38] We observed that the BMI distribution was balanced between the anaesthesia groups, and analysis of the subgroup of patients with BMI data available did not alter the findings from the regression models (Appendix 2). Although PROMs were available at 6 months, it is recognised that we had no early patient reported outcomes available regarding pain and nausea like those collected in trials.[8, 10] Finally, we 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.

Figure 1

Click here to access/download;Figures (Number each one);Figure 1 Selection criteria.jpg

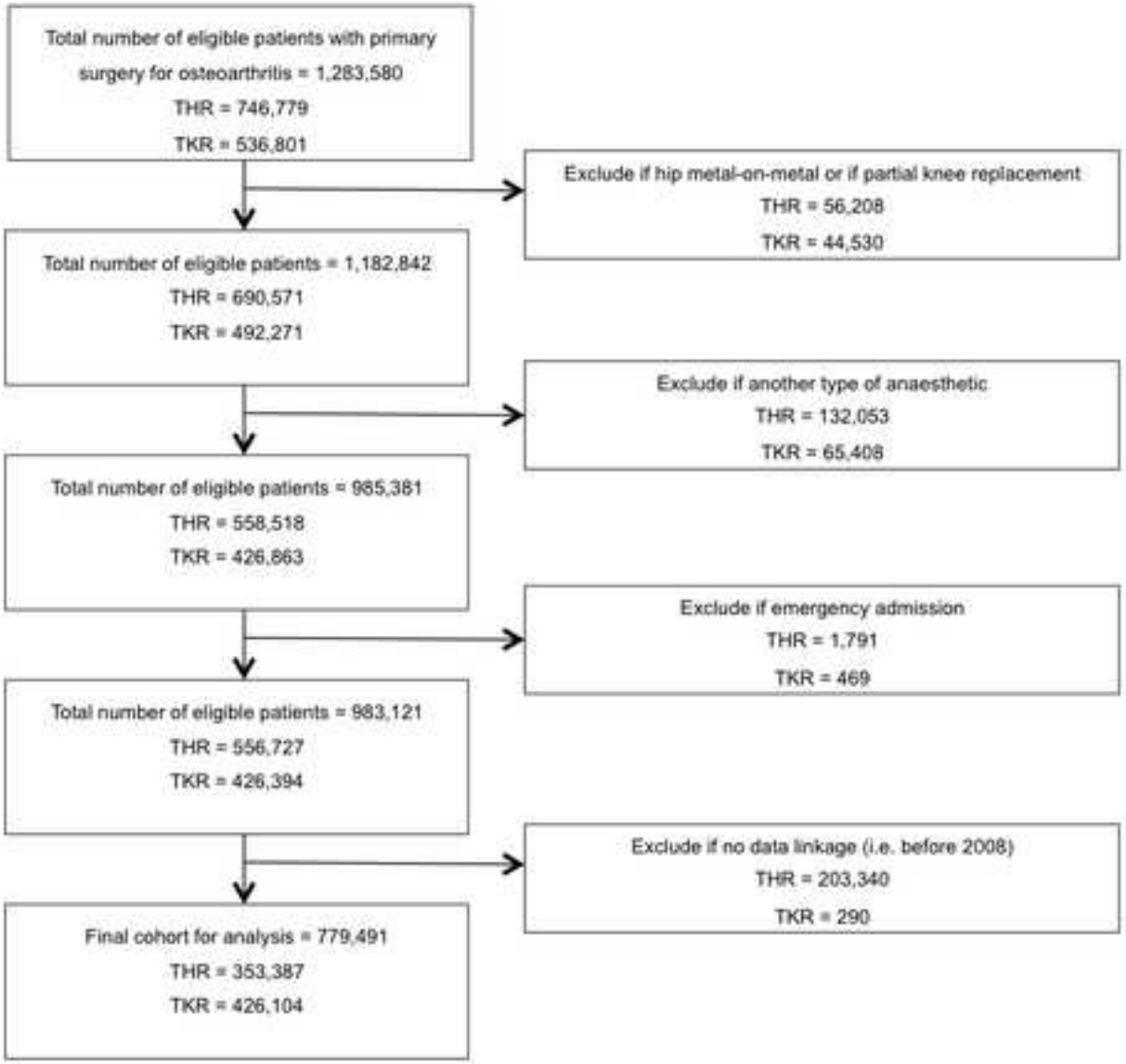

Figure 2

Click here to access/download;Figures (Number each one);Figure 2 Temporal trends.eps

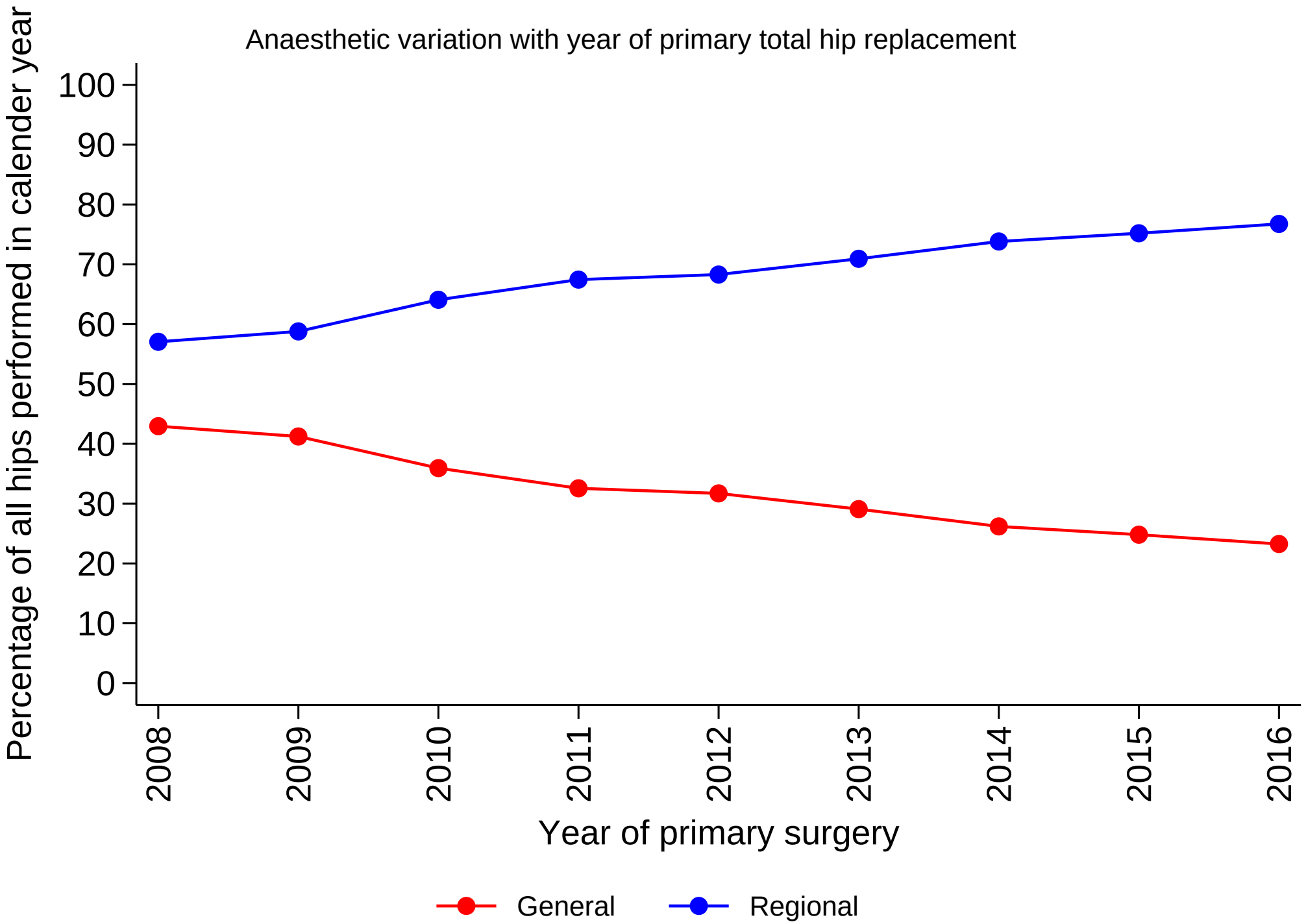

Table 1 Patient and surgical factors in primary total hip and knee replacement

	All primary THRs (n=353,387) (100%)	**General anaesthetic (n=106,782) (30.2%)**	**Regional anaesthetic (n=246,605) (69.8%)**		**All primary TKRs (n=426,104) (100%)**	**General anaesthetic (n=128,089) (30.1%)**	**Regional anaesthetic (n=298,015) (69.9%)**
Covariate							
Sex							
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)
Age at primary (yr)							
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)
BMI (kg/m^2) *							
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)
Deprivation status							
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)
Primary year							
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)
Unit							
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)
Primary ASA grade							
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)
Charlson group							
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)
VTE – chemical							
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)
VTE – mechanical							
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)
Surgeon grade							

Consultant *vs. other*	284,891 (80.6)	86,549 (81.1)	198,342 (80.4)		333,305 (78.2)	100,731 (78.6)	232,574 (78.0)
THR surgical approach Posterior *vs. other*	216,787 (61.4)	65,491 (61.3)	151,296 (61.4)		NA	NA	NA
TKR surgical approach Medial parapatellar *vs. other*	NA	NA	NA		399,552 (93.8)	119,678 (93.4)	279,874 (93.9)
Cup fixation							
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)				
Stem fixation							
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)				
Femoral head size (mm)							
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)				
Bearing surface							
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)				
TKR fixation							
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)
Minimally invasive surgery	12,186 (3.5)	3,601 (3.4)	8,585 (3.5)		9,334 (2.2)	3,436 (2.7)	5,898 (2.0)
Bone graft (femoral)	2,226 (0.63)	591 (0.55)	1,635 (0.66)		4,021 (0.94)	1,307 (1.0)	2,714 (0.91)
Bone graft (acetabular)	12,521 (3.5)	4,141 (3.9)	8,380 (3.4)		NA	NA	NA
Bone graft (tibia)	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

	All primary THRs (n=353,387) (100%)	**General anaesthetic (n=106,782) (30.2%)**	**Regional anaesthetic (n=246,605) (69.8%)**		**All primary TKRs (n=426,104) (100%)**	**General anaesthetic (n=128,089) (30.1%)**	**Regional anaesthetic (n=298,015) (69.9%)**
Length of stay in days 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)
Readmissions within 90 days	41,441 (11.7)	12,953 (12.1)	28,488 (11.6)		58,477 (13.7)	18,361 (14.3)	40,116 (13.5)
Any complication within 90 days	14,547 (4.1)	4,697 (4.4)	9,850 (4.0)		17,364 (4.1)	5,440 (4.3)	11,924 (4.0)
Revision at 90 days	1,355 (0.38)	438 (0.41)	917 (0.37)		387 (0.09)	111 (0.09)	276 (0.09)
Reoperations within 90 days (not including revision)	706 (0.20)	231 (0.22)	475 (0.19)		803 (0.19)	278 (0.22)	525 (0.18)
Mortality at 90 days	1,038 (0.29)	312 (0.29)	726 (0.29)		679 (0.16)	190 (0.15)	489 (0.16)
Specific complications within 90 days							
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)
EQ5D at 6 months * 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))
OHS or OKS at 6 months * 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)**
Length of stay	Coefficient = -0.49 (-0.51 to -0.47) **p<0.001** Based on 342,246 hips	Coefficient = -0.47 (-0.49 to -0.45) **p<0.001** Based on 422,179 knees
Readmissions within 90 days	OR = 0.93 (0.90-0.96) **p<0.001**	OR = 0.91 (0.89-0.93) **p<0.001**
Any complication within 90 days	OR = 0.88 (0.85-0.91) **p<0.001**	OR = 0.90 (0.87-0.93) **p<0.001**
Revision at 90 days	OR = 1.01 (0.88-1.17) p=0.849	OR = 0.99 (0.79-1.23) p=0.899
Reoperations within 90 days	OR = 0.86 (0.73-1.01) p=0.062	OR = 0.79 (0.68-0.92) **p=0.002**
Mortality at 90 days	OR = 0.91 (0.77-1.08) p=0.300	OR = 1.01 (0.86-1.20) p=0.865
Specific complications within 90 days		
VTE (DVT &/or PE)	OR = 0.85 (0.77-0.93) **p=0.001**	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)

	p<0.001	p=0.236
Urinary tract infection	OR = 0.85 (0.77-0.94) **p=0.003**	OR = 0.87 (0.79-0.96) **p=0.007**
Surgical site infection	OR = 0.87 (0.80-0.95) **p=0.001**	OR = 0.84 (0.78-0.89) **p<0.001**
Acute renal failure	OR = 0.78 (0.68-0.89) **p<0.001**	OR = 0.93 (0.82-1.04) p=0.208
Blood transfusion	OR = 0.62 (0.48-0.80) **p<0.001**	OR = 0.96 (0.70-1.31) p=0.780
Anaemia	OR = 0.85 (0.79-0.92) **p<0.001**	OR = 0.89 (0.83-0.95) **p=0.001**
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
EQ5D at 6 months	Coefficient = 0.021 (0.018 to 0.023) **p<0.001** Based on 170,173 hips	Coefficient = 0.019 (0.017 to 0.022) **p<0.001** Based on 208,894 knees
OHS or OKS at 6 months	Coefficient = 0.79 (0.70 to 0.88)	Coefficient = 0.80 (0.71 to 0.88)

	p<0.001 Based on 176,776 hips	**p<0.001** Based on 216,474 knees

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 coagluation 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 pneumonia
J14 Pneumonia due to Haemophilus influenza
J15.X Bacterial pneumonia, not elsewhere classified: bronchopneumonia due to bacteria other than S. pneumoniae and H. influenza
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

Outcome of interest	**THR univariable analysis (n=353,387)**	**THR adjustment for all variables* including BMI (n=249,848)**	**TKR univariable analysis (n=426,104)**	**TKR adjustment for all variables* including BMI (n=304,538)**
Length of stay	Coefficient = -0.56 (-0.59 to -0.54) **p<0.001** Based on 353,365 hips	Coefficient = -0.39 (-0.42 to -0.36) **p<0.001** Based on 249,832 hips	Coefficient = -0.57 (-0.59 to -0.55) **p<0.001** Based on 426,078 knees	Coefficient = -0.37 (-0.40 to -0.34) **p<0.001** Based on 304,520 knees
Readmissions within 90 days	OR = 0.95 (0.93-0.97) **p<0.001**	OR = 0.93 (0.90-0.96) **p<0.001**	OR = 0.93 (0.91-0.95) **p<0.001**	OR = 0.91 (0.89-0.93) **p<0.001**
Any complication within 90 days	OR = 0.90 (0.87-0.94) **p<0.001**	OR = 0.88 (0.84-0.92) **p<0.001**	OR = 0.94 (0.91-0.97) **p<0.001**	OR = 0.90 (0.87-0.94) **p<0.001**
Revision at 90 days	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
Reoperations within 90 days	OR = 0.89 (0.76-1.04) p=0.147	OR = 0.82 (0.68-0.99) **p=0.042**	OR = 0.81 (0.70-0.94) **p=0.005**	OR = 0.73 (0.61-0.87) **p<0.001**
Mortality at 90 days	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
Specific complications within 90 days				
VTE (DVT &/or PE)	OR = 0.80 (0.73-0.87) **p<0.001**	OR = 0.84 (0.75-0.94) **p=0.002**	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) **p=0.002**	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) **p<0.001**	OR = 0.78 (0.66-0.91) **p=0.002**	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) **p<0.001**	OR = 0.82 (0.74-0.90) **p<0.001**	OR = 0.82 (0.77-0.87) **p<0.001**	OR = 0.83 (0.77-0.90) **p<0.001**
Acute renal failure	OR = 0.95 (0.84-1.09) p=0.470	OR = 0.85 (0.72-0.99) **p=0.045**	OR = 1.17 (1.04-1.31) **p=0.011**	OR = 0.95 (0.82-1.10) p=0.495
Blood transfusion	OR = 0.62 (0.48-0.80) **p<0.001**	OR = 0.57 (0.42-0.77) **p<0.001**	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) **p=0.008**	OR = 0.84 (0.77-0.92) **p<0.001**	OR = 0.96 (0.90-1.03) p=0.297	OR = 0.90 (0.82-0.98) **p=0.017**
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) **p<0.001**	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) **p=0.028**
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
EQ5D at 6 months	Coefficient = 0.024 (0.021 to 0.026) **p<0.001** Based on 175,224 hips	Coefficient = 0.023 (0.020 to 0.026) **p<0.001** Based on 127,258 hips	Coefficient = 0.025 (0.023 to 0.027) **p<0.001** Based on 210,816 knees	Coefficient = 0.018 (0.016 to 0.021) **p<0.001** Based on 154,704 knees
OHS or OKS at 6 months	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)

	p<0.001 Based on 182,031 hips	**p<0.001** Based on 132,167 hips	**p<0.001** Based on 218,558 knees	**p<0.001** Based on 160,333 knees

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

Outcome of interest	**THR: GA alone (reference group) vs. GA with nerve block (n=102,206)**	**THR: SA alone (reference group) vs. SA with nerve block (n=246,605)**	**TKR: GA alone (reference group) vs. GA with nerve block (n=124,523)**	**TKR: SA alone (reference group) vs. SA with nerve block (n=298,015)**
Length of stay	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) **p<0.001** Based on 296,002 knees
Readmissions within 90 days	OR = 0.92 (0.87-0.97) **p=0.004**	OR = 0.97 (0.91-1.03) p=0.269	OR = 0.95 (0.92-0.99) **p=0.013**	OR = 0.97 (0.94-1.01) p=0.088
Any complication within 90 days	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
Revision at 90 days	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
Reoperations within 90 days	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
Mortality at 90	OR = 0.90	OR = 0.70	OR = 0.90	OR = 0.88

days	(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
Specific complications within 90 days				
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) **p<0.001**	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
EQ5D at 6 months	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) **p=0.004** Based on 58,837 knees	Coefficient = -0.005 (-0.01 to -0.001) **p=0.022** Based on 148,595 knees

OHS or OKS at 6 months	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

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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