Impact of comorbidities on the safety and effectiveness of hip and knee replacement surgery: an observational study

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Abstract

Background: Access to joint replacement is being restricted for some patients with comorbidities, but there is little consensus about the impact of comorbidities on outcomes. We examined associations between comorbidities and both safety risks and effectiveness after hip and knee replacement.

Methods: 640 832 patients were included who had hip or knee replacements in England between 2009 and 2016. Eleven comorbidities were identified according to ICD-10 codes in administrative records. Safety risks were measured by assessing length of hospital stay (LOS) and 30-day emergency readmissions and mortality. Effectiveness was measured as change in Oxford Hip or Knee Scores (OHS/OKS) on scale from 0 (worst) to 48 (best) and health-related quality of life (HRQoL) measured as changes in EQ-5D from immediately before to 6 months after surgery. Regression was used to estimate adjusted mean differences in LOS and improvement of OHS/OKS and EQ-5D scores and adjusted absolute risk differences in admission rates and mortality.

Findings: Patients with comorbidities had longer LOS and higher readmission rates and mortality than patients without comorbidities. In hip-replacement patients with heart disease for example, LOS was 1.2 days longer and readmission rate was 1.5% and mortality 0.2% higher. Similar patterns were observed for knee-replacement patients. Patients without comorbidities reported large improvements in function (mean improvement in OHS 21.3 and in OKS 15.9). Patients with comorbidities reported only slightly smaller improvements. In patients with heart disease for example, differences in improvement were -0.4 for OHS and -0.6 for OKS. There was no difference in HRQoL.

Interpretation: Comorbidities are associated with small increases in safety risks but they have little impact on improvements in pain and function. For patients with comorbidities, these small increases in safety risks need to be balanced against the consistently large capacity to benefit from joint replacement.

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Research in context

Evidence before this study

Outcomes of elective hip and knee replacement surgery have been reported according to a variety of presence of comorbidities but no consensus has been reached on the impact of comorbidities on both short-term outcomes relating to the safety risks and long-term outcomes relating to effectiveness. In our previous systematic review we identified 70 studies through a search of MEDLINE, Embase and CINAHL Plus (from start of records to 31 May 2017) that reported data on the impact of 11 comorbidities on 10 outcomes (including surgical complications, readmissions, mortality, function, health-related quality of life, pain and revision, surgery). We found that comorbidities had more of an impact on safety outcomes such as hospital readmissions and mortality but less so on outcomes related to effectiveness of surgery. Despite this, the impact of comorbidities on surgical complications and in the long-term on function, quality of life and pain was variable and unclear. Only five papers looked at quality of life outcomes and the majority of studies looking at patient-reported outcomes were small single-centre studies (<2000 patients).

Added value of this study

Our results, to our knowledge, provide the first assessment of both the risks and effectiveness of hip and knee replacement surgery for patients with a variety of comorbidities in the same representative population. This includes not only outcomes that measure safety risks but also outcomes reported by patients that measure the effectiveness of hip and knee replacement surgery in improving hip and knee function and quality of life.

Implications of all the available evidence

The findings about the risks and effectiveness of hip and knee replacement surgery for patients with comorbidities will be of use to both clinicians and patients who together need to make the decision about undergoing surgery. Additionally, our results provide evidence to those commissioning healthcare that any restrictions based on the presence of comorbidities is difficult to justify.

Introduction

Joint replacement surgery has become one of the most successful and cost-effective surgical interventions[1] in medicine offering substantial improvements in pain and function and in turn quality of life in patients with osteoarthritis or inflammatory arthritis[2]. Despite this, in England, as well as in other countries like Canada[3] and New Zealand[4], access to hip and knee replacement surgery has been restricted by commissioners of healthcare due to financial constraints. Eligibility criteria introduced to restrict access have included that a patient's body mass index (BMI) is lower than 30kg/m^2 [5] and that any comorbidities are optimised[6] despite these criteria not being supported by any economic evidence [7] or UK national clinical guidelines[8]. There is also no evidence that limiting access would reduce costs in the long-term as denying patients functional improvement and pain relief could lead to increased costs of treating patients with advanced osteoarthritis of the hip and knee. Advanced hip and knee osteoarthritis has been associated with increased health service use, increased opioid use, decreased mobility and deteriorating mental health[9, 10].

Clinicians and patients need to balance the risks against the benefits when deciding to undergo a hip or knee replacement surgery. An increasing number of patients receiving hip and knee replacement surgery have at least one comorbidity[11]. Currently, the criteria to assess the safety risks and the potential improvements in pain and function for patients with comorbidity who are candidates for hip and knee replacement surgery are based on limited evidence[1]. It is therefore important to understand the impact of comorbidities on both the risks and effectiveness of joint replacement surgery and in order to evaluate whether restrictions on access surgery are justified.

Our previous work, a systematic review and meta-analysis of 70 studies published up until May 2017, found that individual comorbidities had an impact on short-term outcomes related to safety of joint replacement surgery[12]. However, the results presented an inconsistent picture with a variable impact of comorbidities on surgical complications. In addition, the 15 studies (five reporting health-related quality of life) that examined patient-reported outcomes related to effectiveness were all relatively small single-centre studies (<2000 patients). The availability of patient-reported outcome measures (PROMs) data, collected since 2009 for all patients undergoing an elective hip or knee replacement in the English National Health Service (NHS) linked to administrative hospital data provides a unique opportunity to examine the impact of comorbidities on both the short-term outcomes related to safety risks and long-term outcomes patient-reported related to effectiveness.

The aim of our study was to address these gaps in evidence on outcomes of joint replacement surgery for patients with comorbidities. We assessed the impact of comorbidities on the safety risks (length of hospital stay, 30-day readmission rate and mortality) and effectiveness (change in OHS/OKS and EQ-5D from immediately before to 6 months after surgery) of hip and knee replacement surgery.

Methods

Data sources

We used data from the National PROMs Programme for patients undergoing elective hip or knee replacement surgery between April 2009 and November 2016 in the English NHS. All patients participating in this PROMS programme were given a questionnaire to complete before surgery, either on admission or at preoperative assessment, and then sent a follow-up questionnaire 6 months after surgery asking the same questions on the severity of their joint problems and health-related quality of life.

PROMs data were linked at a patient level to data about their hospital admissions extracted from the Hospital Episode Statistics dataset (HES), an administrative database of hospital admissions to NHS hospitals and NHS-funded patients treated in independent sector which also includes date of death according to the Office for National Statistics database for all deaths registered in England[13]. To ensure we only had one record per patient we only included the first primary hip or knee surgery and excluded revision surgeries. In the study of benefits, we also excluded patients who had not returned a postoperative questionnaire with complete information on the main outcome and patients who had a second primary operation before they completed their postoperative questionnaire (Figure 1).

Outcomes

Safety was measured by exploring length of stay (LOS) in hospital and the risk of an emergency readmission or death within 30 days following hip or knee replacement surgery. LOS was measured in days from the date of the operation to the date of hospital discharge according to HES or, if available, the date the patient was ready for discharge. Emergency readmissions and deaths were identified by checking linked HES records for each patient.

Effectiveness was measured using the change (improvement) in the Oxford Hip (OHS), Oxford Knee (OKS) and EQ-5D scores reported by patients immediately before surgery and six months thereafter. The OHS and OKS produce disease-specific scores that are derived from patient responses to 12 questions about pain and limits on physical functioning and everyday activities. Responses to each question are measured on a 5-point scale, and values associated with each response are added up to produce an overall score with the range 0 (worst) to 48 (best). Both scales have been shown to be internally consistent, reliable and to correlate with surgeon-assessed measures of symptoms and disability in patients undergoing hip or knee replacement[14]. The EQ-5D score was used to measure HRQoL and is derived from the EQ-5D profiles. The score ranges from -0.594 (worst) to 1 (best) with 0 reflecting ‘death’. Change scores (differences between the preoperative and postoperative scores)

were chosen as the outcome measure instead of postoperative scores adjusted for preoperative scores, because in nonrandomised studies of pre-existing group (e.g. patients with and without comorbidities) change scores have been shown to be less biased than adjusted postoperative scores [15]. This approach – the analysis of change scores – assumes that without treatment the groups would have had equal change over time, which is a plausible assumption for patients with joint problems, especially with a six months period for patients with and without comorbidities.

Comorbidities

Eleven comorbidities were identified from the list of 12 self-reported comorbidities from the pre-operative PROMs questionnaires included in the questionnaires used by the National PROMs Programme[16]. Arthritis was excluded because it was the reason for surgery rather than a comorbidity. The 11 comorbidities comprised: heart disease; high blood pressure; problems caused by a stroke; leg pain when walking due to poor circulation; lung disease; diabetes; kidney disease; nervous system disease; liver disease; cancer and depression (Supplementary Information). Each comorbidity was mapped to its relevant, International Classification of Diseases, Tenth Revision, (ICD-10) diagnosis codes in hospital records as described in a previous study[17]. The presence of a comorbidity was indicated if a mapped code appeared in any diagnosis field in any hospital admission up to one year prior to a patient's surgery.

Statistical analysis

We conducted multivariable regression exploring the association between the 11 comorbidities and the risk and effectiveness outcomes comparing those patients with and without each comorbidity. We used an ordinary linear regression model to estimate adjusted mean differences in LOS in days between for patients with each of the 11 comorbidities compared to patients without comorbidities with adjustment age, sex, ethnicity and socioeconomic status (Index of Multiple Deprivation[18]), other comorbidities and hospital variation fitted as a random effect. We used the same statistical approach to estimate adjusted mean differences in the change scores for OHS/OKS and EQ-5D scores. We used generalised linear regression model for the binomial family with the identity link function to estimate adjusted absolute risk differences in 30-day emergency readmission rates and mortality. We also investigated the association between number of comorbidities and all outcomes to explore the effect of having multiple comorbidities.

Multiple imputation using chained equations [19] was used to deal with missing values for ethnicity, age, sex and socioeconomic status. Analyses were run on each of the ten imputed data sets and estimated parameters were combined using Rubin's rules. Descriptive results are presented as means

and percentages. Regression results are presented as adjusted differences with 95% confidence intervals. All statistical analyses were carried out using STATA v.15.

Role of the funding source

The funder of the study had no role in the study design, data collection, data analysis, data interpretation or writing of the final report. The corresponding author (BP) and AH had full access to all the data in the study and the final responsibility for the decision to submit for publication.

Results

Study population

We included 640 832 patients who had a primary hip or knee replacement (312 079 hip operations and 328 753 knee operations) between April 2009 and March 2016 in the analyses for the study of the safety risks of hip and knee replacement. Due to missing postoperative questionnaire responses, only 479 632 patients (234 432 hip operations and 245 200 knee operations) were included for the study of effectiveness of hip and knee replacement (Figure 1). Patients who had a hip replacement were on average 68 years of age and 58·2% were women. Of the patients with available information about their ethnicity, 98·3% of hip-replacement patients and 94·5% knee-replacement patients were reported to have a white ethnic background (Table 1). 63·6% of patients who had a hip replacement and 71·3% of those who had a knee replacement had at least one comorbidity. High blood pressure was by far the most prevalent comorbidity (48·4% for patients who had a hip replacement and 57·1% for those who had a knee replacement; Table 2), followed by heart disease (17·1% and 18·5%), lung disease (13·9% and 15·6%), and diabetes (9·5% and 13·6%, respectively).

Safety risks

Safety risk outcomes after hip and knee replacement surgery were associated with all 11 comorbidities. Compared to patients who had a hip replacement without comorbidities, patients who had heart disease for example had an increases in LOS (from 3·7 to 6·0 days; Table 2), readmission rates (from 1·6% to 4·2%), and mortality (from 0·01% to 0·21%). A similar pattern of results was observed for patients who had a knee replacement.

The adjusted differences for all three safety risk outcomes are presented in Figure 2. Compared to patients without comorbidities, patients with comorbidities were more likely to have a longer LOS but the difference varied from 0·14 days (0·08, 0·20) for patients with high blood pressure to 2·1 days

(1·8, 2·4) for stroke patients. Patients with stroke and diseases of the nervous system had the longest stay in hospital compared to patients without comorbidities.

Across both hip and knee patients, the presence of comorbidity was associated with an increased risk in emergency readmission within 30 days, ranging from 0·30% (0·19%, 0·61%) increased risk for patients with hypertension to 2·58% (1·78%, 3·38%) for stroke patients compared to patients without comorbidities. In both hip and knee patients, the highest risk of an emergency readmission within 30 days was for patients with stroke, liver disease; diseases of the nervous system and depression.

There were 347 deaths in the 30 days after elective hip or knee replacement surgery. Across both hip and knee patients, compared to patients without comorbidities, the presence of comorbidity was associated with an increased risk in mortality within 30 days, ranging from -0·01% (-0·05%, 0·02%) increased risk for patients with depression to 0·52% (0·27%, 0·77%) for stroke patients. The highest risk of mortality within 30 days was for patients with stroke, liver disease; diseases of the nervous system and kidney disease.

Effectiveness

On average, hip patients reported a 20-point improvement in the OHS and knee patients reported a 15-point improvement in the OKS after their hip or knee replacement surgery. Similarly, hip patients reported a 0·43-point and knee patients a 0·31-point improvement in the EQ-5D score (Table 2).

Patients with comorbidities tended to have slightly less improvement in pain and mobility issues in their hip or knee than patients without comorbidities. In hip patients, all comorbidities were associated with a slightly smaller improvement in OHS score except for patients with high blood pressure; kidney disease and cancer (Figure 3). For hip replacement, the adjusted differences in the OHS score ranged from 0·40 (95% CI 0·21, 0·60) for kidney disease to -0·74 (-1·17, -0·31) for stroke. For knee replacement surgery, all patients with comorbidities except high blood pressure, kidney disease and cancer were more likely to report a smaller improvement in OKS score. The adjusted differences in the OKS score ranged from 0·32 (0·14, 0·51) for kidney disease to -1·15 (-1·72, -0·58) for liver disease.

In contrast, improvement in HRQoL scores did not vary significantly between patients with and without comorbidities. For hip replacement surgery, only patients with high blood pressure (0·02, 95% CI 0·01, 0·02) and kidney disease (0·02, 0·01, 0·02) had more improvement in HRQoL than patients without comorbidities but the difference was very small. Similarly, for knee replacement surgery, only patients with high blood pressure (0·01, 0·00, 0·01), kidney disease (0·01, 0·00, 0·01) and disease of the nervous system (0·01, 0·00, 0·01) had more improvement in HRQoL than patients without comorbidities but again the difference was marginal.

Multiple comorbidities

The risk of a longer LOS in hospital and emergency readmissions within 30 days increased and the reported improvement in severity of joint problems decreased with increasing number of comorbidities for both hip and knee replacements (Table 3). There was no difference in HRQoL with increasing number of comorbidities. Hip patients with four or more comorbidities stayed three days longer in hospital (3·40, 95% CI 3·29, 3·51) and had a 4·5% (3·97, 5·03) higher risk of an emergency readmission within 30 days, a 0·49% (0·43, 0·54) increased risk of death in 30 days, had a smaller improvement in the OHS (adjusted difference -0·91, 95% CI -1·19, -0·64) and a slightly larger improvement in HRQoL (0·01, 0·00, 0·02) compared to patients with no comorbidities. A similar pattern was observed for patients who had a knee replacement.

Discussion

Currently due to financial constraints, the presence of comorbidity and a high BMI is being used to restrict the access to hip and knee replacement surgery. This is despite this restrictive policy being supported by limited evidence and not being in alignment with national clinical guidelines. Our results demonstrate that while the presence of a comorbidity in patients undergoing hip or knee replacement was associated with a slightly higher risk of safety risks - a longer stay in hospital, an emergency readmission and mortality within 30 days, substantial improvements in severity of joint problems and HRQoL after hip or knee replacement surgery were reported regardless of comorbidity. When examining differences between patients with and without comorbidities in regards to effectiveness of joint replacement surgery, patients with comorbidities reported slightly smaller improvements in joint problems but a similar HRQoL after hip or knee replacement surgery than patients without comorbidities. These differences in improvement in severity of joint problems and increased risk in safety were more pronounced in patients with multiple comorbidities.

While there is a small impact of comorbidities on improvement in severity of joint problems six months after the joint replacement, the differences between patients with and without comorbidities need to be interpreted within the context of how they compare against the '*Minimal Important Difference (MID)*. The MID is the difference in health gain between two independent groups that a patient perceives as beneficial. The differences presented in this study are much smaller than the suggested MID values of five points for the OHS and OKS [20], and 0·08 for the EQ-5D [21]. Even in patients with multiple comorbidities, the differences were less than 1·5 points, much smaller than the MID. It is important to note however, that the number of patients with multiple comorbidities is small as the current practice of selecting patients for joint replacement would make patients with multiple

comorbidities ineligible for surgery[22]. As a result, the findings suggest patients with comorbidities benefit from hip and knee replacement surgery just as much as patients without comorbidities.

To our knowledge, this is the first study to focus on the impact of a range of different comorbidities and the number of comorbidities on multiple outcomes that reflect the safety risks and effectiveness of hip and knee replacement in a large national sample of patients undergoing hip and knee replacement surgery. In the case of safety risks, previous research has predominantly focused on determining the impact of comorbidity on surgical complications [23]. While commonly investigated, the validity and reliability of the coding of these surgical complications in administrative data has been called into question [24]. Furthermore, there is a lack of consensus on how to best measure surgical complications [25]. In this study, we have therefore not explored outcomes that are based on diagnosis or procedure codes and instead focused on process measures.

Our findings are consistent with other studies looking at short-term safety risks in patients with comorbidities undergoing total joint replacement surgery. From our previous systematic review the impact of comorbidities on readmissions within 90 days [26] and mortality within 90 days [27, 28] was highest for patients with liver disease, heart disease, stroke and diseases of the nervous system [12]. Prolonged hospital LOS can have a negative impact on health service use after elective surgery and our findings are consistent with previous studies that have implicated comorbidities in higher LOS [29]. Our findings also corroborate a recent large US study of 516 745 patients undergoing knee replacement that showed that increasing number of comorbidities were associated with longer LOS [29].

In contrast, the previous research on the impact of comorbidities on severity of joint problems and HRQoL after hip and knee replacement surgery has been inconclusive and relied on single-centre studies with small sample sizes [30]. Smaller studies with fewer than 500 patients predominantly found no significant differences [30] but studies with larger samples (>1000 patients) with longer follow-up (>two years) reported an impact of comorbidities on improvement in functional impairment [31]. Consistent with our findings, a large Canadian study investigating the effect of number of comorbidities on HRQoL also found that the effect of comorbidity increased with increasing number of comorbidities but the differences remained below the MID[32]. Our study of almost half a million patients from a nationwide representative sample of patients demonstrates that comorbidities have a marginal impact on the improvement in severity of joint problems and no impact on the improvement in HRQoL after joint problems compared to patients without comorbidities.

Clinicians and patients need to consider the risks and benefits of surgery so they can make an informed decision about undergoing surgery [33]. Orthopaedic surgeons have to operate on increasingly more complex patients [34] who often have more than one comorbidity [35]. This research shows that a decision to operate on patients with comorbidities may be a commitment to managing complications should they arise but the risk remains small compared to the consistently large benefit. Limiting

access to joint replacement surgery therefore, would be denying significant pain relief and functional improvement to patients as well as indirectly increasing costs of care associated with advanced hip or knee osteoarthritis. It is important to also consider the effects of increased use of analgesics such as opioids and deteriorating mental health in patients who are denied surgery. Patients with more comorbidities have been shown to have higher preoperative opioid use which is associated with higher readmissions and revision rates[10]. Similarly, depression has been found to be higher in patients with later-stage hip and knee osteoarthritis suggesting any deterioration in hip or knee function may lead to poorer mental health[9].

In the UK, our previous work on severity of functional status before hip and knee replacement surgery found that patients with comorbidities had more severe pain and poorer functional status just before surgery than patients without comorbidities[36]. When we looked at unpublished data to compare those commissioning regions with restrictive policies to access hip or knee replacement surgery against those that do not have restrictive policies we found little evidence that at the moment in practice patients are being denied surgery. Preoperative severity of hip and knee function just before surgery varied little between commissioning regions with and without restrictive policies. This suggests that patients with comorbidities are not waiting longer for surgery than patients without comorbidities. This may be explained however by the fact that not all the policies are mandatory and that decisions to refer or select patients are ultimately clinician led.

This study has several limitations. The first relates to potential selection bias. Patients undergoing hip and knee replacement surgery are more likely to be healthy than in the general population as patients considered too high risk such as patients with multiple comorbidities may not be selected for hip or knee replacement surgery[37]. Selection for surgery is likely to be based on risk factors that we have no data for or that we capture very poorly. Due to the clinical data being limited it was not possible to account for any selection criteria. Similarly, only patients that returned a postoperative questionnaire were included in the analysis of effectiveness and a previous study found that non-responders were more likely to be severe cases and have more comorbidities[38]. These selection biases may lead to an underestimation of the differences in outcomes between patients with and without comorbidities. The impact of this selection bias one would expect however would be more on isolated comorbidities rather than on patients with multiple comorbidities that are likely to represent a more severe health profile. Contrary to expectations, there was no significant diminishing effect on effectiveness with increasing number of comorbidities.

The second limitation relates to the availability of data on potential confounders. There was a lack of information on other risk factors such as BMI and smoking status. We did however have information about comorbidities that are associated with obesity such as diabetes, heart disease and high blood pressure. Furthermore, a previous study of 2180 patients, which compared patients with normal

weight against patients with a BMI>25kg/m^2, reported that functional outcomes after knee replacement surgery were not influenced by BMI [39].

Our findings suggest that there is a safety risk associated with patients with comorbidities undergoing hip and knee replacement surgery but this remains relatively small compared to the large improvements in functional outcomes and HRQoL. This large improvement persists even in patients with multiple comorbidities. This study therefore provides the evidence that any restriction of access to hip and knee replacement surgery based on the presence of comorbidity alone is unjustifiable.

Figure 1 - Flow chart

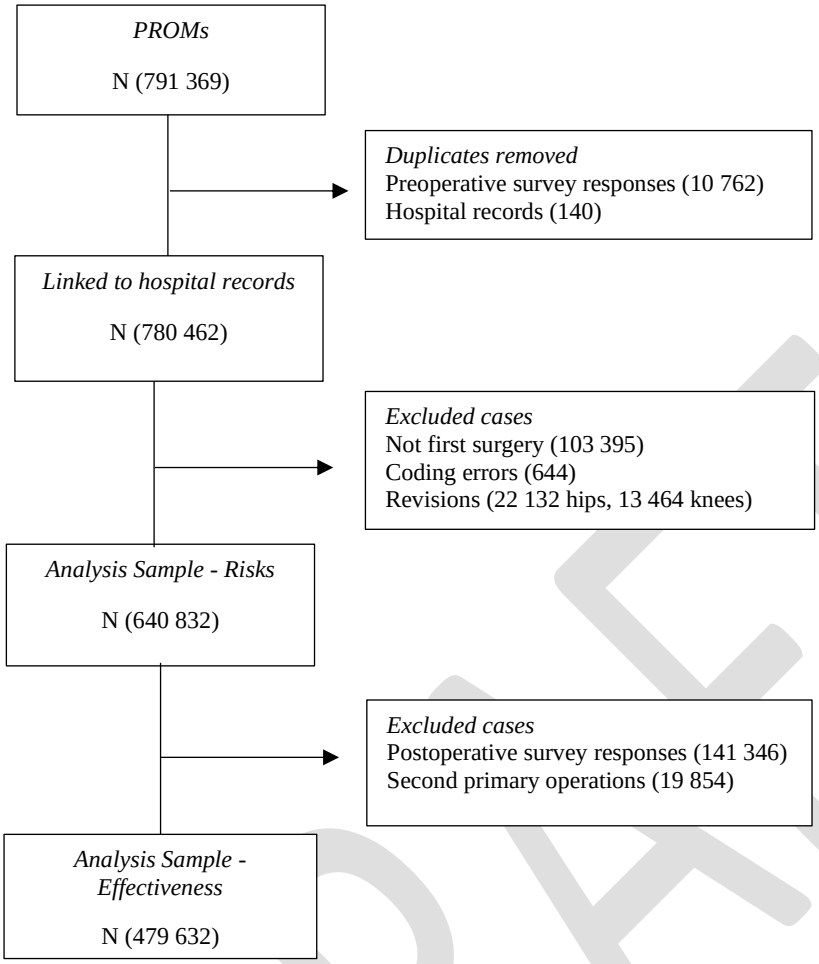

Table 1 - Study population characteristics

	Hip replacement	Knee replacement
Number of patients, n (%)	312 079 (48·7)	328 753 (51·3)
Age (mean, range)	68 (18-105)	69 (18-102)
Gender, n (%)		
Male	126 925 (40·7)	140 971 (43·0)
Female	184 982 (59·3)	187 525 (57·0)
Missing, not stated	172	257
Socioeconomic status by national quintile, n (%)		
1 (least deprived)	74 380 (23·4)	69 582 (21·2)
2	76 164 (24·4)	74 799 (22·8)
3	55 793 (17·9)	62 851 (19·1)
4	52 194 (16·7)	60 177 (18·3)
5 (most deprived)	50 408 (16·2)	58 327 (17·7)
Missing	3 140	3 017
Ethnicity, n (%)		
White or White British	271 959 (98·3)	279 159 (94·5)
Mixed background	546 (0·2)	836 (0·3)
Asian or Asian British	1239 (0·5)	10 445 (3·5)
Black or Black British	1703 (0·6)	3347 (1·1)
Chinese or other ethnic	1150 (0·4)	1706 (0·6)
Missing	35 482	33 260
Count of comorbidity, n (%)		
0	113 479 (36·4)	94 290 (28·7)
1	107 139 (34·3)	119 012 (36·2)
2	59 976 (19·2)	75 202 (22·9)
3	22 929 (7·4)	29 761 (9·1)
4+	8556 (2·7)	10 488 (3·2)

Table 2 – Safety Risks: Length of stay, emergency readmissions and mortality within 30 days (unadjusted)

	Hip replacement (n=312 079)				Knee replacement (n=328 753)			
	Prevalence of comorbidities n (%)	**Length of stay /days Mean (SD)**	**Emergency readmissions within 30 days n (%)**	**Mortality within 30 days n (%)**	**Prevalence of comorbidities n (%)**	**Length of stay / days Mean (SD)**	**Emergency readmissions within 30 days n (%)**	**Mortality within 30 days n (%)**
Patients without comorbidities	..	3·7 (4·4)	1835 (1·6)	6 (0·01)	..	3·9 (3·0)	1635 (1·7)	12 (0·01)
Heart disease	53 277 (17·1)	6·3 (5·7)	2236 (4·2)	113 (0·21)	60 755 (18·5)	5·9 (10·2)	2615 (3·3)	105 (0·17)
High Blood pressure	151 163 (48·4)	5·0 (5·5)	4630 (3·1)	125 (0·08)	187 815 (57·1)	5·0 (9·4)	5912 (3·2)	133 (0·07)
Stroke	3227 (1·03)	7·7 (8·9)	190 (5·9)	14 (0·43)	3530 (1·1)	7·9 (10·1)	189 (5·4)	20 (0·57)
Leg pain due to poor circulation	5140 (1·7)	6·1 (6·1)	244 (4·8)	16 (0·31)	4955 (1·5)	6·1 (7·5)	231 (4·7)	9 (0·18)
Lung Disease	43 481 (13·9)	5·2 (4·7)	1674 (3·9)	54 (0·12)	51 176 (15·6)	5·3 (13·8)	1933 (3·8)	57 (0·11)
Diabetes	29 535 (9·5)	5·4 (5·1)	990 (3·4)	41 (0·14)	44 813 (13·6)	5·4 (8·2)	1637 (3·7)	37 (0·08)
Kidney Disease	16 428 (5·3)	6·5 (7·4)	765 (4·7)	45 (0·27)	18 000 (5·5)	6·5 (17·8)	848 (4·7)	47 (0·26)
Diseases of the Nervous System	8483 (2·7)	6·9 (7·5)	413 (4·9)	11 (0·13)	9741 (3·0)	6·9 (15·4)	516 (5·3)	23 (0·24)
Liver Disease	1888 (0·6)	6·0 (6·1)	92 (4·9)	6 (0·32)	1931 (0·6)	5·7 (5·7)	92 (4·7)	9 (0·47)
Cancer	6354 (2·0)	5·4 (4·9)	255 (4·0)	8 (0·13)	5545 (1·7)	5·3 (4·3)	252 (4·5)	5 (0·09)
Depression	13 367 (4·3)	4·8 (5·4)	559 (4·2)	3 (0·02)	14 814 (4·5)	4·8 (4·5)	651 (4·4)	6 (0·04)

Table 3 – Effectiveness: Improvement in OHS, OKS and EQ-5D (unadjusted)

	Hip replacement (n=234 432)			Knee replacement (n=245 200)		
	Prevalence of comorbidities n (%)	**Improvement in OHS Mean (SD)**	**Improvement in EQ-5D Mean (SD)**	**Prevalence of comorbidities n (%)**	**Improvement in OKS Mean (SD)**	**Improvement in EQ-5D Mean (SD)**
Patients without comorbidities	..	21·3 (9·91)	0·42 (0·33)	..	15·9 (10·0)	0·31 (0·32)
Heart disease	39 594 (16·9)	20·4 (10·6)	0·43 (0·35)	44 914 (18·3)	15·1 (10·4)	0·30 (0·33)
High Blood pressure	114 373 (48·8)	20·9 (10·4)	0·44 (0·34)	139 931 (57·1)	15·7 (10·1)	0·31 (0·33)
Stroke	2423 (1·0)	19·8 (11·1)	0·43 (0·35)	3723 (1·6)	14·4 (10·8)	0·31 (0·35)
Leg pain due to poor circulation	3723 (1·6)	20·1 (10·9)	0·42 (0·36)	3686 (1·5)	14·9 (10·5)	0·29 (0·33)
Lung Disease	30 989 (13·2)	20·6 (10·9)	0·44 (0·35)	36 672 (15·0)	15·2 (10·4)	0·31 (0·34)
Diabetes	21 621 (9·2)	20·4 (10·7)	0·44 (0·35)	32 247 (13·5)	14·7 (10·6)	0·31 (0·34)
Kidney Disease	11 916 (5·1)	21·0 (10·5)	0·43 (0·36)	12 992 (5·3)	15·8 (10·4)	0·32 (0·33)
Diseases of the Nervous System	5723 (2·4)	20·2 (10·9)	0·43 (0·35)	6735 (2·8)	15·2 (10·8)	0·32 (0·35)
Liver Disease	1147 (0·5)	20·8 (11·1)	0·45 (0·37)	1219 (0·5)	14·2 (10·4)	0·29 (0·35)
Cancer	4633 (2·0)	20·9 (10·4)	0·43 (0·34)	4167 (1·7)	15·6 (10·1)	0·30 (0·35)
Depression	8288 (3·5)	20·6 (11·1)	0·43 (0·37)	9549 (3·9)	14·9 (10·6)	0·31 (0·36)

Figure 2- Safety Risks: Forest plot for length of stay (days) and risk of an emergency readmission and mortality in 30 days comparing patients with and without comorbidity after hip and knee replacement with adjustment for age, sex, ethnicity, socioeconomic status, and other comorbidities)

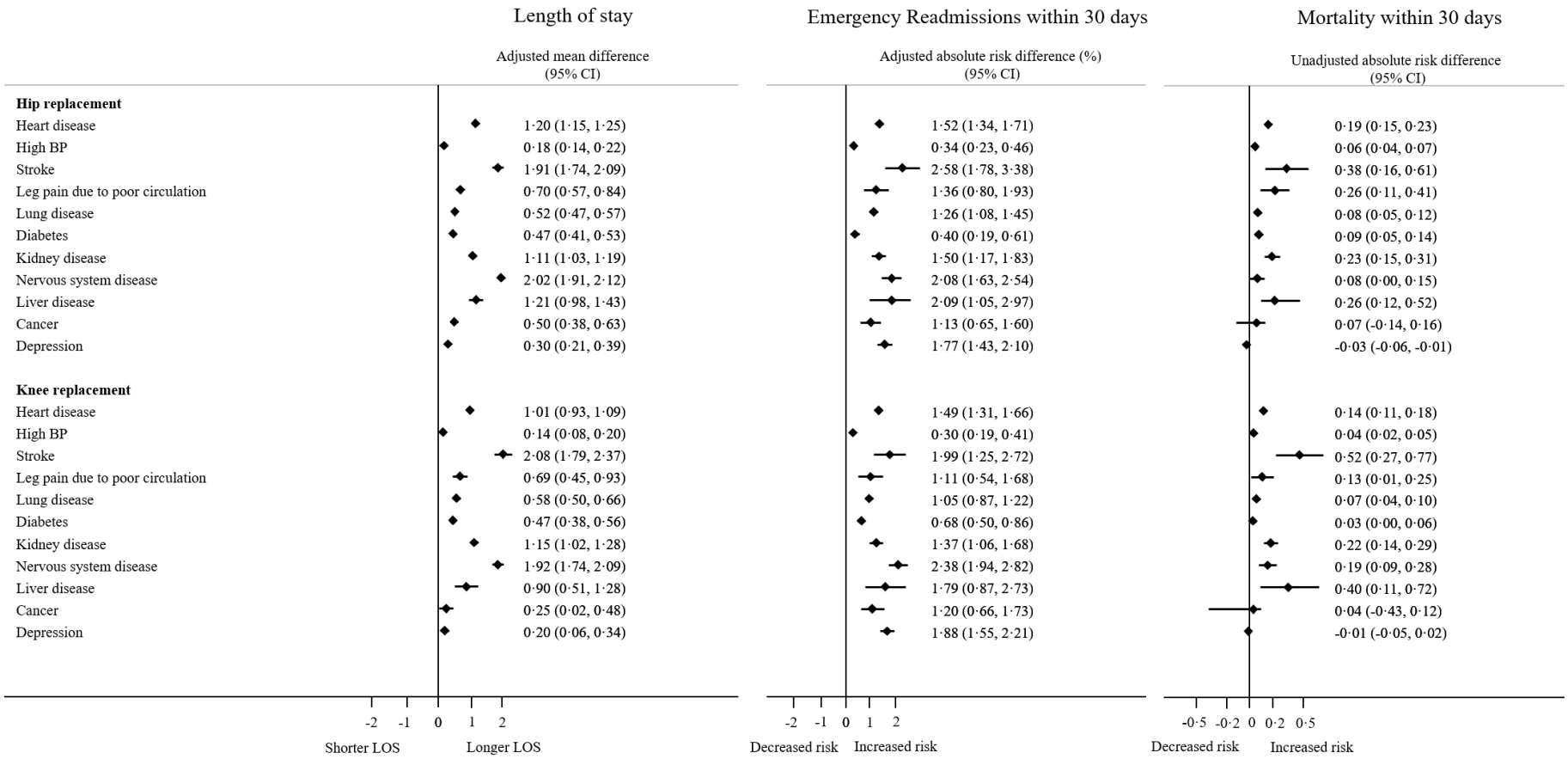

Figure 3 – Effectiveness: Forest plot for improvement in joint problems and health-related quality of comparing patients with and without comorbidities after hip and knee replacement with adjustment for age, sex, ethnicity, socioeconomic status, and other comorbidities.

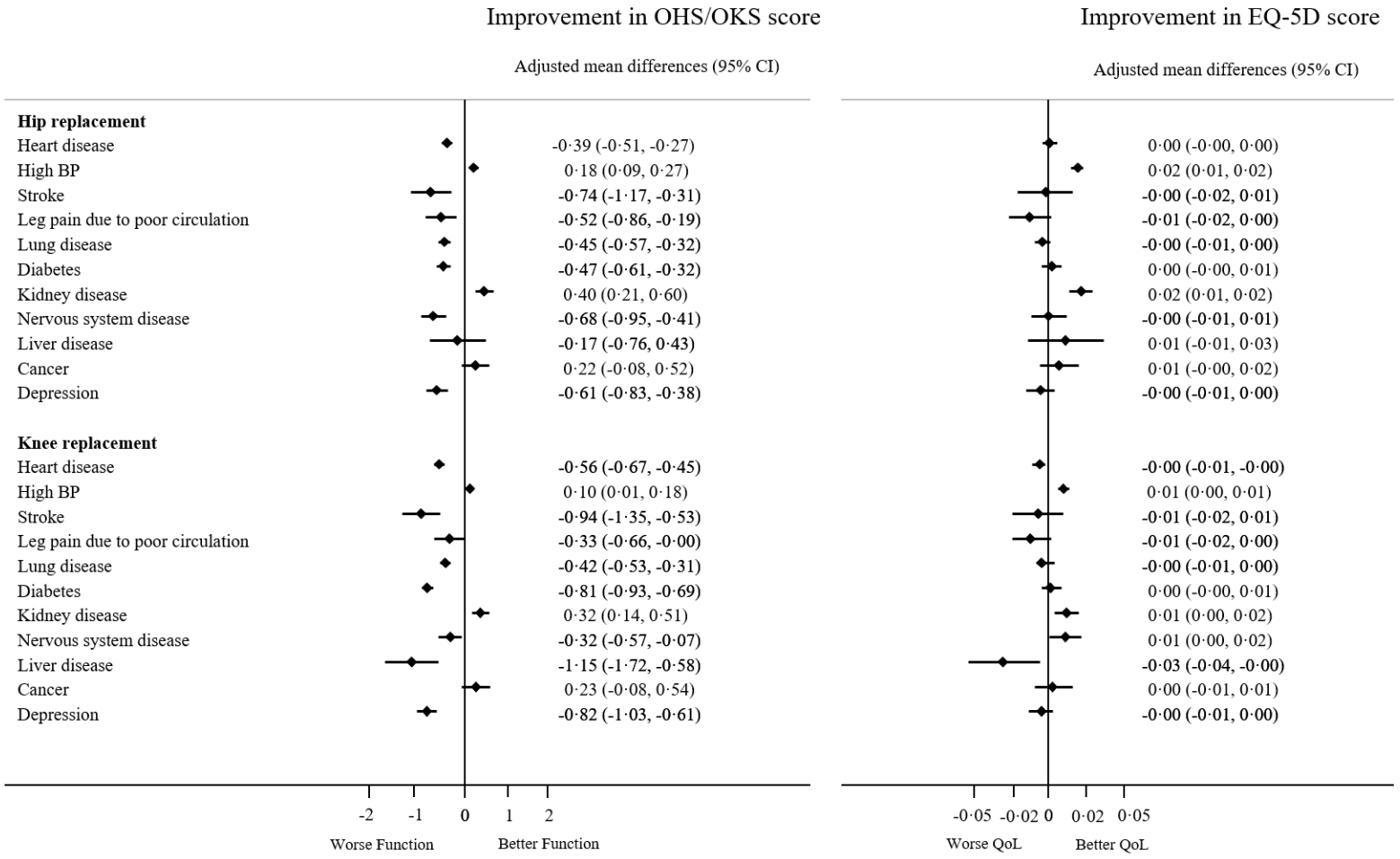

Table 4 – Impact of number of comorbidities on safety risks and effectiveness of hip and knee replacement (with adjustment for age, sex, ethnicity and socioeconomic status)

		Safety Risks						Effectiveness				
Number of comorbidities	**Frequency n (%)**	**Length of stay (days)**		**Emergency Readmission within 30 days**		**Mortality within 30 days**		**Frequency n (%)**	**Improvement in OHS/OKS**		**Improvement in EQ-5D**	
		Mean (SD)	**Adjusted mean difference (95% CI)**	**n (%)**	**Adjusted absolute risk difference (95% CI)**	**n (%)**	**Unadjusted absolute risk difference (95% CI)**		**Mean (SD)**	**Adjusted mean difference (95% CI)**	**Mean (SD)**	**Adjusted mean difference (95% CI)**
Hip replacement												
0	113 479 (36·4)	3·70 (4·4)	Reference**	1835 (1·6)	Reference**	6 (0·01)	Reference**	86 104 (36·7)	21·3 (9·9)	Reference**	0·42 (0·33)	Reference
1	107 139 (34·3)	4·29 (5·0)	0·28 (0·24, 0·32)	2509 (2·3)	0·54 (0·42, 0·66)	32 (0·03)	0·02 (0·005, 0·04)	81 505 (34·8)	21·1 (10·2)	0·02 (-0·08, 0·12)	0·44 (0·34)	0·01 (0·01, 0·01)
2	59 976 (19·2)	5·16 (5·1)	0·99 (0·94, 1·04)	1921 (3·2)	1·29 (1·13, 1·46)	44 (0·07)	0·06 (0·04, 0·09)	44 789 (19·1)	20·7 (10·5)	-0·24 (-0·36, -0·12)	0·44 (0·35)	0·02 (0·01, 0·02)
3	22 929 (7·4)	6·24 (6·0)	1·98 (1·91, 2·06)	1095 (4·8)	2·80 (2·51, 3·09)	(44 (0·19)	0·19 (0·15, 0·22)	16 352 (7·0)	20·3 (10·9)	-0·58 (-0·76, -0·41)	0·44 (0·35)	0·02 (0·01, 0·03)
4+	8556 2·7)	7·71 (7·3)	3·40 (3·29, 3·51)	557 (6·5)	4·50 (3·97, 5·03)	42 (0·49)	0·49 (0·43, 0·54)	5682 (2·4)	19·9 (11·3)	-0·91 (-1·19, -0·64)	0·43 (0·36)	0·01 (0·00, 0·02)
Knee replacement												
0	94 290 (28·7)	3·91 (3·0)	Reference**	1635 (1·7)	Reference**	12 (0·01)	Reference**	71 472 (29·2)	15·9 (10·0)	Reference**	0·31 (0·32)	Reference
1	119 012 (36·2)	4·35 (8·0)	0·23 (0·15, 0·30)	2849 (2·4)	0·52 (0·40, 0·64)	33 (0·03)	0·02 (-0·00, 0·03)	89 798 (36·6)	15·8 (10·1)	-0·10 (-0·20, 0·00)	0·31 (0·33)	0·01 (0·00, 0·01)
2	75 202 (22·9)	5·11 (12·6)	0·89 (0·80, 0·97)	2462 (3·3)	1·29 (1·13, 1·44)	47 (0·06)	0·05 (0·03, 0·07)	55 636 (22·7)	15·4 (10·3)	-0·52 (-0·63, -0·40)	0·31 (0·33)	0·00 (0·00, 0·01)
3	29 761 (9·1)	6·02 (9·9)	1·73 (1·61, 1·84)	1393 (4·7)	2·60 (2·34, 2·85)	45 (0·15)	0·14 (0·11, 0·17)	21 225 (8·7)	15·0 (10·6)	-0·91 (-1·07,-0·75)	0·31 (0·34)	0·01 (0·00, 0·01)
4+	10 488 (3·2)	7·37 (9·5)	3·03 (2·86, 3·21)	687 (6·6)	4·43 (3·96, 4·92)	42 (0·40)	0·39 (0·34, 0·43)	7069 (2·9)	14·4 (10·9)	-1·42 (-1·67, -1·17)	0·31 (0·36)	0·00 (0·01, 0·01)

*Test for trend: ** denotes p value <0.001

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Supplementary information

Supplementary information 1- Comorbidity profile

Comorbidity	Comorbidity sub-category	n	%
Heart disease	Ischemic heart disease	48 555	57·0
	Cardiac arrhythmias	38 492	45·5
	Valvular disease	9377	11·0
	Congestive heart failure	7566	8·9
Stroke	Ischemic stroke	2156	46·3
	Transient Ischemic Attack	745	16·0
	Subarachnoid haemorrhage	52	1·1
	Other Stroke	1806	38·8
Leg pain due to poor circulation	Peripheral vascular diseases	3861	52·1
	Vascular implants	2214	29·9
	Aortic diseases	1844	24·9
	Gangrene	105	1·4
High BP	Primary hypertension	235 890	92·7
	Secondary hypertension	4323	1·7
Nervous system diseases	Epilepsy	4912	39·4
	Parkinsonism	2779	22·3
	Dementia	1713	13·7
	Neuropathies	1004	8·1
	Demyelinating diseases	790	6·3
	Other nervous system (e.g. paralysis, huntington's disease)	1534	12·3
Lung disease	Asthma	47 728	70·5
	COPD	20 574	30·4
	Pulmonary heart diseases	1661	2·5
	Other lung disease (e.g. due to external agents)	1024	1·5
Diabetes	Non-insulin-dependent diabetes	51 787	96·1
	Insulin-dependent diabetes	2290	4·2
	Other	597	1·1
Kidney disease	Chronic renal failure	21 122	84·8
	Glomerular disease	3177	12·7
	Acute renal failure	1191	4·7
Liver disease	Cirrhosis	583	24·6
	Alcoholic liver disease	401	16·9
	Hepatitis	361	15·2
	Hepatic failure	37	1·6
	Any other liver disease	1123	47·4
Cancer	Cancer without metastasis	6934	78·8
	Lymphoma	1708	19·4
	Metastatic cancer	921	10·5
Depression	Depression	16 322	91·5
	Depression linked to anxiety and stress	1721	9·6
	Other depression (linked to schizophrenia and BAD)	15	0·1

Supplementary information 2- Comorbidity profile by number of comorbidities (n (%))

# of Comorbidities	Heart disease	High BP	Stroke	Circulation	Lung disease	Diabetes	Kidney disease	Nervous system disease	Liver disease	Cancer	Depression
1	12 575 (7·3)	117 710 (68·7)	371 (0·2)	805 (0·5)	20 291 (11·8)	6331 (3·7)	1871 (1·1)	3296 (1·9)	437 (0·2)	2235 (1·3)	5380 (3·1)
2	37 623 (37·5)	88 589 (88·2)	1248 (1·2)	1889 (1·8)	24 850 (24·7)	24 166 (24·1)	8394 (8·4)	4024 (4·0)	716 (0·7)	2991 (2·9)	6360 (6·3)
3	23 933 (63·7)	35 564 (94·6)	1482 (3·9)	296 (6·6)	15 220 (40·5)	15 840 (42·1)	8753 (23·3)	2883 (7·7)	636 (1·7)	2144 (5·7)	3780 (10·1)
4	10 377 (81·4)	12 441 (97·6)	1555 (12·1)	2219 (17·4)	7299 (57·2)	7531 (59·1)	5890 (46·2)	2255 (17·7)	577 (4·5)	1430 (11·2)	2317 (18·2)