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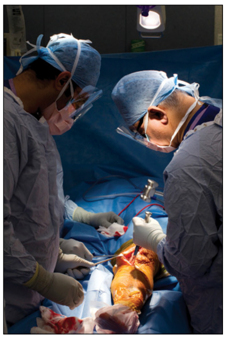
Patient safety after partial and total knee replacement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More than 90 000 people in the UK had knee replacements in 2012, according to the National Joint Registry of England and Wales (NJR).[1] The human cost of this expensive surgery is addressed in two articles in *The Lancet*[2,3] that question conclusions from the NJR, with major consequences for patient safety and the knee replacement industry.

The indications for knee replacement remain poorly defined: a patient with a small wear patch seen on MRI is given the same diagnosis as someone whose knee is severely damaged. Both are told they have osteoarthritis. International Classification of Diseases-10 labels osteoarthritis of the knee as gonarthrosis, M17.1, allowing no separation into compartments, and no classification of severity. So, despite being localised to one compartment in most people,[4] because of poor diagnostic criteria, knee osteoarthritis can be validly approached with two different philosophies. Surgeons who deem knee osteoarthritis a disease excise the entire joint, thereby curing the disease and substituting a total knee replacement (TKR). Alternatively, those who deem it to be predictable wear do the smaller operation of partial, or unicompartmental knee replacement (UKR), relining the part that is worn, preserving the rest of the joint surfaces, and, importantly, the anterior cruciate ligament. In TKR, this important structure is routinely excised, which results in reduced ability to walk,[5] explaining perhaps why TKR is less effective than is total hip replacement,[6] and why life expectancy might also be affected.[7] For patients undergoing either TKR or UKR, if done well, the probability is that this is the last operation that they will need in their lifetime,[8] as results from hundreds of thousands of patients now enrolled into national joint registries around the world confirm.

Unlike tumour registries, which have strict diagnostic inclusion criteria and use death as an endpoint, joint registries are focused on the outcome of the device: anyone with any amount of joint damage can be admitted, only device-related surgical procedures are reported as failures, and death is counted as a success. Because arthrosis is closely related to ageing, the many patients who have died with no need for revision surgery stretch the use of so-called survivorship statistics when reporting the survival of the implant, not the patient.[9]

The NJR now has more than 500 000 knee replacements registered, making it the world's largest registry, so conclusions from it should have a global impact. Set up to give warning of poorly performing devices, with operations leading to exchange of device as the main focus, the registry is now used to compare TKR with UKR. This focus can lead to perverse results: a joint replacement with a problem that can be fixed, curing the pain and restoring the patient's quality of life, is a failure owing to its revision, whereas a painful joint replacement that cannot be revised, condemning the patient to a lifetime of stiffness and pain, is recorded as a success in registry terms.[10] Thus, TKRs are reported as successful despite the fact that 25% are no better or even worse after surgery.[11] On the basis of revision rates alone, registry data continue to encourage surgeons to concentrate on TKR, and avoid UKR.[12–15]

The two *Lancet* papers look at the patients who have had knee replacements rather than their prostheses. Linda Hunt and colleagues[2] undertook a multivariate analysis of 467 779 cases from the NJR. They linked the national Hospital Episode Statistics (HES) with NJR data, in an observational study assessing 45-day mortality associated with knee arthroplasty to treat osteoarthritis. In their analysis, 1183 patients died within 45 days of surgery during the 8-year study period. Mortality decreased with time; from 0·37% in 2003 to 0·20% in 2011, making knee surgery safer than hip replacement, which they reported on last year.[9] They did, however, note a substantial difference in risk of perioperative death dependent on the type of procedure: the smaller, cheaper operation of

UKR was associated with substantially lower mortality than was TKR (hazard ratio [HR] 0·32, 95% CI 0·19–0·54). Despite this finding, Hunt and colleagues stop short of commending UKR. Perhaps this absent recommendation was to avoid conflict with the stream of registry publications promoting TKR over UKR, with revision as the only indicator of failure.[13–17]

Alexander Liddle and colleagues[3] also link HES and NJR data. In addition to mortality, they look at all rates of reoperation, not just revision, and also complications, readmission to hospital, and length of hospital stay. A study group of more than 101 330 matched cases was assembled with propensity score matching to include three TKRs for every UKR (25 334 UKRs were matched to 75 996 TKRs), ensuring the best possible use of data. They report early and late complications separately. Risk of early death after surgery was again significantly lower for UKR than for TKR at all timepoints (30 day: HR 0·23, 95% CI 0·11–0·50; 8 year: 0·85, 0·79–0·92). To avoid one death by 4 years after surgery, the number needed to switch from TKR to UKR is 93, dropping to 62 at 8 years.

Death is not only a very firm and clinically important endpoint, but also a surrogate for more common risks of intraoperative complications, stroke, myocardial infarction, thromboembolism, blood transfusion, and admission to critical care—all much more common after TKR than after UKR. Implant-related complications resulting in operations occur later and were substantially more common after UKR (subhazard ratio [SHR] 2·12, 95% CI 1·99–2·26) at 8 years.[3] These problems, which were mainly loosening and implant failure, were usually treated by a primary TKR. When the same problems of loosening or implant failure resulted in reoperation after TKR, they were often treated by larger so-called revision devices involving stems and augments. Infection, which is the most serious and costly local complication, was half as likely after UKR than after TKR in this large analysis (0·50, 0·38–0·66). In neither study was information available about thresholds for reoperation. By combining these datasets with outcome scores and costs, a formal cost-effectiveness analysis shows that UKR is a cost-effective option, despite the revision rate.[18]

For more on **surgeons** see http://www.njrsurgeonhospitalprofile.org.uk

What can be drawn from these two large studies? When measured in terms of risk of perioperative death or serious morbidity, UKR is unequivocally safer than TKR. This simple message should be of great interest to patients and the clinical commissioning groups and insurers who pay for health care. This finding is at odds with the industry-funded NJR that suggests that UKR should be restricted, if not abandoned, for its high revision rate,[16] despite improved postoperative scores.[1]

Arguments of this sort are not new to surgery. For women with operable breast cancer, for example, lumpectomy and radiotherapy offered substantial advantages, yet were met with fierce resistance from surgeons and centres promoting radical mastectomy. The strategy of radical mastectomy for all malignant breast disease was laid to rest 25 years ago with trial results showing no survival benefit over lumpectomy, despite a substantial reoperation rate for local recurrence in the conservative surgery group.[19] A randomised trial of partial versus radical genuectomy (TKR has been described as internal amputation of the knee) reported at 5, 10, and 15 years showed that the smaller operation of UKR was not functionally inferior at any timepoint.[20] Although in breast cancer survival rightly refers to the patient, and her breast, in the looking-glass of world of implant registries death is a success, and only implant revision counts as a failure. The fairly high mortality in the mainly older population who require knee replacement makes the use of survival statistics challenging when reporting on prostheses, not patients.[9]

So what prevents the smaller, cheaper, and safer operation becoming adopted widely? UKR is a complex operation to learn, yet, in the UK, surgeons and hospitals are paid less for it by private insurers, with NHS reimbursement varying depending on what code is used. Today, many surgeons in the UK have agreed to have their activity and mortality statistics in the public domain as part of the government's focus on patient safety. The NJR goes further though. It reports surgeons to the chief executives of their hospitals, not for excessive mortality, strokes, myocardial infarctions, or infections, but for having a revision rate that is high for TKR, but could be normal for UKR perhaps simply because this small operation is rather easier to fix, if a problem arises. These two papers should provoke a review of knee arthroplasty by policy makers worldwide. Substantial public and private savings are possible: of the 90 000 knee replacements reported in 2012 in England and Wales, only 8% were UKR.[1] If only half of those eligible were offered the more conservative procedure of UKR, the NHS could save an estimated £70 million every year immediately on operative costs alone,[18,21] and, on the basis of these two papers, there would be 170 fewer postoperative deaths annually, and many hundreds of fewer strokes, myocardial infarctions, and infections.

While perverse incentives remain in place, the TKR industry will continue to grow steadily encouraged by statistics based upon revision rates alone. With hundreds of lives and hundreds of millions of pounds at stake every year, a change in knee replacement strategy deserves consideration today, as it did with mastectomy 25 years ago.

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I am on the design team of a novel knee replacement at MatOrtho, and have received grants from MatOrtho, grants and personal fees from CeramTec, grants and personal fees from Stanmore Implants Worldwide, grants from Biomet, been on the speaker panel for Biomet, received grants from DePuy, been the principal investigator for the MHRA study of a novel hip design at JRI, and am cofounder, director, and minority shareholder of Embody, an Imperial start-up company developing patient-matched instruments for hip and knee arthroplasty. I have a patent on designs for knee implants for robotic implantation, and a patent on an anatomical design of acetabulum and femoral head pending.

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Do we need to know whether nitrous oxide harms patients?

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In *The Lancet*, Paul Myles and colleagues[1] investigate the association between nitrous oxide exposure and cardiovascular complications such as non-fatal myocardial infarction, stroke, pulmonary embolism, cardiac arrest, and death, within 30 days of surgery, in patients with known or suspected coronary artery disease having major non-cardiac surgery under general anaesthesia. The rationale for this large, multicentre study, which involved more than 7000 patients from 45 centres, was the observation that short-term exposure to nitrous oxide led to significant increases in plasma homocysteine.[2] Hyperhomocysteinaemia impairs arterial flow and has been associated with cardiovascular disease.[3] The authors report that nitrous oxide did not increase

45-day mortality after 467 779 knee replacements for osteoarthritis from the National Joint Registry for England and Wales: an observational study

Linda P Hunt, Yoav Ben-Shlomo, Emma M Clark, Paul Dieppe, Andrew Judge, Alex J MacGregor, Jon H Tobias, Kelly Vernon, Ashley W Blom, on behalf of the National Joint Registry for England and Wales

Summary

Background Understanding the risk factors for early death after knee replacement could help to reduce the risk of mortality after this procedure. We assessed secular trends in death within 45 days of knee replacement for osteoarthritis in England and Wales, with the aim of investigating whether any change that we recorded could be explained by alterations in modifiable perioperative factors.

Methods We took data for knee replacements done for osteoarthritis in England and Wales between April 1, 2003, and Dec 31, 2011, from the National Joint Registry for England and Wales. Patient identifiers were used to link these data to the national mortality database and the Hospital Episode Statistics database to obtain details of death, sociodemographics, and comorbidity. We assessed mortality within 45 days by Kaplan-Meier analysis and assessed the role of patient and treatment factors by Cox proportional hazards models.

Findings 467 779 primary knee replacements were done to treat osteoarthritis during 9 years. 1183 patients died within 45 days of surgery, with a substantial secular decrease in mortality from 0·37% in 2003 to 0·20% in 2011, even after adjustment for age, sex, and comorbidity. The use of unicompartmental knee replacement was associated with substantially lower mortality than was total knee replacement (hazard ratio [HR] 0·32, 95% CI 0·19–0·54, p<0·0005). Several comorbidities were associated with increased mortality: myocardial infarction (HR 3·46, 95% CI 2·81–4·14, p<0·0005), cerebrovascular disease (3·35, 2·7–4·14, p<0·0005), moderate/severe liver disease (7·2, 3·93–13·21, p<0·0005), and renal disease (2·18, 1·76–2·69, p<0·0005). Modifiable perioperative risk factors, including surgical approach and thromboprophylaxis were not associated with mortality.

Interpretation Postoperative mortality after knee replacement has fallen substantially between 2003 and 2011. Efforts to further reduce mortality should concentrate more on older patients, those who are male and those with specific comorbidities, such as myocardial infarction, cerebrovascular disease, liver disease, and renal disease.

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Introduction

Knee joint replacement is one of the most common surgical procedures, with numbers now exceeding those for hip replacement.[1] Both operations are associated with a short-term increase in mortality.[2,3] Early mortality after hip replacement has decreased in recent years, and several modifiable determinants are associated with mortality, such as surgical approach and type of anaesthesia.[2]

Both knee and hip joint replacement are largely done to relieve pain and disability resulting from advanced osteoarthritis. Research into both osteoarthritis and joint replacement often assumes that knee and hip problems, and their surgical treatments, are very similar, although abundant evidence to the contrary exists. For example, the epidemiological associations of hip and knee osteoarthritis differ, as do the rate of progression and outcomes.[1] Furthermore, advances in knee surgery have led to two quite distinct operative options for the most common form of knee osteoarthritis—anteromedial compartment disease—a unicondylar replacement (UKR) of the medial compartment of the knee or total knee replacement (TKR).

Many surgeons and patients favour TKR over UKR because this option seems to be a more definitive answer to knee osteoarthritis and because of the evidence that UKRs are revised more often than are TKRs.[1] Other researchers have argued that implant survival should not only be looked at in isolation,[4] but also alongside clinical outcomes. If early mortality favoured UKR, opinions and practice might change.

Decision making around knee replacement needs to consider perioperative mortality and patient related outcomes (such as pain, function, and satisfaction) and longevity of implants.[5] We have therefore examined early mortality after knee joint replacement, exploring time trends in early mortality during the past 10 years, and to what extent these trends are determined by patient, surgical, and anaesthetic factors. We postulated that age, sex, year of surgery, surgical approach, thromboprophylaxis, implant type, health status, and serious medical comorbidity would be associated with mortality.

Methods

Data sources

In this observational study, we linked data from three large UK datasets to examine these questions: the National Joint Registry for England and Wales (NJR), the Office of National Statistics (ONS), and the Hospital Episode Statistics for England (HES). The NJR was established in April, 2003, and records all knee replacements done in England and Wales. The ONS accurately records all deaths in England and Wales, and HES records all inpatient episodes for National Health Service (NHS) funded care in England.

For the **ASA Physical Status Classification System** see http://www.asahq.org/For-Members/Clinical-Information/ASA-Physical-Status-Classification-System.aspx

See Online for appendix

Patient details from the NJR were passed to the NHS Personal Demographics Service who provided death dates from the ONS, for which the NHS number was traceable. NJR was further linked to inpatient and day case episodes in HES. We produce part 3 of the annual report of the NJR and, in that capacity, receive the appropriate dataset each year in April. Our HES dataset was received concurrently with the annual report dataset in April, 2012, but contained no entries beyond Sept 30, 2011.

Our base series was 499 695 primary knee operations done between April 1, 2003, and Dec 31, 2011, with valid anonymised person-level identifiers. Of these operations, we included 480 796 for which the only reason for surgery was osteoarthritis. We further excluded simultaneous bilateral operations (done on the same day: 12 866 operations, 6433 patients), and 151 for which the patient's NHS number was not traceable (hence whose deaths could not be ascertained) or for which consent had been withdrawn. Our results are based on the remaining 467 779 operations.

We obtained the HES extract by first searching for records with procedure (OPCS 4) codes relating to primary knee replacements within the NJR. For the patients identified, we extracted HES episodes for hospital admissions for any reason. We then merged the NJR and HES datasets. We restricted our HES records, and therefore the associated comorbidity, to a 5-year period before the relevant knee replacement to give all the knee replacements in NJR the same potential time coverage. Our HES entries went back to April, 1997, which was 5 years before the start of the NJR on April 1, 2003. Every patient, therefore, would have had a potential 5 years of episodes in HES, but those in early years could not have had more than 5 years.

86 841 (19%) of 450 268 primary operations done before Sept 30, 2011 (the last date of our HES extract), had no HES records. Of 86 841, 21 535 (5% of total 450 268) had been done in Wales, 42 587 (9%) were privately funded, and funding was uncertain in 4576 (1%). The remaining 18 143 (4%) operations were NHS funded, but no HES entries. We do not know why these entries were missing; 15 827 of 18 143 operations were NHS funded in independent hospitals or treatment centres, but the remaining 2316 were in English NHS hospitals. HES might not be as complete as it should be.

Procedures

We assessed factors related to time of death from any cause, censoring at 45 days or Dec 31, 2011. We investigated several variables—surgical approach, implant type and fixation, day of the week when surgery was done, anaesthetic type, thromboprophylaxis, age, sex, and body-mass index (BMI), which were all available in the NJR. We used several measures of comorbidity as potential confounders for death. The NJR provided the American Society of Anesthesiologists (ASA) six point scale of surgical fitness. We also used the International Classification of Diseases 10 codes reported in all HES inpatient episodes up to, and including, the primary operation, to define 16 so-called high risk subgroups with increased expected mortality, as originally proposed by Charlson and colleagues.[6,7] To mitigate potential bias due to data incompleteness, calculation of comorbidity was restricted to operations on or before Sept 30, 2011, the last date of our HES extract; the appendix shows further details. We extracted data for ethnic origin and area deprivation score from HES. If the coding of a person's ethnic origin was inconsistent, we used the ethnic group stated most frequently. We used the Lower Super Output Area Level (SOAL)—as defined by the Office for National Statistics—closest in time to the date of the primary operation as our geographical unit of analysis. SOAL was then linked to the English Indices of Multiple Deprivation for 2007[8] and patients were characterised according to the area quintile in which they resided (1=most deprived area, 5=least deprived).

Statistical analysis

We used Kaplan-Meier estimates to describe the 45-day mortality of different sex and age groups. We chose 45 days rather than 90 days because most of the short-term deaths seem to have occurred within this time, although modelling results for 45 days and 90 days proved very similar. During periods longer than 90 days, disengagement of mortality associated with the knee operation from that which would normally be expected because of the patient's age becomes difficult—as shown by a hazard rate that increased at later times, which was similar to that we observed in our previous hip study.[2]

We used Cox proportional hazards models to investigate the effects of patient and treatment factors and secular period, on the risk of death within 45 days. Age (grouped as <55, 55–59, 60–64, 65–69, 70–74, 75–79, and ≥80 years) and sex were included in all models. We first separately examined the effects of year of operation, ASA, surgical approach, mechanical and chemical thromboprophylaxis, anaesthetic used, and implant type, each adjusted for age and sex. We tested for interactions between age and sex, mechanical and chemical thromboprophylaxis, and year of operation and implant type. Proportionality of hazards was checked graphically with a series of plots of –ln(-ln(survivor function) *vs* ln(time), initially for age group and sex together (one adjusting for the other) and then for each of the other variables in turn with adjustment for both sex and age group. We then constructed a series of multivariable models with all the above factors and with further adjustment for comorbidity, BMI, ethnic origin, and social area deprivation.

A high proportion of BMIs was missing, especially in the early phase of NJR, possibly leading to bias in a complete case analysis. We did a series of multiple imputations, assuming that data were missing at random, with the imputation by chained equations procedure (appendix). The imputation models included all predictor variables for the Cox model, together with the outcome variable (Nelson-Aalen estimate and whether or not the patient died) because they had information about missing values of the predictors. We also added other covariates that could help with the imputation model (appendix).

To compare actual mortality with expected mortality, we calculated mortality by age group and sex for every calendar year using national data. For every patient, we calculated the total time at risk within every calendar year (up to a maximum total of 45 days from the primary operation), and calculated expected mortality by multiplying these times at risk by the appropriate rates. These were then summed by year of primary operation (figure 1). Analysis used Stata software (version 11.2, StataCorp LP, TX, USA, 1985–2009).

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. LPH had full access to all the data in the study and AWB had final responsibility for the decision to submit for publication.

Results

During 8 years of follow-up available for the whole cohort, the hazard rate for mortality increased with time from operation (data not shown), with steeper slopes for men and in older age groups. The hazard rate within the first 90 days after the operation (figure 1) suggests a short-term peak risk of death in the perioperative period that subsided by 45 days, which is why we focused on this first period, in which there were 1183 deaths.

45-day mortality increased with age and was higher in men than in women for all age groups (table 1). With adjustment for age and sex, mortality decreased with calendar year of procedure (from 0·37% to 0·20%) with the relative risk reduced by 40% during 8 years (table 2). If we account for the expected population mortality, one can see that the mortality in this cohort is less than expected (healthy selection effect) at all times, but has also shown a progressive reduction in the observed to expected ratio (table 2).

Table 3 shows results of a series of multivariable analyses with the Cox model. First, every variable was assessed in turn, adjusting only for age and sex. No significant interaction was noted between age and sex ($p_{interaction}$=0·47)

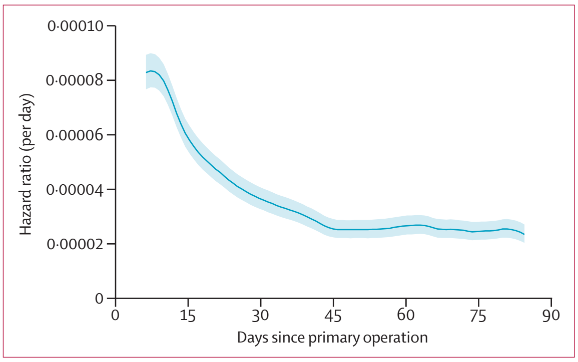

Figure 1: **Smoothed hazard ratio showing change in risk of death changed during first 90 days**
Smoothing calculated from changes in the Nelson-Aalen cumulative hazard estimates and smoothed with band half-width 5; shaded area shows point-wise 95% CI.

	Patients (n)	Deaths (n)	Kaplan-Meier estimate of cumulative % deaths at 45 days (95% CI)
Men			
<55 years	12 575	7	0·06% (0·03–0·12)
55–59 years	17 612	13	0·07% (0·04–0·13)
60–64 years	33 740	34	0·10% (0·07–0·14)
65-69 years	39 028	58	0·15% (0·12–0·19)
70–74 years	40 963	97	0·23% (0·19–0·28)
75–79 years	33 971	148	0·43% (0·37–0·51)
≥80 years	25 045	291	1·15% (1·03–1·29)
Women			
<55 years	17 154	6	0·04% (0·02–0·08)
55–59 years	22 670	10	0·04% (0·02–0·08)
60–64 years	37 557	25	0·07% (0·05–0·10)
65–69 years	45 404	53	0·11% (0·09–0·15)
70–74 years	51 991	78	0·15% (0·12–0·18)
75–79 years	48 645	119	0·24% (0·20–0·28)
≥80 years	41 424	244	0·59% (0·52–0·67)

Table 1: **45-day mortality by age and sex**

For the **mortality risk data from the Office of National Statistics** see http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-276237

	Operations (n)	Kaplan-Meier estimate of cumulative % deaths at 45 days	Hazard ratio* (95% CI), adjusted for sex and age	Deaths within 45 days (n)	Expected number of deaths†	Actual/ expected number of deaths
2003	12 283	0·37%	1 (reference)	46	53·6	0·84
2004	25 141	0·34%	0·96 (0·67–1·37)	88	100·2	0·88
2005	38 309	0·28%	0·78 (0·56–1·11)	108	147·3	0·73
2006	45 503	0·32%	0·89 (0·64–1·24)	146	168·2	0·87
2007	61 563	0·31%	0·89 (0·65–1·23)	194	218·9	0·89
2008	68 899	0·23%	0·67 (0·48–0·93)	161	238·6	0·67
2009	70 789	0·23%	0·65 (0·47–0·90)	160	231·6	0·69
2010	73 109	0·18%	0·53 (0·38–0·73)	134	236·2	0·57
2011	72 183	0·20%	0·60 (0·43–0·83)	146	216·1	0·68

*Cox proportional hazards model. †Calculated from data for mortality risk by age, sex, and year risk from the Office of National Statistics.

Table 2: **Changes in mortality by year of primary operation**

	Separate multivariable analyses (adjusted for sex and age group)*			Multivariable analysis (adjusted for sex and age group)†		Multivariable analysis (adjusted for sex, age group, and comorbidity)‡	
	n	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value
Year of primary operation							
2003–05	75 733	1 (reference)	··	1 (reference)	··	1 (reference)	··
2006–08	175 965	0·92 (0·79–1·07)	0·27	0·91 (0·78–1·07)	0·26	0·89 (0·74–1·07)	0·21
2009–11	216 081	0·67 (0·57–0·79)	<0·0005	0·67 (0·56–0·79)	<0·0005	0·61 (0·50–0·74)	<0·0005
ASA physical status							
P1	68 173	1 (reference)	··	1 (reference)	··	1 (reference)	··
P2	331 888	1·23 (0·99–1·54)	0·068	1·35 (1·07–1·71)	0·012	1·15 (0·88–1·50)	0·31
P3	65 984	2·34 (1·85–2·97)	<0·0005	2·59 (2·02–3·33)	<0·0005	1·40 (1·05–1·87)	0·020
P4/P5	1734	6·93 (4·55–10·56)	<0·0005	7·09 (4·57–11·00)	<0·0005	2·19 (1·31–3·68)	0·003
Approach§							
Lateral parapatella	5567	1·25 (0·77–2·02)	0·36	1·25 (0·77–2·06)	0·37	1·31 (0·76–2·28)	0·33
Medial parapatella	432 666	1 (reference)	··	1 (reference)	··	1 (reference)	··
Midvastus	8242	0·99 (0·64–1·54)	0·96	1·12 (0·72–1·75)	0·61	1·04 (0·62–1·74)	0·88
Subvastus	6590	0·65 (0·36–1·18)	0·16	0·59 (0·32–1·11)	0·10	0·57 (0·28–1·15)	0·12
Other	14 570	0·97 (0·70–1·36)	0·88	0·95 (0·67–1·34)	0·77	1·01 (0·70–1·46)	0·96
Mechanical prophylaxis¶							
No	61 396	1 (reference)	··	1 (reference)	··	1 (reference)	··
Yes	405 072	0·82 (0·70–0·96)	0·014	0·95 (0·80–1·13)	0·57	0·98 (0·81–1·18)	0·80
Chemical prophylaxis¶							
None	61 403	1 (reference)	··	1 (reference)	··	1 (reference)	··
Aspirin(only)	62 355	0·84 (0·67–1·04)	0·11	0·86 (0·68–1·07)	0·18	0·82 (0·63–1·06)	0·14
Heparin (+/–aspirin) only	293 808	0·90 (0·76–1·06)	0·21	0·91 (0·77–1·09)	0·31	0·93 (0·76–1·14)	0·47
Others/other combs	48 902	0·81 (0·64–1·03)	0·091	0·93 (0·72–1·20)	0·58	0·86 (0·64–1·17)	0·34
Anaesthesia type||							
Spinal only	180 669	1 (reference)	··	1 (reference)	··	1 (reference)	··
General only	100 560	0·98 (0·83–1·15)	0·79	1·02 (0·87–1·20)	0·82	1·01 (0·84–1·22)	0·89
Epidural only	19 319	1·22 (0·93–1·60)	0·14	1·17 (0·90–1·54)	0·24	1·03 (0·76–1·40)	0·84
Nerve block only	6255	1·08 (0·65–1·77)	0·77	1·04 (0·63–1·71)	0·87	1·06 (0·62–1·81)	0·83
Spinal and general	30 999	1·14 (0·90–1·43)	0·28	1·21 (0·96–1·53)	0·11	1·36 (1·05–1·75)	0·019
Spinal and epidural	9446	1·57 (1·14–2·17)	0·006	1·32 (0·95–1·83)	0·096	1·20 (0·85–1·70)	0·31
Spinal and nerve block	29 032	0·94 (0·73–1·21)	0·63	0·96 (0·75–1·24)	0·78	0·95 (0·72–1·26)	0·75
General and epidural	11 105	1·01 (0·69–1·49)	0·96	0·96 (0·65–1·42)	0·83	1·00 (0·65–1·53)	>0·995
General and nerve block	60 854	1·04 (0·86–1·25)	0·68	1·03 (0·85–1·24)	0·75	1·06 (0·86–1·30)	0·61
Other combinations	5275	1·09 (0·64–1·85)	0·76	1·07 (0·63–1·82)	0·81	1·19 (0·69–2·08)	0·53
Knee type**							
Cemented	388 608	1 (reference)	··	1 (reference)	··	1 (reference)	··
Uncemented	26 503	1·11 (0·87–1·40)	0·40	1·03 (0·80–1·33)	0·81	1·14 (0·85–1·53)	0·38
Hybrid	6546	1·02 (0·63–1·65)	0·94	1·03 (0·64–1·66)	0·91	0·84 (0·47–1·53)	0·58
Patello-femoral	5655	0·85 (0·38–1·90)	0·69	0·91 (0·40–2·03)	0·81	1·10 (0·45–2·67)	0·83
Unicondylar	40 428	0·37 (0·25–0·54)	<0·0005	0·37 (0·25–0·56)	<0·0005	0·32 (0·19–0·54)	<0·0005
Myocardial infarction††							
No	353 106	··	··	··	··	1 (reference)	
Yes	10 321	··	··	··	··	3·46 (2·89–4·14)	<0·0005
Congestive heart failure							
No	356 178	··	··	··	··	1 (reference)	
Yes	7249	··	··	··	··	3·41 (2·81–4·14)	<0·0005
Peripheral vascular disease							
No	356 903	··	··	··	··	1 (reference)	
Yes	6524	··	··	··	··	1·19 (0·89–1·58)	0·23

(Table 3 continues on next page)

	Separate multivariable analyses (adjusted for sex and age group)*			Multivariable analysis (adjusted for sex and age group)†		Multivariable analysis (adjusted for sex, age group, and comorbidity)‡	
	n	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value
(Continued from previous page)							
Cerebrovascular disease							
No	356 101	..	..	..	..	1 (reference)	
Yes	7326	..	..	..	..	3·35 (2·70–4·14)	<0·0005
Dementia							
No	362 485	..	..	..	..	1 (reference)	
Yes	942	..	..	..	..	1·39 (0·72–2·69)	0·33
Chronic pulmonary disease							
No	315 710	..	..	..	..	1 (reference)	..
Yes	47 717	..	..	..	..	1·15 (0·96–1·37)	0·12
Connective tissue disease or rheumatic disease							
No	349 008	..	..	..	..	1 (reference)	..
Yes	14 419	..	..	..	..	1·27 (0·95–1·68)	0·11
Peptic ulcer disease							
No	357 732	..	..	..	..	1 (reference)	..
Yes	5695	..	..	..	..	1·17 (0·81–1·69)	0·41
Liver disease							
No	361 230	..	..	..	..	1 (reference)	..
Mild	1834	..	..	..	..	1·49 (0·74–3·00)	0·27
Moderate/severe	363	..	..	..	..	7·20 (3·93–13·21)	<0·0005
Diabetes							
No	321 595	..	..	..	..	1 (reference)	..
Without complications	39 759	..	..	..	..	1·32 (1·10–1·57)	0·002
With complications	2 073		..		..	1·46 (0·87–2·46)	0·15
Paraplegia or hemiplegia							
No	361 960	..	..	..	..	1 (reference)	
Yes	1467	..	..	..	..	0·46 (0·23–0·95)	0·037
Renal disease							
No	354 968	..	..	..	..	1 (reference)	
Yes	845	..	..	..	..	2·18 (1·76–2·69)	<0·0005
Cancer							
No	348 657	..	..	..	..	1 (reference)	
Cancer	13 192	..	..	..	..	1·01 (0·76–1·34)	0·97
Metastatic cancer	1578	..	..	..	..	3·01 (1·70–5·33)	<0·0005

ASA=American Society of Anesthesiologists. *Separate multivariable analyses for each of the listed variables in turn, namely year, ASA, approach, mechanical and chemical prophylaxis, anaesthetic and knee type, in each case adjusting only for age and sex (subgroup sizes in left hand column). †Fully-adjusted multivariable analyses for year, ASA, approach, prophylaxis (mechanical and chemical), anaesthetic and knee type, with further adjustment for sex and age group (452 490 cases with complete information; 1127 deaths within 45 days). ‡Multivariable analysis as for † but with further adjustment for 16 comorbidity subgroups (349 905 cases with complete information; 903 deaths within 45 days). §Approach 144 (0·03%) missing; ¶1311 (0·28%) missing; ||14 265 (3·05%) missing. **Unsure for 39 (0·01%). ††No comorbidity for 104 352 either with no Hospital Episode Statistics records or with the primary operation done after Sept 30, 2011.

Table 3: **Cox proportional hazards models of 45-day mortality by variables**

and, after adjustment for age and sex, no significant interaction was noted between mechanic and chemical prophylaxis ($p_{interaction}$=0·43). Compared with cemented TKRs, mortality was lower in unicondylar (p<0·001), but not in uncemented, hybrid, and patellofemoral types. The effect of implant type did not change significantly across the three groups by year ($p_{interaction}$=0·92) and persisted in our fully adjusted multivariate analysis, which adjusted for all the other variables as well as age and sex, and also with further adjustment for the Charlson comorbidities. Both of these sets of analysis are shown in table 3. Of note, HIV was excluded because there were only six cases and none died. Further adjustment for BMI, ethnic origin, and area deprivation did not change the results much (appendix).

Graphical checking did not suggest that hazard rates were substantially non-proportional (curves non-parallel) during this fairly short interval of 45 days. A global test based on Schoenfeld residuals, as implemented in Stata software (Stata version 11.2, StataCorp LP, Texas, 1985–2009), for the model with age, sex, year, ASA, and implant type was not significant (p=0·38)

Surgical approach, mechanical and chemical thromboprophylaxis, and type of anaesthesia did not affect mortality, except that spinal and general anaesthetic combined was associated with increased mortality compared with spinal alone (table 3). Day of the week when surgery was done was not related to mortality (appendix).

Worse general health measured by the ASA grade and some comorbidities were associated with increased risk of mortality (table 3). Cerebrovascular disease, congestive cardiac failure, and myocardial infarction were associated with a three-fold and severe liver disease with a seven-fold increase in relative risk of death within 45 days of surgery (table 3).

When our model included BMI, we recorded that being overweight at the time of surgery (BMI 26–30 kg/m²) was associated with reduced 45-day mortality (HR 0·69, 95% CI 0·54–0·88, p=0·003) referenced to a normal BMI of 19–25 kg/m² (appendix). The hazard ratio of individuals with a BMI greater than 30 kg/m² was 0·79 (95% CI 0·61–1·01, p=0·06) and for those with BMI less than 19 kg/m² was 1·31 (0·41–4·11, p=0·65). However, data for BMI were either missing from the NJR or the values were deemed out of range (<10 kg/m² or >60 kg/m²) for 266 514 of (57%) 467 779 of operations, therefore these results should be interpreted with caution. Our reanalysis with several multiple imputation strategies produced almost identical results to the complete case analysis (appendix). As explained in some detail in our previous publication[2] about mortality after hip replacement, the number of cases recorded in the NJR has risen greatly during the studied period because of increased compliance with uploading data, rather than increased activity (figure 2).

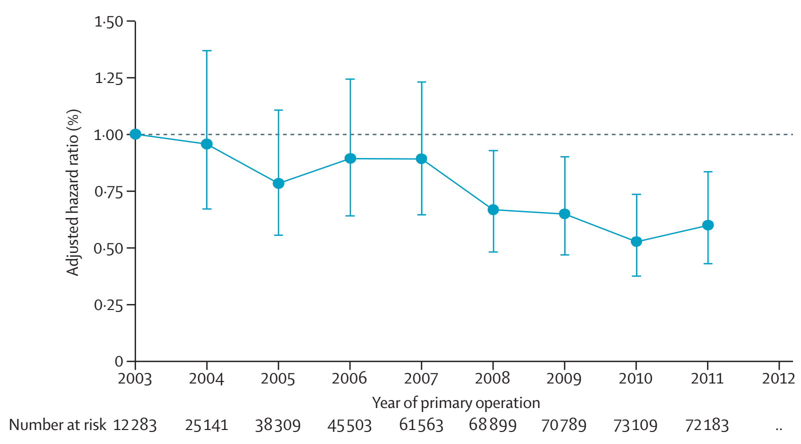

Figure 2: **Changes in 45-day mortality with time**
Hazard ratios with 95% CI for every year of primary after adjustment for sex and age. *Numbers shown underneath the plotted values are the number of primary operations done that year.

Discussion

We have shown a fall in early mortality after total knee replacement undertaken for osteoarthritis in England and Wales between 2003 and 2011 (panel). This result is similar to our findings for hip replacements for osteoarthritis.[2] One possible explanation in the case of hip replacement is the shift to surgical and anaesthetic techniques with reduced risk,[2] but this shift is not the case for knee replacement. We believe that the most likely explanation is that patients coming to surgery are generally fitter and less frail, because evidence shows worldwide trends to increased longevity. However, this evidence does not fully explain the magnitude of the decrease during a fairly short period, because the trends we recorded persisted after adjustment for comorbidity. Patients undergoing knee replacement have lower observed than expected mortality for their age and sex. This difference is most probably due to a so-called healthy-surgery effect whereby high risk patients are excluded from elective surgery.

As would be expected, older people and men are the most likely to die. The increased risk associated with cardiovascular, hepatic, and renal comorbidities argues strongly for routine screening for and careful counselling of patients who have these problems.

Our findings for BMI are much the same for the knee as for the hip—being overweight, but not obese, is associated with a reduced risk of mortality, a finding recorded in other arthroplasty cohorts[26] and in patients with cardiovascular disease.[27] These findings challenge the accepted definition of what constitutes an ideal BMI for these patients. We have recorded a U-shaped relation between mortality and BMI. WHO has defined normal BMI between 19 kg/m² and 25 kg/m². However, we noted that BMI 25–30 kg/m² is associated with the lowest mortality, suggesting that the ideal BMI for our study population, who are old (median age 70 years), European, and have advanced osteoarthritis, might differ from the ideal BMI of the world population as a whole. Some evidence suggests that the apparent so-called protective effect of obesity on mortality is seen in the general population, but has only emerged recently and is seen in a subgroup of older people with comorbidity, as noted in the NHANES-III dataset.[28] This result might show a healthy survivor effect such that obese individuals who survive to older age are less susceptible to the usual causes of premature mortality (cardiometabolic disease). In these cases, increased bodyweight might also be associated with greater muscle mass and perhaps reduced frailty, thereby being more resistant to the acute stresses that follow an operative procedure. However, they might also be because of residual confounding and thus need to be investigated further in other cohorts.

Using the NJR to explore 90-day mortality after hip replacement, we showed that surgical approach, anaesthetic technique, and thromboprophylaxis had important associations with postoperative mortality.

However, we found little evidence that the equivalent variables were associated with mortality after knee replacement once the data were adjusted for age and sex, although we did record an increased hazard ratio for combined spinal and general anaesthetic, which might be a type I error since no increased risk was associated with general anaesthetic. These findings were surprising and presumably relate partly to the fact that knee and hip osteoarthritis are quite different disorders, and that hip and knee replacement are very different operations. This argues for the disease in the two joints to be considered separately, and not, as so often happens in research studies, linked together. Surgical techniques to replace these joints are also quite different—for example, a tourniquet is used during knee replacement, but not during hip replacement, effectively isolating the operative site from the rest of the body. These operative differences could relate to the absence of any apparent effect of thromboprophylaxis on mortality and might account for low frequency of pulmonary embolism and death from pulmonary embolism after knee replacement compared with hip replacement.[27] Despite the fact that NICE[29] concluded that there was "no significant evidence on the effects of thromboprophylaxis on fatal and non fatal PE [pulmonary embolism] in TKR", and that there is no evidence that the use of thromboprophylaxis is of benefit in reducing all cause mortality, the use of thromboprophylaxis is recommended in NICE guidelines. Our data support the view that if there is a substantial risk of TKR causing bleeding, thromboprophylaxis should not be used. Indeed, new anticoagulants are associated with increased risks of bleeding.[29,30]

Lower mortality after UKR than after TKR was perhaps to be expected because UKR is a less invasive operative procedure than is TKR; most of the native knee is preserved and postoperative adverse events are uncommon.[31] Despite the fact that UKR was associated with a substantially reduced mortality, this association is unlikely to have contributed much to the overall decline in early mortality after knee replacement that we recorded; UKR accounted for only 8·6% of knee replacements, and no discernible increase in use of UKR was recorded during the 8 year follow-up.

Many, but not all, patients with osteoarthritis of the knee are suitable for either TKR or UKR. Both the patient and the surgeon need to consider several factors when choosing between them, including the risk of perioperative death, the risk of major complications, the chances of good relief of pain and disability, and survival of the implants. Decreased mortality and complications will obviously be regarded as a major advantage by patients, but they have to weigh up this advantage against the higher rates of revision that are consistently reported for UKR than for TKR.[1] Whether UKR results in better clinical outcomes than does TKR is unclear, with researchers reporting opposing findings.[24,25] The TOPKAT study,[22] which is a continuing multicentre trial comparing UKR with TKR, should elucidate comparative patient-based outcomes.

Aylin and colleagues[23] suggested that operations done at the end of the week increased the risk of mortality. Their analysis combined several procedures, including TKR. Our findings show that day of the week did not affect mortality after TKR for osteoarthritis in the first 45 days.

Panel: Research in context

Systematic review

We searched the Cochrane Library, Medline, and Embase from Jan 1, 1995, to Nov 30, 2013, for studies of total knee arthroplasty and mortality. Our search terms were total knee replacement, unicompartmental arthroplasty, prosthesis, and mortality. We found two systematic reviews,[9,10] eight national registry studies,[11–18] one large regional registry study (>10 000 patients),[19] and two large institutional registry studies (>10 000 patients).[20,21] Five national registry studies[9–11,22,23] were based on the same registry (the Nationwide Inpatient Sample, an all-payer inpatient discharge database from the USA) and so were considered together as Nationwide Inpatient Sample (NIS). One systematic review[24] analysed 80 studies that investigated mortality after hip or knee arthroplasty, and identified only non-significant trends of lower 90-day mortality in women. The NIS studies reported decreasing in-hospital mortality with time, although one[10] showed a slight increase between 2000 and 2004 compared with the earlier time periods, 1990–94, and 1995–99, based on 3 830 420 arthroplasties. Only one national registry study used longer-term mortality, based on the Swedish Knee Arthroplasty Register with up to 28 years' follow-up.[12] This study showed initial reduced mortality in the first 12 postoperative years for patients aged younger than 55 years at the time of their primary knee arthroplasty compared with the general population, but from 12 years onwards, increased mortality compared with the general population. One systematic review[25] analysed 64 studies that investigated outcomes after total joint arthroplasty for osteoarthritis, and identified older age and male sex as predictors of mortality. The remaining registry studies identified older age,[9–11,13,16,17,22,23] male sex,[9–11,13,15,22,23] higher numbers of comorbidities,[9–11,13,16,17,22,23] (with specific comorbidities of cardiovascular disease[9–11,22,23] dementia,[9–11,22,23] renal disease,[9–11,22,23] cerebrovascular disease,[9–11,22,23] and cardiopulmonary disease[17]), and high ASA grade[16] as patient related predictors of mortality. One institutional registry study[17] of 22 540 consecutive total knee arthroplasties identified higher mortality in cemented than in uncemented prostheses. One national registry study[14] of 35 878 total knee arthroplasties showed no difference in mortality with or without the use of epidural anaesthesia. Although all national registry studies were linked to national databases for identification of mortality, only two[9–11,15,22,23] were linked to national databases that allowed accurate study of comorbidities, suggesting potential underlying confounding for any associations seen.

Interpretation

The National Joint Registry of England and Wales has the biggest joint replacement database in the world, allowing us to analyse more than 450 000 primary knee operations between April, 2003, and September, 2011, reducing problems that can arise from selection bias. Linkage to Hospital Episode Statistics (a data warehouse containing details of all admissions to National Health Service hospitals in England with records of clinical information about diagnoses) allowed us to accurately assess comorbidities, and thereby control for confounding. Our findings show that all-cause mortality at 45 days has decreased between 2003 and 2011, echoing the previous findings of a reduction in in-hospital mortality. Similar to other registry studies, we have identified increasing age, male sex, and comorbidities, particularly cardiovascular and liver disease, as predictors of mortality. Furthermore, we identified that unicompartmental knee replacement is associated with decreased mortality. Efforts to further reduce mortality should concentrate more on older patients, those who are male and those with specific comorbidities, such as myocardial infarction, cerebrovascular disease, liver disease, and renal disease.

The strengths of this study include the large size and comprehensive coverage of the NJR, enhancing confidence in the validity and generalisability of the findings. Weaknesses are the facts that observational data cannot prove causality and that all potential confounders could not be accounted for. Confounding by indication remains a possibility, especially for the data on implant type.

Thus, we have shown that 45-day mortality after knee replacement is declining. Male sex, age, and specific comorbidities are strongly associated with increased mortality and efforts to reduce mortality should concentrate on these patients.

Contributors

LPH, YB-S, EMC, PD, AJ, AJM, JHT, and AWB designed the study. LH and KV managed and analysed the data. EMC and AWB reviewed the literature. All authors contributed to data interpretation and preparation of the report.

Declaration of interests

AJ has received consultancy fees from Anthera Pharmaceuticals, Servier, the UK Renal Registry, and Oxford Craniofacial Unit, and received a research grant from Roche. The University of Bristol has a research grant from Stryker. All other authors declare no competing interests.

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Adverse outcomes after total and unicompartmental knee replacement in 101 330 matched patients: a study of data from the National Joint Registry for England and Wales

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Summary

Background **Total knee replacement (TKR) or unicompartmental knee replacement (UKR) are options for end-stage osteoarthritis. However, comparisons between the two procedures are confounded by differences in baseline characteristics of patients undergoing either procedure and by insufficient reporting of endpoints other than revision. We aimed to compare adverse outcomes for each procedure in matched patients.**

Methods **With propensity score techniques, we compared matched patients undergoing TKR and UKR in the National Joint Registry for England and Wales. The National Joint Registry started collecting data in April 1, 2003, and is continuing. The last operation date in the extract of data used in our study was Aug 28, 2012. We linked data for multiple potential confounders from the National Health Service Hospital Episode Statistics database. We used regression models to compare outcomes including rates of revision, revision/reoperation, complications, readmission, mortality, and length of stay.**

Findings **25 334 UKRs were matched to 75 996 TKRs on the basis of propensity score. UKRs had worse implant survival both for revision (subhazard ratio [SHR] 2·12, 95% CI 1·99–2·26) and for revision/reoperation (1·38, 1·31–1·44) than TKRs at 8 years. Mortality was significantly higher for TKR at all timepoints than for UKR (30 day: hazard ratio 0·23, 95% CI 0·11–0·50; 8 year: 0·85, 0·79–0·92). Length of stay, complications (including thromboembolism, myocardial infarction, and stroke), and rate of readmission were all higher for TKR than for UKR.**

Interpretation **In decisions about which procedure to offer, the higher revision/reoperation rate of UKR than of TKR should be balanced against a lower occurrence of complications, readmission, and mortality, together with known benefits for UKR in terms of postoperative function. If 100 patients receiving TKR received UKR instead, the result would be around one fewer death and three more reoperations in the first 4 years after surgery.**

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Introduction

Total knee replacement (TKR), usually undertaken for end-stage osteoarthritis, is one of the commonest surgical procedures, with more than 76 000 TKRs done every year in the UK.[1] International trends suggest that this number will rise substantially, largely because of the ageing population and an increased prevalence of risk factors, including obesity.[2]

TKR is a highly successful and cost-effective procedure. In terms of implant survival, more than 95% are in situ 10 years after surgery.[1,3,4] However, implant survival is an imperfect measure. With this measure, patients who have died, those who undergo reoperations that are not regarded as revisions (such as debridement for infection or manipulation under anaesthetic for stiffness), and those who have poorly functioning, but unrevised, knee replacements, are all classed as successes.[5]

The proportion of TKRs that is judged successful changes with the use of different outcome measures. 90-day mortality after TKR is 0·4%,[6] by 4 years, 3·8% of patients undergo a non-revision reoperation;[7] 8·5% of patients have worse patient-reported outcome measures 6 months after knee replacement than they had beforehand;[8] and up to 20% are dissatisfied after TKR.[9]

A large proportion of patients who are eligible for TKR are also eligible for unicompartmental knee replacement (UKR) in which only the parts of the knee affected by osteoarthritis are replaced.[10,11] Better patient reported outcomes can be obtained with UKR than with TKR, and mortality and major complications are lower after UKR than after TKR.[4,12] However, unadjusted data from national registries show a significantly higher revision rate for UKR than for TKR.[1,3,4] Because revision rate has traditionally been regarded as the most important factor to determine implant choice, only 8% of knee replacements done each year in the UK are UKRs, and most knee surgeons do not do them.

As such, the use of UKR in the treatment of end-stage osteoarthritis is controversial. Fair comparison of TKR and UKR is hampered by differences in the baseline characteristics of patients being offered each procedure

	Crude		p value	Matched*	
	TKR	UKR		TKR	UKR
Number of patients	315 767	25 982		75 996	25 334
Age at surgery (years)	70·4 (9·1)	64·3 (9·7)	<0·0001	64·7 (9·3)	64·7 (9·4)
Unit type					
Public hospital	269 857 (86%)	22 085 (85%)	0·044	64 179 (85%)	21 544 (85%)
Independent hospital	33 542 (11%)	2872 (11%)	0·030	9141 (12%)	2801 (11%)
Independent sector treatment centre	12 368 (4%)	1025 (4%)	0·822	2676 (4%)	989 (4%)
Thromboprophylaxis					
Drugs					
Unfractionated or low molecular weight heparin	209 221 (66%)	15 816 (61%)	<0·0001	48 546 (64%)	15 438 (61%)
Aspirin	34 668 (11%)	3924 (15%)	<0·0001	9519 (13%)	3858 (15%)
Warfarin	3447 (1%)	211 (1%)	<0·0001	727 (1%)	208 (1%)
Direct thrombin inhibitor	12 487 (4%)	1101 (4%)	0·025	2654 (4%)	1050 (4%)
Other	23 410 (7%)	1927 (7%)	0·986	5205 (7%)	1830 (7%)
None/unspecified	32 514 (10%)	3003 (12%)	<0·0001	9345 (12%)	2950 (12%)
Mechanical					
Thromboembolic deterrent stockings	203 878 (65%)	16 772 (65%)	0·965	49 246 (65%)	16 323 (64%)
Foot pumps/intermittent calf compression	67 884 (22%)	5820 (22%)	0·001	16 686 (22%)	5653 (22%)
Other	4129 (1%)	272 (1%)	<0·0001	1012 (1%)	266 (1%)
None/unspecified	39 876 (13%)	3118 (12%)	0·003	9052 (12%)	3092 (12%)
Indices of multiple deprivation (quintiles)[13]					
1	48 598 (15%)	2951 (11%)	<0·0001	8744 (12%)	2915 (12%)
2	59 609 (19%)	4361 (17%)	<0·0001	12 247 (16%)	4291 (17%)
3	70 398 (22%)	5791 (22%)	0·983	16 723 (22%)	5666 (22%)
4	71 870 (23%)	6179 (24%)	<0·0001	19 070 (25%)	5986 (24%)
5	65 292 (21%)	6700 (26%)	<0·0001	19 212 (25%)	6476 (26%)
Hypertension	140 581 (45%)	8926 (34%)	<0·0001	26 542 (35%)	8851 (35%)
Sex (male)	135 515 (43%)	13 547 (52%)	<0·0001	39 573 (52%)	13 106 (52%)
Fixation					
Cemented	285 749 (91%)	23 407 (90%)	0·033	68 776 (91%)	22 822 (90%)
Uncemented	26 135 (8%)	1 944 (8%)	<0·0001	5684 (8%)	1912 (8%)
Hybrid	3883 (1%)	631 (2%)	<0·0001	1536 (2%)	600 (2%)
Ethnic origin					
Undefined	38 832 (12%)	3654 (14%)	<0·0001	9983 (13%)	3593 (14%)
White	263 333 (83%)	21 506 (83%)	0·010	63 547 (84%)	20 934 (83%)
Mixed race	615 (<1%)	54 (<1%)	0·647	114 (<12%)	51 (<1%)
Asian	8587 (3%)	515 (2%)	<0·0001	1643 (2%)	511 (2%)
Black	2992 (1%)	120 (1%)	<0·0001	471 (1%)	116 (1%)
Other	1408 (1%)	133 (1%)	0·127	238 (<1%)	129 (1%)
Cases done by consultant	231 151 (73%)	22 255 (86%)	<0·0001	34 998 (86%)	21 628 (85%)
Cases per consultant per year	73·9 (52·5)	85·7 (56·6)	<0·0001	84·7 (58·8)	84·8 (55·5)
Comorbidities (Charlson index)[14]					
None	240 663 (76%)	20 865 (80%)	<0·0001	60 935 (80%)	20 291 (80%)
Mild	60 152 (19%)	4298 (17%)	<0·0001	12 560 (17%)	4233 (17%)
Moderate	11 389 (4%)	642 (3%)	<0·0001	1988 (3%)	635 (3%)
Severe	3563 (1%)	177 (1%)	<0·0001	513 (1%)	175 (1%)
American Society of Anesthesiologists score[15]					
1	36 461 (12%)	5885 (23%)	<0·0001	16 050 (21%)	5463 (22%)
2	228 079 (72%)	17 725 (68%)	<0·0001	53 268 (70%)	17 507 (69%)
3+	51 227 (16%)	2372 (16%)	<0·0001	6678 (9%)	2364 (9%)

Data are n (%) or mean (SD). TKR=total knee replacement. UKR=unicompartmental knee replacement. *No significant differences after matching.

Table 1: **Baseline and matched demographics**

(known as confounding by indication); for instance, UKR is often offered to younger patients who, because of their higher activity levels, tend to have better functional outcomes, but increased failure rates.[1,3,4]

The aim of this study was to comprehensively compare the rates of adverse outcomes after TKR and UKR, with large datasets from the National Joint Registry for England and Wales (NJR), Hospital Episode Statistics (HES), and the Office for National Statistics (ONS). We have studied multiple outcomes, including complications, readmission, reoperation, and death.

Methods

Data source

We analysed NJR records linked to data from the HES database. The NJR began collecting data in 2003 and contains details of more than 1 million joint replacements, making it the largest joint registry in the world.[1] For this study, we extracted data for all knee replacements done between the start of data collection on April 1, 2003, and Aug 28, 2012. Where possible, we linked these data to corresponding records in the HES database. Records could be linked to HES if they took place in, or were funded by, an NHS trust in England. HES provides additional information for every patient (including detailed comorbidity information and deprivation indices), and about every procedure (including length of stay and need for blood transfusion or critical care). Additional linked records contain details of readmissions, reoperations, and revisions not recorded in the NJR database. Data for all-cause mortality are provided by the ONS; these data are linked periodically to the NJR database. The data used here were extracted from the NJR shortly after the latest NJR–ONS linkage. Patients consent for their data to be collected from the NJR. The National Information Governance Board (now the Confidentiality Advisory Group) gave us permission to link the datasets (application number ECC 1-02 (FT3)/2013). We consulted the National Research Ethics Service who confirmed that we did not need local research ethics committee approval.

Procedures

We did analyses to compare the outcomes of TKR and UKR by six measures: rates of revision, revision/reoperation, and readmission; length of stay, complications of surgery, and mortality. To address the problem of confounding by indication, we have matched patients with propensity scoring techniques. We compared the reasons for revision (as reported by the operating surgeon) and the revision operation (exchange of modular components or secondary patellar resurfacing, conversion to primary TKR, complex revision) for the two procedures. Complex revisions were defined as revisions to hinged components or components with stems or wedges, or two-stage procedures. We restricted our analyses to patients older than 18 years undergoing primary knee replacement for osteoarthritis. We excluded patellofemoral replacements, so-called complex primary knee replacements, and primary operations with augmentation and stems (implying a complex deformity). We showed significant differences in baseline characteristics between groups (table 1).

Statistical analysis

We used propensity score matching to generate matched cohorts for comparison.[16] First, we estimated the effects of each confounder on treatment allocation using a logistic regression model. Using these estimates, we generated a score representing the probability of each knee receiving UKR; we matched three TKR patients to every one UKR patient on the basis of this propensity

	Survival for TKR (%; 95% CI)	Survival for UKR (%; 95% CI)	Hazard*/subhazard† ratio (95% CI)	NNT (95% CI)
Revision				
4 years	96·4% (96·2–96·5)	92·7% (92·3–93·1)	1·97 (1·84–2·12)	30·0 (26·1–34·7)
8 years	94·6% (94·2–94·9)	87·0% (86·2–87·9)	2·12 (1·99–2·26)	17·6 (15·6–19·9)
Revision/ reoperation				
Overall	87·2% (86·7–87·8)	80·4% (79·4–81·4)	1·38 (1·31–1·44)	14·7 (13·2–16·6)
0–3 months	..	..	0·46 (0·38–0·56)	..
3 months–8 years	..	..	3·34 (2·75–4·07)	..
Mortality				
30 days	99·76% (99·71–99·81)	99·94% (99·88–99·97)	0·23 (0·11–0·50)	543·6 (467·2–839·6)
90 days	99·53% (99·45–99·59)	99·78% (99·68–99·85)	0·47 (0·31–0·69)	399·0 (309·9–696·7)
1 year	99·22% (99·15–99·28)	99·47% (99·37–99·55)	0·69 (0·58–0·83)	420·2 (303·9–778·2)
4 years	95·66% (95·46–95·84)	96·71% (96·41–96·98)	0·75 (0·68–0·82)	93·5 (75·6–732·7)
8 years	88·52% (87·85–89·16)	89·10% (88·06–90·06)	0·85 (0·79–0·92)	62·1 (43·4–115·5)

Hazard ratios less than 1 favour unicompartmental knee replacement. The revision/reoperation hazard ratios are split because of time-varying hazard (see text); survival and NNT are provided at 8 years. NNT=number needed to treat (ie, number of patients switching treatment to avoid one adverse event). TKR=total knee replacement. UKR=unicompartmental knee replacement. *Hazard ratios are provided for mortality (Cox regression). †Subhazard ratios are provided for revision and revision/reoperation (competing risks regression).

Table 2: **Propensity-score matched survival models by timepoints up to 8 years by outcome**

score. When calculating the propensity score, we included confounders consisting of age, sex, ethnic origin, Charlson comorbidity index, American Society of Anaesthesiologists (ASA) score, Index of Multiple Deprivation (in quintiles and by each subgroup), implant fixation, type of mechanical or chemical thromboprophylaxis, unit type (public, private, independent sector treatment centre), surgical caseload (the combined number of TKRs and UKRs done by the surgeon in charge in the year of surgery), and the grade of the primary surgeon (consultant or trainee). Body-mass index (BMI) had a large proportion of missing data and, we therefore did not include it in the propensity score analysis. As a sensitivity analysis, we calculated estimates for complete case datasets, with and without BMI, and after completing the missing values using multiple imputation (appendix).

See Online for appendix

We used proportional hazards regression to examine survival outcomes (revision, revision/reoperation, and mortality). Because mortality can be regarded as a competing risk for revision surgery, we used competing risk regression when examining revision and revision/reoperation;[17] we used Cox regression for the mortality comparison. We examined continuous outcomes (length of stay) using linear regression and binary outcomes (complications during the primary admission) using logistic regression, and examined readmission rate (within the first year) using a zero-inflated Poisson model.

For the survival models, we tested the proportional hazards assumption using Schoenfeld's residuals. If the proportional hazards assumption was violated, we analysed survival hazards in sections, with breaks being placed at the points of divergence from proportionality. Results of these models are presented as overall survival percentages, hazard ratios, and numbers needed to treat (NNT, representing the number needing to switch from one procedure to the other to avoid one adverse event, calculated with Altman and colleagues'[18] method).

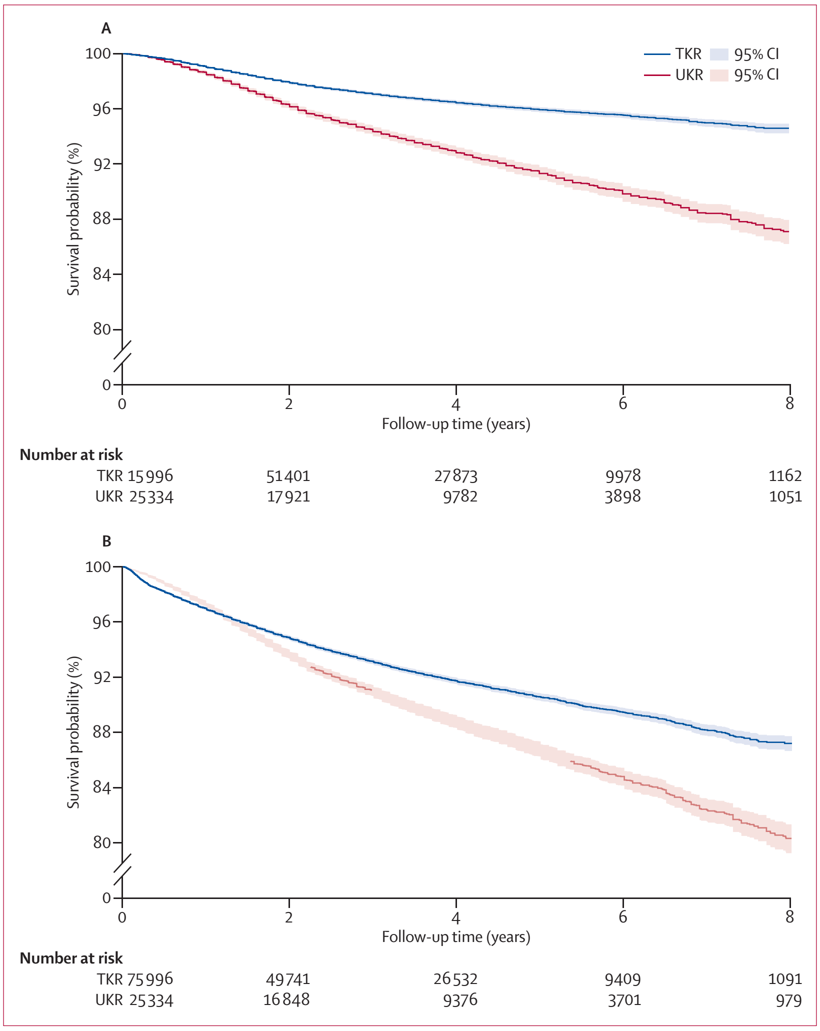

Figure 1: **Kaplan-Meier curve of revision (A) and revision/reoperation (B) to 8 years in matched patients**
UKR=unicompartmental knee replacement. TKR=total knee replacement.

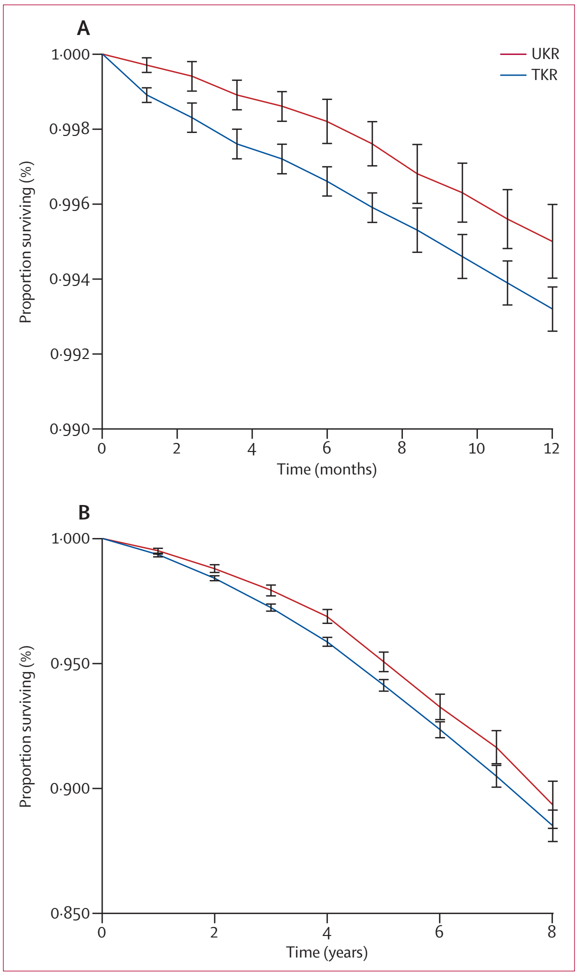

Figure 2: **Survival curves showing comparison of mortality at 1 year (A) and 8 years (B)**
UKR=unicompartmental knee replacement. TKR=total knee replacement. Error bars show 95% CI.

We used Stata (version 12.1) for all statistical analyses, and used R (R Foundation for Statistical Computing, Vienna, Austria) to do the matching on the basis of propensity score.

Role of the funding source

The sponsors of the study had no role in the design or conduct of the study. All authors had full access to the data and take responsibility for the contents of the study and the decision to proceed to publication. DWM is the guarantor.

Results

From a pool of 552 015 records from the NJR, and after exclusion of patellofemoral and complex primary knee replacements, a total of 341 749 records (315 767 TKRs and 25 982 UKRs) could be linked to HES records. We recorded significant differences in several baseline variables (table 1). On the basis of propensity score, 25 334 (98%) of 25 982 UKRs could be matched to TKRs. Because we matched on a ratio of three TKRs to each UKR, the matched study group consisted of 101 330 knees, of which 75 996 were TKRs. After matching, we achieved balance with respect to confounding factors (table 1).

After matching, implant survival at 8 years (with all-cause revision as the endpoint) was greater for TKR than for UKR (table 2, figure 1). Inclusion of all reoperations reduced overall survival values and attenuated the difference between TKR and UKR. At 8 years, implant survival (with revision/reoperation as the endpoint) was greater for TKR than for UKR (subhazard ratio 1·38, 95% CI 1·31–1·44; table 2). The survival hazard for reoperation varied with time. More reoperations were done for TKR than for UKR in the first 3 months before the TKR hazard became shallower and the hazards crossed at around 15 months (figure 2). Therefore, a break was introduced at 3 months; in the first 3 months, the revision/reoperation rate was significantly higher for TKR than for UKR; between 3 months and 8 years the risk of revision/reoperation was significantly higher for UKR than for TKR (table 2).

Mortality was significantly higher for TKR at all timepoints (table 2). At 30 days, 90 of 76 074 patients (cumulative mortality rate 0·24%, 95% CI 0·19–0·29) had died in the TKR group compared with seven of 25 358 (0·06%, 0·03–0·12) in the UKR group. Hazard ratios were 0·23 (0·11–0·50) at 30 days and 0·47 (0·31–0·69) at 90 days. Although the hazard ratio fell with time, the absolute difference in death rates increased to 1·1% (0·7–1·4%) at 4 years, before decreasing to 0·7% (–0·5 to 1·9) at 8 years (figure 2).

Mean length of stay was 1·38 days shorter for UKR than for TKR (mean 5·52 [SD 3·97] for TKR; 4·14 [2·24] for UKR; 95% CI 1·33–1·43, p<0·0001) and readmission within the first year was significantly less likely in UKR than in TKR (incidence rate ratio 0·65, 0·58–0·72). Intraoperative complications, blood transfusion, thromboembolism, stroke, and myocardial infarction were significantly less likely for UKR than for TKR (table 3).

	Crude comparisons		Propensity matched comparisons	
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Intraoperative complications	0·70 (0·57–0·87)	0·001	0·73 (0·58–0·91)	0·006
Critical care admission	0·72 (0·60–0·86)	<0·001	0·84 (0·69–1·02)	0·075
Blood transfusion	0·18 (0·12–0·26)	<0·001	0·25 (0·17–0·37)	<0·0001
Thromboembolism	0·42 (0·34–0·52)	<0·001	0·49 (0·39–0·62)	<0·0001
Stroke	0·28 (0·13–0·63)	0·002	0·37 (0·16–0·86)	0·021
Myocardial infarction	0·32 (0·20–0·52)	<0·001	0·53 (0·31–0·90)	0·018

Odds ratios less than 1 favour unicompartmental knee replacement.

Table 3: **Crude and matched logistic models for complications**

	TKR		UKR		Hazard ratio (95% CI)	p value
	Rank	N (%)	Rank	N (%)		
Loosening/lysis	1=	351 (25·1)	1	385 (30·1)	3·17 (2·75–3·67)	<0·0001
Infection	1=	351 (25·1)	7	61 (4·8)	0·50 (0·38–0·66)	<0·0001
Pain	3	152 (10·9)	2	264 (20·6)	5·08 (4·16–6·21)	<0·0001
Instability	4	141 (10·1)	8	58 (4·5)	1·20 (0·88–1·62)	0·254
Malalignment	5	107 (7·7)	6	76 (5·9)	2·04 (1·52–2·75)	<0·0001
Stiffness	6	99 (7·1)	11	12 (0·9)	0·36 (0·20–0·66)	0·001
Other reasons	7	88 (6·3)	4	135 (10·6)	4·40 (3·36–5·76)	<0·0001
Dislocation/dissociation	8	30 (2·2)	5	92 (7·2)	10·01 (6·52–15·38)	<0·0001
Wear	9	30 (2·2)	9	27 (2·1)	2·49 (1·48–4·20)	0·001
Progression of disease	10	27 (1·9)	3	144 (11·3)	15·09 (10·00–22·78)	<0·0001
Periprosthetic fracture	11	15 (1·1)	10	22 (1·7)	4·24 (2·19–8·18)	<0·0001
Implant fracture	12	5 (0·4)	12	3 (0·2)	1·68 (0·40–7·05)	0·478
Total	..	1396	..	1279	..	..

Percentages are the percentage of all revisions that are done for the reason given. Hazard ratios represent the overall risk of being revised for each reason at 8 years. Hazard ratios less than 1 favour unicompartmental knee replacement. TKR=total knee replacement. UKR=unicompartmental knee replacement.

Table 4: **Reasons for revision in unicompartmental knee replacement (UKR) and total knee replacement (TKR; matched analysis, revisions recorded in NJR only)**

Reasons for revision differed between TKR and UKR (table 4). Although aseptic loosening was the commonest reason for revision after either operation, significantly more TKRs than UKRs were revised for infection and stiffness. Progression of arthritis and bearing dislocation are modes of failure that were almost exclusive to UKR, and as a result, the odds ratio for revision for either reason greatly favoured TKR. Unexplained pain, aseptic loosening, malalignment, wear, periprosthetic fracture, and other unspecified reasons for revision were significantly more common in UKR than in TKR. The proportion of patients being revised for instability or implant fracture was much the same for the two operations (table 4).

Although most revisions in TKR required augments or constrained implants, most of those recorded for UKR in the NJR were conversions to a primary TKR. These conversion-type operations accounted for the difference

	TKR			UKR			Hazard ratio (95% CI)	p value
	N	% of revisions	% of all cases	N	% of revisions	% of all cases		
Bearing/patella	259	19%	<1%	81	6%	<1%	0·90 (0·70–1·16)	0·430
Revision to primary total knee replacement	247	18%	<1%	854	67%	3%	10·07 (8·74–11·62)	<0·0001
Complex revision	890	64%	1%	344	27%	1%	1·12 (0·99–1·27)	0·068
Total	1396	..	..	1279	..	..	..	..

Hazard ratios less than 1 favour unicompartmental knee replacement. TKR=total knee replacement. UKR=unicompartmental knee replacement.

Table 5: **Type of revision operation (matched analysis, revisions recorded in NJR)**

in the revision rate between UKR and TKR. The probability of part revisions (including secondary patellar resurfacing in TKR, and bearing exchange in UKR) did not differ between TKR and UKR, nor did they for complex revisions (table 5).

Discussion

This study shows a significantly higher risk of revision/reoperation in patients undergoing UKR than for matched patients undergoing TKR. However, patients undergoing TKR are at increased risk of medical complications; they are twice as likely to have a venous thromboembolism, myocardial infarction, or deep infection, three times as likely to have a stroke, and four times as likely to need blood transfusions. As a result, these patients are four times more likely to die in the first 30 days after surgery and about 15% more likely to die during the first 8 years. Inpatient stays are longer, and readmissions are more likely after TKR than after UKR. Revisions of TKRs are more commonly due to stiffness or infection, whereas revisions of UKR are more usually done for unexplained pain, arthritis progression, or other unspecified reasons. Most revisions of UKR are conversions to a primary TKR, whereas most revisions of TKR are more complex procedures requiring larger components and increased levels of constraint—constrained implants introduce more tibiofemoral conformity to address the instability caused by the loss of the normal soft-tissue and bony constraints during revision knee surgery. Conversion-type operations accounted for all the difference in the revision rate between UKR and TKR.

In patients with disease suitable for TKR or UKR, the decision of which procedure to offer should take into account the advantages and disadvantages of each, both in terms of functional results and of adverse outcomes. Although previous studies have examined functional outcomes, we have focused on adverse outcomes.[19,20] In the short term, UKR has proved to have clear advantages, with reduced hospital stays, complications, readmissions, and mortality; however, it does have the disadvantage of an increased revision and reoperation rate. The difference in revisions largely consists of conversion-type operations, which are similar to a primary TKR. When offered a choice of elective surgical procedures, patients are likely to rate mortality and major complications (such as myocardial infarction and stroke) as the worst possible outcomes. As such, these outcomes should be as, or more, important factors in the decision about which procedure to offer compared with the risk of reoperation/revision. Although revision is a deeply undesirable result after joint replacement, mortality after elective surgery is devastating.

Revision, reoperation, and death are uncommon outcomes of either procedure. At 4 years, the NNT to avoid a revision is 30 cases and to avoid a death is 93, whereas 8 years the NNT to avoid a revision is 18 cases and to avoid a death is 62. However, because knee replacement is very common, even small percentage differences affect large numbers of patients. Although estimates of the proportion of patients eligible for UKR vary (and have been estimated at up to 47%[10]), a conservative estimate from a previous study[11] suggested that, at present, 21% of patients undergoing TKR meet the criteria for UKR. At 4 years, if 21% of the patients in the NHS currently undergoing TKR underwent UKR instead, a potential annual saving of 169 deaths, at the cost of 405 additional revisions, would result. However, as the revision rate of UKR tends to decrease with increasing surgeon volume, if these surgeons perform more UKRs per year, there might be fewer additional revisions.[21]

The difference in revision rates between UKR and TKR has been well described (panel).[1,3,4] In this study, this difference is smaller than that shown in registry reports (which are unadjusted for patient characteristics)[3,4,11] and observational studies (which have varying degrees of adjustment).[23,24] This difference suggests that patient selection for UKR or TKR exerts a powerful effect on ultimate revision rate. Inclusion of reoperations, which registries do not class as revisions, effaces this effect further. Reasons for the residual difference are multifactorial and include the presence of additional failure mechanisms in UKR (mainly progression of disease), more subtle patient factors (such as the degree of cartilage damage before surgery),[30] and threshold for revision. UKR is easier to revise than TKR, and revision usually results in a primary TKR. As a result, UKR is five times more likely to be revised than a TKR with the same patient-reported outcome.[19]

Differences in mortality between the two procedures have been previously reported;[28] however, as far as we are aware this study is the first to confirm this finding in matched patients and the first to show an effect in the medium term. The reasons for the differences recorded have been discussed in the accompanying paper,[31] but the primary reason is likely to be that UKR surgery is less invasive, both for soft tissue and bone, than is TKR.[12,32] Similar factors explain the findings for perioperative morbidity. In addition to the short-term effect, this study shows that, although the effect of surgery on mortality is attenuated over time, an effect is seen into the medium term. Causality is more difficult to prove at longer follow-up times, but might be related to long-term consequences of complications of surgery, such as myocardial infarction, stroke, venous thromboembolism, or prosthetic joint infection, which we have shown to be more common in TKR than in UKR.

The strengths of this study include the use of an unselected registry sample, reducing the likelihood of sampling bias. The use of linked NJR/HES datasets allows adjustment for a very large set of potential confounders. The use of propensity score matching allows comparison of comparable cohorts and addresses the risk of confounding by indication.[16] This study is the most comprehensively matched study of these two treatments so far.

Weaknesses relate to the observational nature of the study. To address sources of bias, we matched the patients, which raises the possibility that some of the findings, particularly differences in long-term mortality, could result from inadequate matching. If matching were inadequate, then the difference in mortality would be expected to progressively increase over time. However, although the survival curves for mortality diverge progressively for 4 years, they become parallel or converge slightly in the second half of the study, which is what would be expected because medical complications of surgery would only affect mortality for a limited time.

The matching process might also restrict the external validity of the study by excluding unmatchable patients. However, the crude differences between the groups were not large, and 25 329 (97·5%) of 25 982 UKRs could be matched to a TKR. This finding could be attributable to the fact that patients who are eligible for UKR could be offered TKR or UKR, dependent on their surgeon's views, and suggests that the findings shown here might be generalisable to the wider population of patients who are appropriate for UKR.

Propensity score matching has been used for more than 30 years and has gained popularity in diverse specialties of medicine, social sciences, and economics.[33,34] In that time, the understanding of the strengths and limitations of propensity score matching has increased.[35] Although the aim of propensity score matching is to recreate the conditions of a randomised trial in an observational study, this can only be the case if all causes of confounding by indication are eliminated by the matching process (the principle of strong ignorability[33]). In reality, all observational studies will have a degree of unmeasured confounding and the results of propensity score matched studies such as this must be interpreted with this in mind.[35] In this study, patients were matched for 20 variables, and the effect of a 21st, BMI, was examined after matching and shown not to affect outcome (appendix). Potential sources of unmeasured

Panel: Research in context

Systematic review

We searched Medline, Embase, and the Cochrane Library on July 31, 2013, to retrieve all studies comparing unicompartmental knee replacement (UKR) and total knee replacement (TKR) in terms of revision rate, mortality, or complications. Clinical trials and observational studies were included in the review. Additionally, the latest annual reports of six major NJRs (England and Wales, Australia, New Zealand, Sweden, Norway, and Denmark) and one large regional joint registry (Emilia-Romagna, Italy) were retrieved and interrogated. The search identified two randomised trials,[20,22] two retrospective cohort studies,[12,23] and three case-control studies.[24–26] One retrospective study (examining patients with UKR in one knee and TKR in the other) was excluded from the review because it studied a design of UKR that has subsequently been withdrawn as a result of design factors leading to a high revision rate.[27] Only two randomised control trials comparing the two procedures exist. The first, a study of 102 patients at 15 years, reported implant survival at 89·8% (95% CI 74·3–100) for UKR and 78·7% (56·2–100) for TKR, with better functional outcomes with UKR than with TKR.[20] However, substantial attrition was noted, with 45 (44%) of 102 knees in patients who died before 15 years. The second, of 104 knees at very early follow-up, reported better survival with TKR than with UKR at the cost of a higher rate of deep vein thrombosis and a greater fall in haemogolobin concentration with TKR.[22] All major joint registries show a higher revision rate for UKR than for TKR. Unmatched data from the NJR annual report shows hazard ratios between 2·9 and 3·7;[1] similar data from Australia show similar hazard ratios of 2·59 (95% CI 2·50–2·69) and from New Zealand of 2·72 (2·47–2·99).[3,4] Mortality in UKR and TKR has been little studied. The NJR 7th annual report shows hazard ratios of 0·36 (95% CI 0·22–0·58) at 90 days and 0·64 (0·58–0·72) at 5 years, adjusted for age, sex, and American Society of Anaesthesiologists' grade.[28] A large observational study of 2840 TKRs and UKRs adjusted for age, sex, body-mass index, and comorbidities showed significantly increased rates of manipulation under anaesthesia (odds ratio 13, p<0·001), admission to critical care (7·4, p=0·049), and postoperative transfusion (8·5, p=0·036), and for complications overall (2·8, p<0·001).[12] In a smaller study, Lombardi and colleagues[26] reported a shorter length of stay (1·4 days for UKR *vs* 2·2 days for TKR, p<0·001); similar differences are reported in two other small studies.[25,29] In Lyons and colleagues'[23] retrospective cohort study, reduced survival for UKR was reported with an institutional database (5606 TKRs and 279 UKRs, 10 year survival 95% for TKR, 90% for UKR), and in the small case-control study of Amin and colleagues.[24]

Interpretation

Our study is the most comprehensive comparison of UKR and TKR that has been done so far. The NJR is the largest joint replacement database in the world, and our study is the first to address the problem of confounding by indication with propensity score techniques. Most previous comparisons of the two techniques have compared survival alone, and this is the first study to compare TKR and UKR with such a wide selection of endpoints. This study has supported finding of a higher revision and revision/reoperation rate reported by earlier joint registery studies, but has also shown important advantages of UKR in terms of speed of recovery, rate of readmission, ease of revision, morbidity, and mortality. Patient-reported outcomes have not been examined in this study, but previous work has suggested that they could be better in TKR than in UKR. Future studies should examine patient-reported outcomes.

confounding include the radiological stage of disease (patients with only partial loss of cartilage thickness are more prone to revision than those with full-thickness cartilage defects[30]); differences in complexity of operation (although cases with augmentation and those labelled as complex primaries are excluded, there might be more subtle differences between procedures); more detailed patient-level comorbidity data (although reliability of HES comorbidity data are well established[36,37]), and level of preoperative activity. A randomised trial would be required to address these limitations; such a trial is in progress.[38] However, the primary outcomes of this trial are patient-reported outcome measures; the size of a randomised controlled trial that would be required to produce meaningful information about rarer outcomes such as mortality is prohibitive. Such questions are best answered with observational study designs.

The choice of which procedure to offer will depend on the individual patient. Decisions about treatment should be made on the basis of all outcome measures, not merely the revision rate of each procedure. This study should provide important evidence for making such decisions.

Contributors

ADL conceived the study, did the statistical analyses, and drafted the manuscript. AJ contributed substantially to the statistical design and analysis and made major contributions to the writing of the paper. HP made substantial contributions to the conception of the work and the drafting of the manuscript. DWM contributed substantially to the conception and design of the study and made significant revisions to the manuscript. All authors approved the submitted version and agree to be accountable for all aspects of the work.

Declaration of interests

ADL declares that he has no competing interests. HP has been a paid speaker for Biomet, who are manufacturers of orthopaedic implants including unicompartmental and total knee replacements. DWM receives royalties related to the Oxford UKR and is paid consultancy fees by Biomet. AJ has received honoraria from Roche, held advisory board positions (which involved receipt of fees) for Anthera, and received consortium research grants from Servier; none of these entities were related to this study. The Nuffield Department at Oxford receives research funding from Biomet, Stryker, and Zimmer, all of whom are manufacturers of orthopaedic implants. None of these companies were involved in the funding or conduct of this study.

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