Failure of Unicompartmental Knee Replacement

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Doctor of Philosophy

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Abstract

Failure of Unicompartmental Knee Replacement
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Unicompartmental knee replacement (UKR) is the principal alternative to total knee replacement (TKR) in the treatment of end-stage knee osteoarthritis. It involves less tissue resection, resulting in lower rates of morbidity and faster recoveries compared to TKR. However, UKR has a significantly higher revision rate compared to TKR. As a result, whilst over a third of patients are eligible for UKR, only around 8% receive it.

A comprehensive comparison of matched patients undergoing TKR and UKR was undertaken using a large dataset from the National Joint Registry for England and Wales (NJR). Failure rates (revision, reoperation, complications and mortality), length of stay and patient-reported outcomes (PROMs) were studied. Whilst patients undergoing TKR had lower reoperation and revision rates, they had higher rates of morbidity and mortality, longer hospital stays, and inferior PROMs compared to UKR. The main reason for revision in UKR was loosening.

In view of the high revision rate in UKR, NJR data was studied to identify modifiable risk factors for failure in UKR. Important patient factors were identified including age, gender and pre-operative function. Surgeons with a higher UKR caseload had significantly lower revision rates and superior patient-reported outcomes. Increasing usage (offering UKR to a greater proportion of knee replacement patients) appears to be a viable method of increasing caseload and therefore of improving results. Surgeons with optimal usage (around 50% of patients, using appropriate implants) achieved revision/reoperation rates similar to matched patients undergoing TKR.

Two clinical studies were conducted to establish whether the use of cementless fixation would improve fixation and reduce the revision rate of UKR. Cementless UKR was demonstrated to be safe and reliable, with PROMs similar or superior to those demonstrated in cemented UKR. Patients with suboptimal cementless fixation were examined and pre-disposing technical factors were identified. Finally, using NJR data, the effect of the introduction of cementless UKR on overall outcomes was examined. The number of cementless cases was small, and no significant effect on implant survival was demonstrated. However, patients undergoing cementless UKR demonstrated superior PROMs.

These studies demonstrate that UKR has numerous advantages over TKR in terms of morbidity, mortality and PROMs. If surgeons perform high volumes of UKR (achievable by increasing their UKR usage), these advantages can be attained without the large difference in revision rates previously demonstrated. Cementless UKR is safe and provides superior fixation and outcomes in the hands of high-volume surgeons. Further work is needed to quantify the revision rate of cementless UKR, and to assess its results in the hands of less experienced surgeons.

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To my father

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Abbreviations

ACL	Anterior Cruciate Ligament
AMOA	Anteromedial Osteoarthritis
ANCOVA	Analysis of Covariance
AOANJRR	Australian Orthopaedic Association National Joint Replacement Registry
ASA	American Society of Anaesthesiologists (grading system)
ASCII	American Standard Code for Information Interchange
BMI	Body Mass Index
CI	Confidence Interval
DTI	Direct Thrombin Inhibitor
EQ5D	EuroQuol 5 domain quality of life questionnaire
HA	Hydroxyapatite
HES	Hospital Episode Statistics
HR	Hazard Ratio
HSCIC	Health and Social Care Information Centre
HTO	High Tibial Osteotomy
ISTC	Independent Sector Treatment Centre
IMD	Index of Multiple Deprivation
IQR	Inter-Quartile Range
KOOS	Knee Injury and Osteoartirits Outcome Score
KSS	(American) Knee Society Score
LOWESS	Locally-Weighted Scatterplot Smoothing
MCID	Minimal Clinically Important Difference
MCL	Medial Collateral Ligament

MCS	Mental Component Summary of the SF-12
MI	Multiple Imputation
MINORS	Methodological Index for non-randomised studies
NJR	National Joint Registry
OA	Osteoarthritis
OKS	Oxford Knee Score
OR	Odds ratio
OUKR	Oxford Unicompartmental Knee Replacement
PCL	Posterior Cruciate Ligament
PCS	Physical Component Summary of the SF-12
PMMA	Poly Methyl Methacrylate
PROMS	Patient Reported Outcome Measures
PTIR	Patient-Time Incidence Rate
RA	Rheumatoid Arthritis
RCT	Randomised Controlled Trial
RSA	Radiostereometric analysis
SD	Standard Deviation
SF-12	Short-form 12-question quality of life questionnaire
TAS	Tegner Activity Scale
TEDS	Thromboembolic Deterrent Stockings
TKR	Total Knee Replacement
UHMWPE	Ultra-High Molecular Weight Polyethylene
UKR	Unicompartmental Knee Replacement
VAS	Visual Analogue Scale
WOMAC	Western Ontario and McMaster Arthritis Scale

Chapter 1 Introduction and literature review

1.1. Background and aims

Unicompartmental Knee Replacement (UKR) is an alternative to Total Knee Replacement (TKR) in osteoarthritis (OA) of the knee. Whilst TKR involves resection of the entire joint surface and one or more ligaments of the knee, UKR only replaces the parts of the knee that are affected by the disease process. By preserving the unaffected joint surfaces and ligaments, it restores the normal, ligament-driven kinematics of the knee, resulting in a higher rate of return to high-demand activities[1,2]. The operation involves a smaller incision and less bone resection, and as a result, previous studies have provided evidence that UKR is associated with shorter hospital stays, less need for blood transfusion and lower rates of associated morbidity and mortality[3-5].

However, data collected from National Joint Registries (NJRs) consistently demonstrate that patients who have received UKR are around 2.5-3.5 times more likely to undergo revision surgery compared to those who have received TKR at up to ten years[6-9]. Whilst between one third and half of all patients are eligible for UKR, only around 8% receive it. The revision rate reported by NJRs contrasts with that reported in case series from high-volume units, where ten-year survival figures are similar to those reported in series of TKR[10-13]. This discrepancy suggests that many of the factors leading to the high revision rate are modifiable, either by changes in patient selection or surgical practice.

[*] Elements of this chapter were published as part of three review articles: "Knee Replacement for osteoarthritis" (Maturitas 2013), "Cementless Unicondylar Knee Arthroplasty (Orthopaedic Clinics of North America 2013), and "Unicompartmental Knee Arthroplasty: state of the art and future developments" (Archivio di Ortopedia e Rheumatologia, 2012).

In addition to being more frequent, revisions of UKR in NJRs appear to be performed for different reasons from those in published series. The commonest reason for revision in NJRs is loosening of the implant-bone fixation, which is an uncommon reason for revision in published series[10-13]. This suggests that modifications to the implant, to make fixation more reliable in less-experienced hands, may also represent an important avenue to improve the revision rate of UKR.

The aim of this thesis is to determine and address modifiable risk factors for failure of UKR so as to reduce the failure rate overall. As such, this thesis has three broad aims:

- To delineate the failure rate of UKR in national data, using multiple metrics, and to compare it to the failure rate of TKR.
- To determine the modifiable factors, in terms of patient selection and surgical practice, affecting the failure rate of UKR.
- To determine whether the introduction of a new design of implant can reduce the failure rate of UKR by improvement of bone-implant fixation.

1.2. Osteoarthritis and the knee

Osteoarthritis (OA) is a very common condition amongst older adults, although precise estimates of prevalence are difficult to obtain due to differences in diagnostic criteria[14]. In the knee, evidence of OA is apparent on radiographs in up to 50% of the population over the age of 75, whilst up to one third have symptomatic knee OA[15]. Use of more sensitive tests such as Magnetic Resonance Imaging (MRI) demonstrates evidence of osteoarthritis in up to 89% of people over the age of 50, irrespective of the presence of symptoms[16]. Whilst most people with osteoarthritis remain asymptomatic, end-stage osteoarthritis requiring knee replacement is increasingly common. In the USA, the

incidence of Total Knee Replacement (TKR) has increased from 402,100 per year in 2005 to 676,000 in 2009, and has been projected to increase to 3.5 million per year by 2030[17,18].

The principal symptom of OA is pain, with varying degrees of stiffness and deformity. Whilst OA is a progressive disease, the level of pain associated with it often fluctuates and can be affected by factors such as a patient's weight or activity level, or by extraneous factors such as climate or time of day. The level of pain experienced by patients with osteoarthritis correlates with radiological measures of disease severity, but this is not consistent and a proportion of patients with radiographs demonstrating severe end-stage disease can remain asymptomatic[19].

Osteoarthritis can be considered to be a disorder of cartilage homeostasis, in which the repair mechanisms of cartilage, mediated by chondrocytes, fail, tipping the balance in favour of cartilage degradation[20]. In response to inflammation and cartilage degeneration, significant remodelling occurs in subchondral bone leading to the characteristic radiological features of subchondral sclerosis and osteophyte formation[21].

Risk factors for knee OA include obesity, increasing age, family history, previous knee injury (particularly anterior cruciate ligament (ACL) and meniscal injury), and abnormal loading caused by limb malalignment[21,22]. On a microscopic level, osteoarthritis is considered a disease of the entire joint, but in most cases, the macroscopic defect is primarily restricted to a single compartment of the knee, usually the medial tibiofemoral joint (Figure 1-1)[23]. Progression to the remainder of the joint is largely dependent on the status of the ACL, the attritional rupture of which is associated with progression to tricompartmental disease[24].

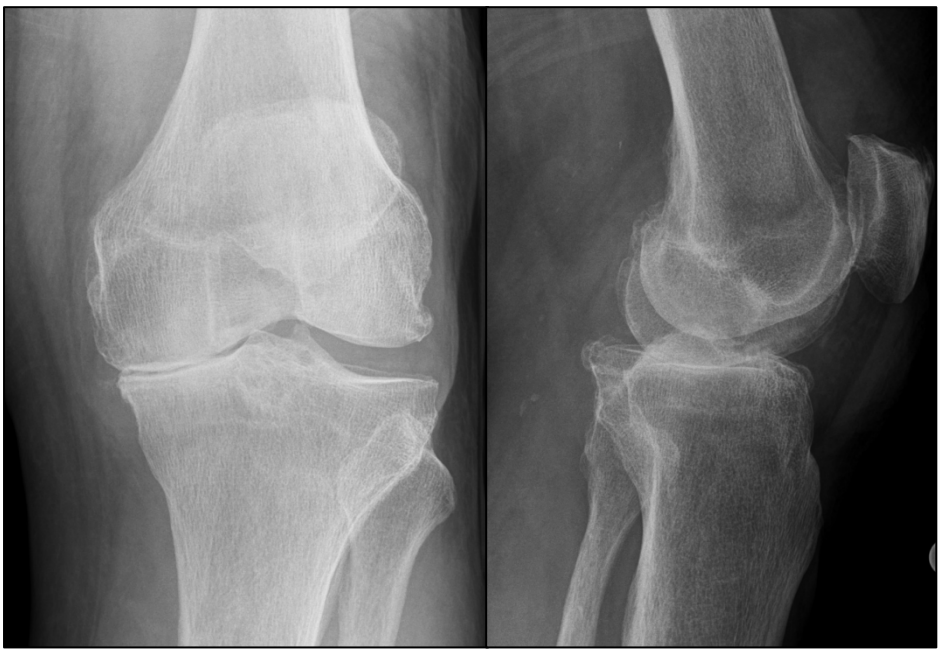


Figure 1-1: Medial compartment osteoarthritis (anteroposterior and lateral radiographs). Pre-operative radiograph of a patient from the multicentre study reported in Chapter 7 of this thesis.

1.3. Non-arthroplasty treatment for osteoarthritis

Even amongst patients referred to orthopaedic surgeons to be considered for knee replacement, up to two thirds are considered ineligible, often because symptoms have not reached the stage where joint replacement is indicated[25]. Whilst knee replacement is the only treatment for osteoarthritis that is considered curative, it is only indicated for end-stage disease and several treatments are indicated for disease which has not yet reached this stage[26-28]. Strong evidence exists that regular exercise, physiotherapy, weight loss (if overweight), orthotics and walking aids are helpful for patients with osteoarthritis, alone or in combination with simple analgesics and non-steroidal anti-inflammatory drugs[26,28,29].

In terms of pharmacological therapies, there is weak evidence for the use of glucosamine[30] or chondroitin[21,31], and these are not currently recommended for use in the UK by the National Institute for Health and Care Excellence (NICE)[27]. Injected

corticosteroids appear to provide only short-term relief from symptoms, and injection of hyaluronic acid derivatives may produce a longer-lasting effect, although they take longer to act[26]. There is significant interest in the development of disease-modifying drugs for OA and several candidates (including therapies based on growth-factors, bone morphogenic proteins and calcitonin) are being investigated in pre-clinical trials[32]. Risedronate, a bisphosphonate usually used in osteoporosis, has been shown in clinical trials to have an effect on biomarkers of cartilage degradation but has not demonstrated any clinical or radiological effect on disease progression[33]. Strontium, another drug used in osteoporosis, has been found to confer benefits both in terms of symptoms and disease progression in a large, multi-centre trial[34]; however, concerns relating to the cardiovascular risks associated with strontium have led to its withdrawal from the market. The latest NICE draft guideline does not recommend the use of any disease modifying pharmaceutical treatments for OA outside the research setting[35].

Non-arthroplasty surgical treatments, such as arthroscopic debridement and lavage, have little evidence of effectiveness and are reserved for patients with mechanical symptoms or radiographic evidence of loose bodies[21,27]. Focal cartilage defects can be treated by techniques that stimulate the production of fibrocartilage (such as microfracture). Alternatively, such defects may be treated using transfers of cartilage from non-weight-bearing parts of the knee (mosaicplasty), or using sheets of chondrocytes, grown in culture after being harvested during an earlier arthroscopic procedure (Autologous Chondrocyte Implantation, ACI). These procedures are reserved for small, focal defects and are usually performed in younger patients[36]. High tibial osteotomy (HTO), which can be performed with or without cartilage or soft tissue procedures, are intended for younger patients with malalignment and normally early, unicompartmental osteoarthritis[37]. Acceptable results have been demonstrated with

osteotomy in more severe disease, in carefully selected patients, but it is largely considered a pre-arthroplasty procedure[38]. In most cases, knee replacement surgery remains the intervention of choice for patients with end-stage, symptomatic knee osteoarthritis.

1.4. Knee replacement

Most Total Knee Replacements in use today are modifications of the Total Condylar Replacement design, first introduced in the 1970s[39]. Likewise, most TKRs are performed using the medial parapatellar approach first described by von Langenbeck in 1874[40]. In the medial parapatellar approach, the knee joint is accessed through a midline skin incision and the patella and extensor mechanism are everted laterally to allow access to the joint surfaces (Figure 1-2). Various minimally-invasive surgical (MIS) techniques have been described with the aim of minimising trauma to the extensor mechanism. Examples include sub-vastus, mid-vastus, and quadriceps-sparing approaches[41]. Whilst there is some evidence that these techniques allow function to return more quickly following surgery, they are more technically challenging and are associated with longer tourniquet times and a higher rate of intra-operative complications[41]. As a result, they have not gained widespread popularity, and only around 3% of TKRs in England and Wales are performed using MIS techniques[6].

Once the joint is exposed, the ACL is excised and the tibial plateaux are resected using horizontal saw cut. The distal femoral joint surfaces are resected in their entirety using a transverse cut, and anterior and posterior cuts and chamfers. Depending on the severity of disease and surgeon preference, the posterior cruciate ligament (PCL) and the patellar joint surface may also be resected. Before the implants are inserted, the surgeon ensures that the resected surfaces of the tibia and femur are parallel to each other and an equal

distance apart in flexion and extension. This 'balancing' ensures that the knee is stable and that any pre-operative deformity is corrected. Balance can be achieved either by 'measured resection' where bony cuts are made according to bony landmarks, and residual soft tissue deformity is corrected with sequential ligamentous and capsular releases, or by 'gap balancing', where the femoral cuts are made parallel to the tibial cuts with the ligamentous structures in equal tension[42].

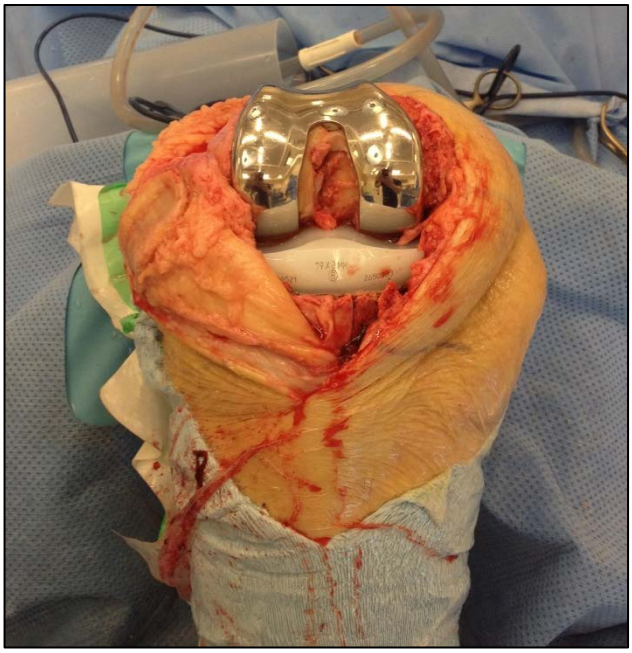


Figure 1-2: Medial parapatellar approach to TKR.
The patella and extensor mechanism is everted and TKR components are *in situ*

The tibial joint surface is replaced by an ultra-high molecular weight polyethylene (UHMWPE) bearing, normally attached to a metal base-pate, whilst the distal femur is resurfaced using a metal component. If there is patellofemoral osteoarthritis, the patella may be resurfaced using a UHMWPE 'button'. The excision of the menisci and cruciate ligament(s) necessitates the imposition of a degree of constraint between the tibia and femur, which is normally achieved by dishing of the tibial component with or without a cam-post mechanism to replicate PCL function. In most cases, the implants are cemented into place, but in around 5% of cases, the implants are coated to encourage bone

ingrowth and fixation without cement[6]. Cementless fixation is considered in more detail in Section 1.11.

1.5. Unicompartmental Knee Replacement

1.5.1. Rationale for Unicompartmental Knee Replacement

Whilst total condylar replacement became the pre-eminent design for knee replacements in the early 1970s, attempts to replace a single compartment of the knee were made as early as the mid-1950s. MacIntosh, and later McKeever described the use of metal or acrylic hemiarthroplasty to replace either the medial, lateral or both tibial plateaux[43,44]. In common with earlier attempts at knee replacement, the primary indication was rheumatoid arthritis (RA), with the authors recommending osteotomy for patients with OA. This is no longer the case: as RA is a disease of the entire joint, it is now considered a contra-indication to UKR (see Section 1.5.3). In current practice, the majority of UKRs are performed for OA.

The observation that even severe osteoarthritis is often macroscopically restricted to the medial compartment has been confirmed by long-term follow-up studies on un-treated patients[45]. Recent cross-sectional studies have demonstrated that around three quarters of patients with radiographic evidence of OA have disease restricted to the medial compartment on radiographs[23].

When osteoarthritis is present medially in the presence of intact cruciate ligaments, wear is commonly restricted to the anterior part of the medial compartment (anteromedial osteoarthritis, AMOA)[46]. Rupture of the ACL represents a threshold point, after which osteoarthritis progresses beyond the medial compartment, resulting in tricompartmental disease[47,48]. The preservation of full-thickness posteromedial cartilage in AMOA allows

any varus deformity to correct in flexion, maintaining the length of the medial collateral ligament (MCL) and allowing passive correction of the deformity in extension[49]. This prevents shortening of the MCL and allows the intra-articular varus deformity to be corrected in UKR without the need for the ligament releases used in TKR[50]. By restoring the anatomical and kinematic attributes of the joint to normal, UKR prevents secondary rupture of the ACL, with the aim of arresting progression of OA, whilst maintaining a normally-functioning knee.

1.5.2. Development and principles of Unicompartmental Knee Replacement

Following the early work of MacIntosh and McKeever, the first true Unicompartmental Knee Replacements were the Marmor and the St Georg 'Sled'[51,52], both of which were introduced in the late 1960s. The St Georg prosthesis (Link GmbH, Hamburg, Germany), and a modification of the Marmor prosthesis (the 'Journey' Knee, Smith and Nephew), remain in use today, and most UKR prostheses on the market work on similar design principles (Figure 1-3).

Figure 1-3: St Georg 'Sled' (left) and Journey UKRs*

When performed for AMOA, UKR restores pre-disease knee kinematics by restoring the height of the affected compartment and normalising ligament tension[1]. Therefore, in

* Images reproduced by permission of Waldemar Link GmbH and Smith and Nephew inc.

contrast to the situation in TKR, UKR should be no more constrained than the native knee to allow normal tibiofemoral movement under ligamentous control.

In most designs of UKR, including the Marmor and the St Georg, the metal femoral component is polyradial, to match the geometry of the native femoral condyle. In order to minimise implant constraint, the tibial component (which is made from UHMWPE, with or without metal-backing) is flat. The use of a more conforming fixed bearing leads to high shear stresses at the bone-implant interface and a high rate of failure, and such implants are no longer used[53,54]. Three designs, the Oxford Knee (OUKR, Biomet, Bridgend, UK), the Balansys Uni (Mathys, Bettlach, Switzerland) and the AMC/Uniglide (Corin, Cirencester, UK), use an unconstrained, UHMWPE mobile bearing between metal femoral and tibial components[49,55,56]. Whilst the Uniglide and Balansys have polyradial femoral components, the OUKR uses a single radius of curvature, rendering the articulation congruent throughout the range of knee flexion, minimising wear[57]. The OUKR accounts for around 70% of UKRs implanted in the UK, and will be covered in greater detail in Section 1.6[6,58-60].

Figure 1-4: Mobile-bearing UKR: Uniglide (left) and Oxford*.

* Images reproduced by permission of Corin Ltd. and Biomet Inc.

1.5.3. Indications for Unicompartmental Knee Replacement

The principal indication for UKR is anteromedial OA[47]. UKR for other indications (such as osteonecrosis and post-traumatic arthritis) is less common[61,62]. As such, this thesis considers UKR primarily in terms of its use for OA.

On the basis of the current literature, depending on indications, anywhere from 5% to 47% of patients with OA are eligible for UKR[63-65]. The optimal indications for UKR have been controversial since the introduction of UKR in the 1970s[64], and a large proportion of patients currently undergoing TKR may be eligible for UKR[66]. Indications have broadened with improvements in implant design, fixation and polyethylene durability. Indications may vary between implants, particularly between fixed and mobile-bearing designs[67].

There is broad agreement on the four factors which should be present for UKR to be indicated in AMOA[68]. Firstly, UKR should be performed for end-stage disease: results are significantly worse in patients with partial-thickness cartilage loss in the affected compartment and the threshold for performing UKR should be no lower than to perform any other joint replacement[69,70]. Secondly, the lateral tibiofemoral compartment should be functionally normal, with full-thickness cartilage preservation (although fibrillation or superficial cartilaginous damage may be safely ignored)[47,63]. The only exception to this is the presence of a full-thickness ulcer on the medial aspect of the lateral femoral condyle, which is associated with impingement by the tibial spine in severe varus deformity with subluxation, and which is un-loaded when the deformity is corrected[71].

The third universal criterion for UKR is the presence of intact, functional ligaments, most importantly the ACL[72,73]. Performance of UKR in ACL-deficient knees is associated with higher rates of wear[74] and loosening[47]. Given the ACL's role in restricting the disease to

the medial compartment, patients with radiographic appearances of AMOA have an intact ACL in the vast majority of cases, meaning that intra-operative conversion to TKR due to ACL deficiency should be rare[75]. Recently, cases have been proposed in which UKR may be performed without a functional native ACL. In carefully selected young patients with instability and medial compartment OA secondary to ACL rupture, combined ACL reconstruction and UKR has produced good results[76-78], whilst one study exists demonstrating success in the very short term for clinically stable elderly patients with a deficient ACL[79]. The final undisputed criterion is the absence of inflammatory disease, which is considered to affect the entire joint, ruling out any partial replacement[47,63,80].

Further contra-indications remain controversial. Early UKRs demonstrated a very high failure rate through polythene wear and aseptic loosening[74], leading some authors to propose very strict criteria based on disease morphology and patient factors[63,80]. In more than twenty years following the publication of these 'ideal patient' criteria[80], a combination of refinements in implant design and a growing body of evidence on UKR has suggested that the indications should be significantly wider[64]. Of these contra-indications, which include excessive weight[81], high activity level[64,82]; presence of patellofemoral disease (excluding severe lateral facet disease)[67,83-85]; lateral tibiofemoral pain[84,86] or chondrocalcinosis[64,87], none have been demonstrated to have any effect on outcome following UKR. Younger patients have a higher revision rate, but this finding is also seen in TKR[6] and good results have been demonstrated in younger patients[88]. The use of broad indications is further supported by the excellent results reported by units using them[12,13,55,89,90]. However, the majority of surgeons performing UKR perform very few, implying the continued use of narrow criteria for eligibility[91]. The influence of

patient factors on the performance of UKR is further considered in Section 1.10.1 and Chapter 4. The influence of differences in surgical practice is considered in Chapter 5.

1.6. Development of the Oxford Knee

1.6.1. Introduction and initial development

The Oxford Knee was first introduced in 1976 for bicompartmental implantation, and it has been used for UKR since 1982[92-94]. It is the most commonly-used UKR in the UK (as well as in New Zealand and Australia) and accounts for around 70% of all UKRs implanted in England and Wales[95-97]. Since its introduction, the design has been through two major modifications. The first modification (Phase 2) was intended to facilitate unicompartmental implantation and the second (Phase 3) facilitated minimally-invasive implantation. However, the design principles of the Oxford Knee have remained unchanged throughout these phases (Figure 1-5)[49].

Figure 1-5: Oxford Knee (Phase 1)*

*Image taken from Murray DW, Goodfellow JW, O'Connor JJ. The Oxford medial unicompartmental arthroplasty: a ten-year survival study. J Bone Joint Surg [Br] 1998;80-B:983-989, reproduced with permission and copyright © of the British Editorial Society of Bone and Joint Surgery

The Oxford Knee was designed to allow unconstrained tibiofemoral articulation whilst eliminating the excess wear which is a consequence of the point-loading resulting from the round-on-flat design of other UKRs[57]. To achieve that, the Oxford Knee employs an unconstrained mobile bearing with a flat under-surface and a concave upper surface, articulating with the flat tibial component and the hemispherical femoral component respectively (allowing fully-congruent articulation throughout the range of knee flexion without the imposition of constraint)[57].

1.6.2. Early results and rationalization of indications

The first clinical results for the Oxford Knee (as a bicompartmental prosthesis) were published in 1986[93]. This study reported 125 knees in 107 patients, 74 with osteoarthritis and 51 with rheumatoid arthritis. Patients were considered suitable for surgery if they could achieve at least 75° of flexion, had a flexion deformity of no greater than 40°, and varus or valgus deformity no greater than 30°. Posterior cruciate deficiency was considered a contra-indication but ACL deficiency was not. The reported implant survival was 88%, although patients who were well-functioning following implant-retaining re-operations (largely due to dislocation of the meniscal bearing) were excluded from this figure.

For unicompartmental implantation, the initial indication was end-stage single-compartment osteoarthritis, with a correctible deformity (as evidenced by stress radiographs) and an intact posterior cruciate ligament[94]. Soon after the introduction of the Oxford Knee, it was observed that the absence of a functional ACL was the greatest predictor of failure[94], and ACL deficiency became a contra-indication for OUKR (see Section 1.5.3). AMOA, in which an intact ACL leads to isolated medial compartment disease with preservation of full thickness cartilage posteriorly and a correctible deformity, was described in 1991 and has become the principal indication for OUKR[46].

With these indications, the first long-term study of the OUKR demonstrated 98% implant survival at 10 years[98]. Whilst indications have been refined in the light of poor results in patients undergoing OUKR following high tibial osteotomy[99], and those with partial thickness disease[70], the indications used in this first series are largely observed today.

1.6.3. Subsequent development of the OUKR

Phase 2 of the Oxford Knee (pictured in Figure 1-6) was introduced in 1987 and was designed for unicompartmental implantation. Femoral preparation in the Phase 1 design was by chamfer cuts using a saw and a cutting-block, as is common in TKR. In phase 2, a femoral mill was introduced which produces a cut femoral surface which is spherical. The non-articulating surface of the femoral component was redesigned to fit the prepared femur.

Figure 1-6: Oxford Knee (Phase 2)*

*Image taken from Murray DW, Goodfellow JW, O'Connor JJ. The Oxford medial unicompartmental arthroplasty: a ten-year survival study. J Bone Joint Surg [Br] 1998;80-B:983-989, reproduced with permission and copyright © of the British Editorial Society of Bone and Joint Surgery

Phase 1 and 2 were performed using a medial parapatellar approach similar to that used for TKR. UKR using the MIS technique, where implantation is performed through a short paramedian arthrotomy without eversion or dislocation of the extensor mechanism, was first popularised by Repicci[100]. The first MIS OUKR was performed in 1996, and the Phase 3 OUKR, which was designed specifically for MIS implantation, was introduced in 1998. Studies of MIS OUKR have demonstrated reduced blood loss and faster recovery times than conventional surgery, with no loss of accuracy of implantation when the Phase 3 instrumentation is used[101-103].

Since the introduction of the Phase 3 OUKR in 1998, there have been incremental changes in the design of the prosthesis. 'Anatomical' bearings were introduced shortly after the introduction of the Phase 3, with the aim of reducing the rate of bearing dislocation. An alternative design of femoral component with two pegs was introduced to confer improved security of fixation in deep flexion[104], and a domed tibial component was introduced specifically for lateral-compartment implantation[105]. The cementless OUKR was introduced in 2004 to provide reliable fixation whilst eliminating the problems associated with cement[106]. The results of the cementless OUKR form a substantial part of this thesis.

1.7. Study of outcome in joint replacement

Adequate assessment of outcome following medical interventions is essential for evidence-based practice. The assessment of outcome in joint replacement is particularly challenging given the large numbers of different systems on the market and the relative infrequency of poor outcomes and revision surgery.

Evidence for interventions in joint replacement is assessed on the basis of clinical studies. In 2000, the Oxford Centre for Evidence-Based Medicine established a hierarchy of study designs based on their innate susceptibility to bias[107]; this hierarchy has been adapted for orthopaedic studies (Table 1-1)[108]. Whilst the higher levels are considered to provide the strongest evidence, the choice of study design is influenced by a number of factors (including feasibility, ethics and cost). Each study type has inherent advantages and disadvantages and each type of study plays a role in establishing the evidence-base for new interventions.

Level	Study types
1	High-quality randomised controlled study (RCT) Systematic review or meta-analysis of level 1 RCTs.
2	Prospective comparative study (including registry studies) Non- level 1 RCTs (high levels of loss to follow-up or insufficient blinding) Systematic review of level 2 studies
3	Case-control study Retrospective comparative study Systematic review of level 3 studies
4	Case series
5	Case report Expert opinion

Table 1-1: Levels of evidence for therapeutic studies in orthopaedic surgery (adapted from the CEBM 2000 levels of evidence)

A number of these study designs are used within this thesis; these are explored further in Chapter 2. In this Section, the different types of study which are used when interventions are compared within orthopaedic surgery will be briefly described. Following that, in Section 1.8, the different outcome metrics used in orthopaedic studies will be discussed.

1.7.1. Controlled studies in joint replacement

The Randomised Controlled Trial (RCT) is one of two designs of study that are considered to provide 'level 1' evidence for an intervention (the other being the systematic review of many RCTs). Randomisation of patients to one intervention or

other leads to balanced groups and addresses the issue of selection bias. Blinding of patients and assessors addresses detection bias[109]. As such, a well-conducted RCT is considered to be the study design least susceptible to bias.

However, in surgery, and orthopaedic surgery in particular, there are specific challenges which make RCTs difficult to perform. Important challenges include the difficulties of blinding surgical interventions, and strong surgical and patient preferences for one intervention or another (which can cause problems with recruitment to trials)[110,111]. The effect of heterogeneity of disease and differences in surgical expertise may represent unmeasured confounders. The fact that RCTs are normally performed in expert centres, and that they often have strict inclusion and exclusion criteria, limits the external validity of such studies.

There are also substantial logistical difficulties with the conduct of orthopaedic RCTs. As joint replacement is an intervention with a generally high level of success, detection of significant differences between implants is difficult, particularly when only an incremental improvement is expected with the new intervention being tested (as is often the case when new implants are introduced). If hard endpoints such as revision are used, very large numbers of patients need to be recruited and followed up for a long time before a significant difference can be demonstrated. This also has important cost implications[112].

The numbers of randomised trials are increasing within orthopaedic surgery, due to two main mechanisms[113]. The first is the development of new outcome measures (see Section 1.8) and the introduction of innovative trial designs, which allow relatively small RCTs to provide meaningful results[114,115]. The second factor is the development of structures to allow increased co-ordination and funding of large, multi-centre randomised trials[116].

1.7.2. Observational studies

Whilst RCTs provide the strongest evidence for any intervention, the evidence for most, if not all, of the interventions currently in use in orthopaedic surgery has come from observational studies. With the increased focus on evidence-based medicine and the increased ease with which data can be collected, it is likely that observational studies will become more, rather than less, important within orthopaedic surgery[117].

Observational studies can be divided into two broad groups: comparative studies (cohort or case-control studies), and non-comparative studies (case series). National Joint Registries, which represent a specialised form of observational study, are covered in more detail in Section 1.7.3.

Whilst RCTs control for potential confounders by the use of randomisation, observational studies control for measured confounders during the analysis phase of the study. As inclusion criteria are generally broader for observational cohort studies compared to RCTs, the external validity of cohort studies may be greater than that of RCTs. However, even after adjusting for measured confounders, observational studies may be susceptible to bias from a number of sources. Selection bias (or confounding by indication) is a particular problem with observational studies[117]. Newer statistical methods have been developed to address this problem by matching patients based on their baseline factors[118,119]. However, these methods depend on accurate and comprehensive recording of all possible confounders, and there remains the risk of confounding by unknown and unmeasured factors[120].

Case series are very common within orthopaedic surgery, and play an important role in the assessment of joint replacements. Case series are the main method by which survival of joint replacements can be assessed, as they allow large numbers of patients to be

recruited and followed-up. Survival analyses within case series are the principal source of data used for benchmarking of new implants by bodies such as the Food and Drug Administration (FDA) in the USA and the Orthopaedic Data Evaluation Panel (ODEP) in the UK[121]. Whilst case series are of limited use when comparing one intervention to another, they are particularly useful in examining the safety and durability of implants. The ability to include large numbers of implants and follow them up for long periods allows even relatively rare complications to be quantified.

1.7.3. Joint Registries

In Joint Registries longitudinal data is collected from large numbers of participating institutions before being assembled centrally. In most cases, a report is issued annually and raw data are released on request for research studies[122]. The principal aim of joint registries is to facilitate the identification of poorly-performing implants at the earliest possible stage, allowing modification or abandonment of such implants before large numbers are implanted[123].

The first national joint registry (NJR) was established in Sweden in 1975[124]. Since then, NJRs have been established in Finland (1980), Norway (1987), Denmark (1995), Australia, and New Zealand (both 1998), amongst others. The National Joint Registry for England and Wales was established in 2003, as a direct consequence of the poor results of the 3M Capital hip, which remained in widespread use for eight years in spite of very high early revision rates secondary to femoral loosening[125]. The NJR for England and Wales is currently the largest database of joint replacements in the world[6]. Evaluation of data from the NJR for England and Wales forms the basis of the first part of this thesis, and is covered in more detail in Chapter 2.

The principal advantage of NJRs is the large number of cases they report. In most cases, participation is near-universal (and in some cases is obligatory), which removes the problems of reporting and publication bias which may affect other longitudinal studies. The fact that NJRs study the population as a whole allows great diversity within cases studied, in terms of implant type, surgical technique and experience, patient selection and postoperative regimen. The large overall number of cases allows the study of these subgroups with acceptable power to draw accurate conclusions. The contemporaneous reporting of outcomes is intended to allow action to be taken to address poorly-performing implants (at least, if the poor performance is apparent early in the implant's life) before large numbers are implanted. NJRs have additional benefits in allowing surgeons to compare their results with their peers', and to allow easy identification of implants in the case of recall.

However, NJRs remain imperfect tools to measure outcome[126]. The large number of cases reported, and the reliance on operating units to report their cases, limits the quantity of data that can be gathered on each patient. In all NJRs, the primary measure of outcome is the rate of revision surgery; whilst this has the benefit of being objective and easy to measure, it has several deficiencies, which are covered in more detail in the next Section. Likewise, the divide between those gathering the data and those interpreting it may lead to a large amount of missing data[127] and may lead to difficulties in verifying more subjective variables (such as precise reasons for revision). In common with all observational studies, comparisons between interventions need to be adjusted for confounders. The reporting of raw comparisons without controlling for confounding factors may fail to highlight the demographic differences between groups receiving each implant, and the comparison of two types of joint replacement (such as UKR and TKR)

may fail to take into account innate differences between the two which may affect revision rate (in this case, the ease of revision of UKR as compared to TKR)[128].

1.8. Outcome metrics in joint replacement

The success or failure of a joint replacement may be measured by one of a number of metrics. Each metric has advantages and disadvantages, and the choice of outcome metric should be informed by the study design, the procedure being studied, and the practicalities of collection. Outcomes in joint replacement can be divided into solid end-points, such as the death of the patient or implant revision, and functional outcomes, which are normally collected using patient- or physician- completed questionnaires. A third category, 'objective' outcomes (such as radiological measures), are used less often. Each metric has strengths and weaknesses: in order to accurately assess the performance of a joint replacement, a multimodal approach is necessary[129].

1.8.1. Implant survival

Implant survival is the most commonly used outcome metric following joint replacement, and represents the principal outcome reported by the NJRs. It is a solid end-point, and has been described as the point at which both the surgeon and the patient agree that revision is preferable to continuing with the prosthesis in situ[130]. It is normally defined as the removal or exchange of any of the components of the joint replacement and can be reported for the entire joint replacement or specific parts (such as femoral or acetabular survival in total hip replacement)[7]. The addition of an extra component, such as secondary resurfacing of the patella after TKR, or the addition of a lateral or patellofemoral replacement to a medial UKR in the case of osteoarthritis progression, may also be considered to be a revision.

Revision rate is normally expressed as the proportion of implants that have been revised by a specific time-point, using Kaplan-Meier or life-table estimates, but may be expressed as the number of revisions per 100 implant years. The latter form of expression allows more straightforward statistical analysis and allows comparison of older and newer implants on a like-for-like basis. However, this form assumes a linear and constant revision hazard, which is rarely the case.

As a measure of implant function, however, revision rate has a number of deficiencies. The decision to revise an implant has several components, not all of which relate to the implant (or the knee joint) itself. In addition to the severity of the patient's symptoms, the health of the patient, the ease of the revision procedure, the chance of improvement following revision, and the resources available within the department all affect the decision to revise. As a result, revision rate alone may be insensitive to patients who have poorly functioning implants *in situ* but for whom revision is not deemed to be the best course of action (for instance, due to co-morbidity, or the expectation of poor results from revision). Bullens *et al* demonstrated a 5 year success rate of 96.7% for TKR on the basis of revision rate, but this fell to 73.3% if patient satisfaction scores was added as an endpoint[131]. Murray and Frost reported a similar effect if pain was added as an endpoint[132]. In addition, re-operations such as manipulation under anaesthetic for stiffness, or debridement for infection, are not considered to be revisions for the purposes of survival analyses[133].

Comparison of different classes of implant is further complicated by different thresholds for revision. Therefore, in two classes of implant with identical functional outcomes, the implant that is easier to revise will have an artificially high revision rate[128]. This is particularly pertinent to the comparison of UKR to TKR, where the revision rate of the former is higher despite better overall functional outcomes[134]. Likewise, if an implant has

a higher mortality rate (either due to patient selection or the surgery itself), patients who have died with the prosthesis in situ are censored from the analysis and can be considered successes on the basis of implant survival alone[135].

Finally, revision is a rare and often late outcome, even in poorly-functioning implants. At seven years, the worst-performing TKR reported by the NJR for England and Wales remains unrevised in 96.5% of the patients in whom it was implanted[6]; its revision rate differed by only around 2% from the best-performing. A randomised trial would need to recruit in excess of 1,000 patients in each group, and to follow the patients up for seven years, to detect a significant difference between these implants. As a result, there are significant logistical challenges to the use of implant survival, particularly in the setting of RCTs.

1.8.2. Measures of functional outcome

Many of the problems associated with the use of survival as an outcome measure may be addressed by the use of measures of pain and function. Outcome measures can be either surgeon-reported[136] or patient-reported[137], or can use a combination of the two[138]. Likewise, scores can be generic or specific to the knee joint, and it is likely that a combination of the specific and generic scores provides the most reliable measure of outcome following joint replacement[139].

Patient-reported outcome measures (PROMs) have the advantage over physician-reported scores in that they can be completed by post or in the presence of non-specialist assessors, as well as being less susceptible to optimism bias due to the surgeon assessing his own work[140]. PROMs ask questions relating to pain and function. Numerous PROMs exist, but the most commonly used are the Knee Society Functional Score (KSS-Fcn), and the Oxford Knee Score (OKS), both of which are used in this thesis and are covered in

more detail in Chapter 2. The Knee Society Objective Score (KSS-Obj) is a physician-completed measure (with domains including alignment and range of motion) and is often completed alongside the KSS-Fcn; again, this is considered later. The Western Ontario and McMaster Universities Arthritis Index (WOMAC) works on similar principles to the KSS-Fcn and the OKS, but may be used for assessment of both the hip and the knee. Details of these and other scores are contained in Table 1-2[141].

Outcome measure	Type	Reported by	Range	Notes
HSS	OA and knee Specific	Observer	0-100	Now obsolete – modified to become KSS.
KSS-Fcn	OA and knee Specific	Patient	0-100	Modified in 2012; this version still in widespread use
KSS-Obj	OA and knee Specific	Observer	0-100	Modified in 2012; this version still in widespread use
Bristol Knee Score	OA and knee Specific	Mixed	0-100	
WOMAC[a]	OA Specific	Patient	0-96	Reported as % or 3 subsets (pain, stiffness, function)
KOOS[a]	OA and knee specific	Patient	100-0	Reported as overall scale or 5 subsets (eg pain, QOL)
Oxford Knee Score	OA and knee specific	Patient	0-48	Previously reported as a scale from 60-12
SF-12	General QOL	Patient	0-100	Reported as SF-12 MCS and SF-12 PCS, both 0-100[b]
EQ5D	General QOL	Patient	-0.594-1	Also general health VAS, scored 0-100
Tegner Activity Scale	Activity questionnaire	Patient	0-10	0-10, 0 being unable to work, 10 being elite athlete

Table 1-2: Outcome measures used in joint replacement
Ranges are given as worst possible score – best possible score. [a]KOOS contains all the questions used by the WOMAC questionnaire, and hence the latter can be calculated from the KOOS. [b]Physical Component Score and Mental Component Score. OA – Osteoarthritis. HSS – Hospital for Special Surgery; KSS – Knee Society Score; Fcn-Functional component; Obj – Objective component; WOMAC – Western Ontario and MacMaster University Arthtiits scale; KOOS – Knee Injury and Arthritis Scale; SF – Short Form; EQ5D – EuroQol 5 Domain questionnaire.

Both the WOMAC and OKS have been extensively studied and are widely used. Both have been demonstrated to be reproducible (i.e., to give similar results if tested and re-tested on the same population), valid (to give similar results to other questionnaires on the same subject), and sensitive to change[137,142].

However, caution must be exercised when interpreting PROMs. Knee-specific scores may be affected by comorbidities, by disease in other joints and by age[143-147]; as a result, a decline in PROMs over time may be considered a normal finding[148]. Concerns exist about the floor and ceiling effects of such scores. Most were devised with the aim of

assessing the outcomes of elderly patients following TKR, and as a result, most focus on the assessment of pain and simple activities of daily living (examples are given in Appendix 2)[149]. As more evidence has emerged confirming the reliability and longevity of knee replacement, the patients undergoing such procedures are now younger and more active; these patients have higher expectations and may not consider themselves to have had a satisfactory result despite attaining levels of PROMs traditionally regarded as sufficient. In particular, differences between patients undergoing TKR and UKR may be masked by the ceiling effect of widely used PROMs; as a result, 'high activity' PROMs, such as the OKS Activity and Participation Questionnaire (OKS-APQ, which is a high-activity supplement to the OKS) and the High Activity Arthroplasty Score (HAAS) have been developed. It is hoped that the broader scope of these PROMs will allow the more accurate distinction between the outcomes of patients who place higher demands on their joint replacements[149,150].

General quality of life questionnaires include the EuroQol 5 domain (EQ5D) and Short Form-12 and 36 questionnaires (SF-12 and SF-36). Both ask a series of questions on health-related quality of life, including sections on pain, emotional wellbeing and physical disablement. Both general scores are in widespread use and have demonstrated acceptable reproducibility, validity and sensitivity to change[151,152]. There is significant agreement between the SF-36 and the EQ5D[153]. The SF-36 can be distilled into physical and mental component summary scores (PCS and MCS); the EQ5D can be presented by domain or as a summary score which ranges between -0.594 to 1. The EQ5D also records a visual analogue scale (VAS) for general health, which is reported separately.

1.8.3. 'Objective' measures

In medical studies, 'objective' outcome measures such as radiological or biochemical markers are often used as primary or secondary outcomes, often playing the role of

surrogates for a longer-term outcome such as mortality (see Section 1.8.4 below). Following joint replacement, 'objective' measures include physiological and radiological measures. The measurement of gait, using an instrumented treadmill, can quantify differences between pre-operative patients and those with unicompartmental or total knee replacement[154]. Radiological techniques may be used to estimate prosthetic wear or loosening. In both cases, interpretation of these radiographs can be qualitative (i.e. to record the presence or absence of radiolucent lines around the prosthesis, see Section 1.12[155]) or quantitative. Quantitative measures include the measurement of lines and angles on standard radiographic projections or the use of radiostereometric analysis (RSA)[156]. In RSA, pairs of synchronised, orthogonal radiographs are taken to provide a stereo image of the prosthesis. In some cases, radio-opaque marker balls of less than 1mm diameter are fixed to the bone at the time of surgery, and migration of the prosthesis is measured relative to these[157]. Alternatively, the thickness of polyethylene components can be measured using the metal components as reference points and compared to standard measurements to estimate the degree of polyethylene wear[158]. Non-radiographic objective measures of outcome include the assessment of gait prior to, and following joint replacement.

1.8.4. Surrogate outcome measures

As discussed in Section 1.8.1, implant revision is a rare and often late outcome, even in poorly performing implants. One approach for dealing with this problem is the development of surrogate measures of implant failure. Such measures have been developed in other areas of medicine where interventions are used to reduce the incidence of a rare or late end-point (Table 1-3). Early surrogates (also termed biomarkers) may be used as the primary endpoint in phase 2 clinical trials, where the

viability of a new intervention is tested before investing significant amounts of time and money in phase 3 trials to examine the ultimate outcome (in this case, implant revision).

Setting	Surrogate end-point	'Hard' end-point
Osteoporosis	Bone mineral density / FRAX score	Fracture[159]
Osteoarthritis	MRI with T2 mapping / dGEMRIC	Joint replacement[160]
Prostatectomy	Prostate-Specific Antigen doubling time	Survival[161]
Renal transplantation	Glomerular Filtration Rate	Transplant rejection[162]
Venous thromboembolism	Asymptomatic DVT on ultrasound	Fatal Pulmonary Embolism[163]

Table 1-3: Surrogate measures used in medical trials

Surrogate measures can include any factor which is present soon after primary surgery. Potential surrogate measures may include radiological measures such as RSA[164]; measures of postoperative pain (such as the level of analgesic usage[165]); or PROMs[134].

1.9. Clinical results of unicompartmental knee replacement

As UKR has been in widespread clinical use for over 30 years, there is now considerable evidence in the literature concerning its use. The aim of this literature review is to summarise the evidence for UKR in terms of survival and functional measures, and to present the results of studies comparing UKR and TKR. The latter include both clinical studies and NJR data.

1.9.1. Search strategy

An initial literature search was performed in December 2011, and this was repeated in July 2013. In both cases, Medline was searched with the string "Unicompartmental [OR] unicondylar [AND] knee". The initial search revealed 1076 studies; the second search revealed 1278. Studies were selected for further screening on the basis of title, and the abstracts of the selected studies were read. Review articles and previous departmental theses were read to identify any studies of interest which had not been retrieved during

the Medline search. A total of 326 studies were retrieved, read in full and indexed. From this library, long-term survival studies of UKR, and all studies comparing UKR to TKR were identified and are presented below. Inclusion criteria for each review are stated in the corresponding Section. The quality and risk of bias of the studies were assessed using validated scoring systems. Details of these quality assessments are given in Section 1.9.5.

1.9.2. Survival studies of UKR

As described in Section 1.8, survival analysis is the method by which most implants are assessed in clinical studies. In this Section, all existing survival analyses of UKRs in current use are summarised. Results for withdrawn implants are presented if their replacement represents only a re-branding (e.g. AMC to Uniglide), or minor modification (Marmor to Journey; Miller-Galante to ZUK; Oxford Phase 1 to Phase 3). Only studies with at least 50 patients and at least 10 years of follow-up are presented. In series where multiple follow-up intervals have been published, only the latest is presented. Full details of the studies are given in Table 1-4 and Table 1-5.

Twenty-two series meet these inclusion criteria, and data are reported on seven implants. All but two of the studies concern one of four implants, the Marmor, St Georg (both pictured in Figure 1-3, page 9), Miller-Galante (Zimmer inc., Warsaw IN), and the OUKR. The OUKR has been discussed in detail in Section 1.6. The other three implants have similar geometry to one another, with flat, fixed-bearing tibial components and polycentric femoral components. Tibial components are made from UHMWPE, either monoblock or with metal-backing. Originally, the Marmor and St Georg had monoblock tibiae, although metal-backed versions of each are now available. The Miller-Galante is only available with a metal-backed tibial component.

The remaining two studies report the results of the Genesis and Unix prostheses. The Genesis (Smith and Nephew) is similar to the Marmor implant, and is available with metal-backed or monoblock tibiae. It is available as both a cemented and a cementless implant. The Unix is a cementless implant which is described in more detail in Section 1.12. In common with the majority of UKRs, it has a polycentric femoral, and flat tibial component.

1.9.2.1. Studies of fixed-bearing prostheses

Six studies examine the Marmor prosthesis, with survival ranging from 70 to 93% at ten years[166-170]. The majority of the revisions in this series (42/70 in studies reporting revision reasons, 60%) were for loosening or subsidence, with a particular problem reported for smaller sizes. Of the remaining reasons for revision, the commonest was disease progression.

A single, large series of the St Georg 'Sled' from Bristol has been reported at various intervals[171-173]. 10 year survival has been reported as 87% at ten years[172]. A subsequent paper reports that, of those reaching ten years, 86% will survive to twenty years[90]. In common with the Marmor, loosening was a common reason for revision (6/19 revisions, 32%), but disease progression was the commonest reason given.

Five long-term survival studies exist for the Miller-Galante prosthesis[10,89,174-176]. All five series report functional outcomes in addition to survival. Several different outcome measures are reported, but overall outcomes are good (scores are given in full in Table 1-5). Loosening is less prevalent than observed in series of the Marmor prosthesis, and the commonest reason for revision (25/47 revisions, 53%) is disease progression, either to the lateral or patellofemoral compartments. Wear (8/47, 17%) and loosening (6/47, 13%) are the other major reasons for revision.

Heyse *et al* report a series of 223 patients below the age of 60 years, receiving the Genesis prosthesis[11]. All femora were cemented, but cemented monoblock (88 patients) and both cemented and cementless metal-backed tibiae (30 and 55 patients respectively) were used KSS-Fcn was reported as ranging between 92.0 and 96.1 depending on whether monoblock or metal-backed components were. The single long-term series of the Unix prosthesis (see Section 1.12) reports 92% survival at ten years but does not report functional outcomes[177].

1.9.2.2. Results of mobile-bearing UKR

The OUKR is the only mobile-bearing UKR with published long-term results. Eight series exist that meet the inclusion criteria for this review; two are from the designing centre, Murray *et al*'s series from 1998 (using the Phase 1 and Phase 2 prostheses) and Pandit *et al*'s series from 2011 (using the Phase 3 prosthesis)[13,98]. No functional outcomes were reported in the first series; Pandit *et al* report a mean OKS of 24.7 (SD 8.7) pre-operatively and 41.0 (7.5) at latest follow-up.

Seven further series originate from non-designing centres, with survival ranging from 82-94%[13,178-183]. The series with the lowest survival, by Vorlat *et al*, contained patients who had undergone previous HTO and these are noted to fare particularly poorly. Similarly, in the series of Kumar *et al*, four of the seven revisions were attributed to un-diagnosed inflammatory disease. As with the series of the Miller-Galante, clinical outcomes are good overall (Table 1-5). Around one third of revisions (56/171, 33%) were for disease progression, and 32/171 (19%) were for bearing dislocation. 24/171 (14%) revisions were for loosening, 18/24 of which were in two series, those of Vorlat *et al* and Price *et al*. There were no revisions for wear.

Author	Year	Prosthesis	Knees (lateral)	Design	Age (yrs)	Male (%)	Min. f/u	Survival given at	Number at risk	Survival %	Survival (95% CI)	Comments	MINORS (max 16)
Argenson	2013	Miller-Galante	160	Fixed, metal-backed	66	-	-	20	70	74	67-81	Survival given as 94% at ten years (NAR 160)	11
Kristensen	2013	Oxford 3	695	Mobile	64	53	0	10	<18.5	85	79-90	Mean f/u 2.9yrs; max 10.7yrs.	11
Rachha	2013	Miller-Galante	74	Fixed, metal-backed	64	-	5	10	-	95	-	Functional score (KSS-Fcn) 75.5 (45-90)	10
Foran*	2012	Miller-Galante	62 (3)	Fixed, metal-backed	68	33	15	15	19	93	83-98	10 year survival of 98% (96-100) in previous study[184]	10
Hall	2012	Unix	85 (20)	Fixed, metal-backed	65	57	8	10	34	92	83.8-100	Cementless fixation	10
Heyse*	2012	Genesis	251 (78)	Fixed / m-b / all poly	54	44	5	10	-	94	-	Cemented (147 knees) or hybrid fixation	9
Lim	2012	Oxford 3	400	Mobile	69	-	1	10	22	94	90.1-98.0		10
John	2011	Miller-Galante	94 (9)	Fixed, metal-backed	67	64	2	10	-	94	-		8
Pandit*	2011	Oxford 3	1000	Mobile	66	48	1	10	121.5	96	92.1-99.2		12
Price	2011	Oxford 1-3	682	Mobile	70	45	0.5	15	97	92	87.2-97.4	Survival given as 94% at ten years.	12
Emerson	2008	Oxford 2	55	Mobile	64	42	9	10	-	85	-		11
Vorlat	2006	Oxford 2	149	Mobile	66	-	5	10	74.5	82	74.3-88.9	84% in non-HTO patients	8
O'Rourke	2005	Marmor	136	Fixed, all-poly	71	-	21	20	-	84	-		-
Naudie	2004	Miller-Galante	113	Fixed, metal-backed	68	54	3	10	86	90	87-93		11
Rajasekhar	2004	Oxford 2	135	Mobile	70	57	2	10	24.5	94	84.0-97.8		10
Kumar	1999	Oxford 1 & 2	100	Mobile	71	38	1	10	-	85	78-92		9
Squire	1999	Marmor	140 (15)	Fixed, all-poly	68	50	15	15	140	87	78-95	Survival given as 89% at ten years	9
Murray*	1998	Oxford 1 & 2	143	Mobile	71	45	-	10	33	98	92.7-100		12
Tabor	1998	Marmor	67	Fixed, all-poly	61	42	5	10	-	84	74.2-93.8	Survival given as 79% at 15 years	10
Ansari	1997	St Georg	461	Fixed, all-poly	70	32	1	10	133	88	81-93		11
Cartier	1996	Marmor	207	Fixed, all-poly	65	-	10	10	54	93	80.7-100	Survival figure may be lower; see text.	9
Heck	1993	Marmor / C1 / C2	294 (39)	Fixed, all-poly	68	37	10	10	294	91	86.0-97.0	12 year survival as.6%. HSS good/excellent in 86%.	9
Marmor*	1988	Marmor	60 (7)	Fixed, all-poly	63	30	10	10	60	70	-	50% rated as 'excellent' on HSS scale.	11

Table 1-4: Long-term survival studies of unicompartmental knee replacement.
Series from designing centres are indicated by an asterisk next to the first author's name.

Author	Year	Prosthesis	Knees (lateral)	Outcome measure	Pre score	Latest score	Revisions	Revision reasons
Argenson	2013	Miller-Galante	160	KSS-Fcn	-	88 (45-100)	19	Disease progression (12), loosening (2), wear (5), infection (1)
Kristensen	2013	Oxford 3	695	-	-	-	49	Disease progression (16), loosening (11), pain (10), infection (4), fracture (2), other (6)
Rachha	2013	Miller-Galante	74	KSS-Fcn	-	75.5 (45-90)	5	Disease progression (2), pain (2), infection (2)
Foran*	2012	Miller-Galante	62 (3)	HSS	-	80% 'excellent'	5	Disease progression (2), pain (1), Component dissociation (1), not stated (1)
Hall	2012	Unix	85 (20)	OKS	-	38 (13-48)	Not given	Not given
Heyse*	2012	Genesis	251 (78)	KSS-Fcn	43.8 (SD 8.5)	92.0-97.2*	15	Wear/loosening (6), disease progression (4), Pain (3), Instability (2)
Lim	2012	Oxford 3	400	OKS	25.8 (SD 8.3)	37.8 (8.4)	14	Bearing dislocation (12), disease progression (1), infection (1)
John	2011	Miller-Galante	94 (9)	BKS	-	43.6 (28-50)	7	Disease progression (5), loosening (2)
Pandit*	2011	Oxford 3	1000	OKS	24.7 (SD 8.7)	41.0 (SD 7.5)	29	Disease progression (9), bearing dislocation (6), infection (6), pain (6), other (2)
Price	2011	Oxford 1-3	682	-	-	-	29	Disease progression (10), loosening (9), infection (5), pain(3), bearing dislocation (2)
Emerson	2008	Oxford 2	55	KSS-Fcn	56	90	5	Disease progression (7), loosening (1) impingement (1)
Vorlat	2006	Oxford 2	149	-	-	-	24	Disease progression (9), loosening (7), bearing dislocation (4) other (4)
O'Rourke	2005	Marmor	136	KSS-Fcn	-	53	19	Disease progression (9), Loosening (8), pain (2)
Naudie	2004	Miller-Galante	113	KSS-Fcn	53 (10-90)	80 (20-100)	11	Disease progression (4), wear (3), loosening (2), pain (1), traumatic ligament rupture (1)
Rajasekhar	2004	Oxford 2	135	KSS-Fcn	-	76 (51-100)	5	Loosening (3), pain (1), bearing dislocation (1)
Kumar	1999	Oxford 1 & 2	100	KSS-Fcn	45	71	7	Patient selection (see text, 4), disease progression (2), fracture (1)
Squire	1999	Marmor	140 (15)	KSS-Obj	42	71	14	Disease progression (7), tibial subsidence (6), pain (1)
Murray*	1998	Oxford 1 & 2	143	-	-	-	5	Disease progression (2), infection (1), pain (1), loosening (1)
Tabor	1998	Marmor	67	KSS-Fcn	-	77 (5-100)	11	Subsidence (6), Disease progression (2), inflammatory disease (2), not stated (1)
Ansari	1997	St Georg	461	BKS		79-86	19	Disease progression (9), loosening (6), pain (3), implant fracture (2), infection (1)
Cartier	1996	Marmor	207	KSS (both)	-	75% 'excellent'	7	Not given
Heck	1993	Marmor / C1 / C2	294 (39)	Various	-	-	16	Loosening (11), disease progression (4), infection (1)
Marmor*	1988	Marmor	60 (7)	HSS	-	50% 'excellent'	21	Loosening (11), disease progression (8), other (2)

Table 1-5: Survival studies of UKR: PROMs and revision reasons

1.9.3. Studies comparing UKR and TKR

A small number of studies exist comparing the outcomes of TKR and UKR, generally consisting of small studies which are often retrospective and of low methodological quality. Two studies are RCTs, six are cohort studies, three are case-control studies and two are self-controlled studies of patients receiving TKR in one knee and UKR in the other. Details are given in Table 1-6. Two studies are not included in this review as they compare prostheses which are now obsolete: these are detailed at the end of this Section.

1.9.3.1. RCTs

Newman *et al* performed the first RCT comparing St Georg UKR (50 knees) to Kinematic TKR (Howmedica, Rutherford NJ, 50 knees)[185]. The mean age of patients in each group was around 70 years; at the latest follow-up (15 years) a large number had died (45 cases), could not attend (17) or were lost to follow-up (3). Final analysis compared 24 UKRs to 23 TKRs. At 15 years, superior PROMs were reported in UKR, with 15/21 UKRs (71%) reporting 'excellent' results compared with 10/19 TKRs (53%). 3/52 UKRs and 4/50 TKRs were revised. The difference in survival between the two groups was not found to be statistically significant.

Sun *et al* randomised 56 patients to either an Oxford UKR, or an AGC (Biomet) TKR; results are reported with a mean follow-up of 52 months[186]. The UKR group had a shorter operative time, less blood loss, fewer DVTs and a lower transfusion requirement than TKR. KSS-Obj and mean range of movement was higher in the UKR group, but neither are described as being statistically significant. Seven patients in the UKR group required revision for tibial loosening (six patients) or subsidence. The authors attribute this to the learning-curve effect, as all were performed within the first two years of use of the OUKR. There were no revisions in the TKR group.

Noticewala *et al* reported a retrospective analysis of prospectively-collected data from their institutional database, comparing 70 UKRs to 128 TKRs[4]. WOMAC and SF-12 questionnaires are reported, adjusted for age, gender, comorbidities, diagnosis and pre-operative scores using linear regression. They report significant mean differences in all measures favouring UKR.

Sweeney *et al* performed a retrospective cohort study of 317 OUKRs to 425 Advance TKRs (Wright Medical Technologies, Arlington, TN) from a single institution[187]. The authors used hierarchical linear modelling to estimate the treatment effect of UKR and TKR at different time-points allowing for clustering by surgeon and adjusting for age and gender. At six months, there is no significant difference between TKR and UKR.

Brown *et al* conducted a retrospective cohort study specifically examining complication rates with TKR and UKR[188]. Minimum follow-up was 90 days. Overall, complications were more common in TKR (Odds Ratio 2.8, $p<0.001$). Specifically, stiffness (OR 13.0, $p<0.001$), transfusion (OR 8.5, $p=0.036$), and admission to critical care (OR 7.4, $p=0.049$) were significantly more common in TKR. Death, readmission and all other complications were more common in TKR, but none reached the threshold for statistical significance.

Lyons *et al* performed a retrospective analysis of 5606 TKRs and 279 UKRs (various designs of each were used)[189]. No adjustment was made for differences in pre-operative function. There were no significant differences in any WOMAC domain in terms of change score. KSS-Fcn was significantly superior in the UKR group both post-operatively and by change score ($p<0.001$). KSS-Obj was similar post-operatively, but as the UKR group had a higher pre-op score, the change scores were significantly better in the TKR group ($p=0.001$). The SF-36 Physical Component Score was significantly superior in UKR, both in post-operative and change scores ($p=0.005$, $p=0.03$,

respectively). There was no difference between groups in terms of Mental Component Score. The rate of implant survival was significantly higher in the TKR group.

Walton *et al* retrospectively compared 183 UKRs with a non-matched group of 142 TKRs, reporting a mean OKS of 37.8 in the UKR group and 35.5 in the TKR group, a significant difference ($p=0.04$)[190]. Weale *et al* retrospectively compared cohorts of patients undergoing Oxford UKR (31 patients) and AGC TKR (130 patients), reporting inferior survival in the UKR group with similar functional outcomes to TKR[191].

Manzotti *et al* conducted a case-control study of 68 knees, comparing computer-navigated TKR with controls who had undergone UKR, matched for age, gender and pre-operative knee function[192]. They recorded Knee Society Scores (functional and objective) and They reported significant differences in KSS-Fcn and GUIM score (a UKR-specific surgeon-completed score devised by the Italian UKR Users' Group[193]) No significant difference was detected in KSS-Obj.

A second case-control study, by Lombardi *et al*[3], compares early (1-52 months, mean 31 months) outcomes for TKR and UKR, with particular emphasis on speed of recovery. 103 consecutive UKR patients (115 knees) were matched to the same number of TKR patients (and knees) on the basis of age, gender, BMI and bilaterality. The number of revisions was similar as were the number of complications. Stiffness requiring manipulation under anaesthetic was significantly more common in TKR (7/115 v 0/115, $p=0.007$). Patients with UKR had a higher mean haemoglobin at discharge (12.1g/dL v 11.3 g/dL, $p<0.001$), shorter hospital stays (1.4 days v 2.2 days, $p<0.001$) and a better mean range of movement (77^{o} of flexion v 67^{o}, $p<0.001$). There was no difference in KSS-Fcn or KSS-Obj.

Amin *et al* matched 54 consecutive UKRs with 54 TKRs on age, gender, BMI, range of movement and pre-operative function[194]. At a mean follow-up of 59 months, there was a

superior range of movement, but inferior survival, in UKR compared to TKR. There were no differences in the outcome scores.

Two studies have been published comparing outcomes for UKR and TKR in the same patient. Costa *et al* performed simultaneous bilateral knee replacement in 34 consecutive patients, performing UKR in one knee and TKR in the other[195]. Five knees from the UKR group were revised, four of which had peri-prosthetic fractures (attributed to a poorly-designed drill guide), and one of which had unexplained pain. All revised patients received the EIUS system (Stryker, Marwar, NJ), which has since been recalled due to its unacceptably high revision rate. The authors could not detect any difference between the groups on the basis of KSS-Fcn or KSS-Obj scores. Dalury *et al* performed a retrospective review of all patients in a single centre who had received both a TKR on one side and a UKR on the other[196]. Range of motion was greater in the UKR group (123^{o} v 120^{o}), but there was no difference in functional scores between the groups. Of the 23 patients, 12 expressed a preference for their UKR knee, and none expressed a preference for their TKR knee.

Two further studies comparing UKR to TKR are excluded from this review as they used implants that have subsequently been discontinued. Similar to the Dalury *et al* study, a study by Laurencin *et al* compared TKRs to UKRs in patients who had received both, reporting a superior range of motion in UKR (123^{o} v 110^{o}). In this study, 44% of patients expressed a preference for their UKR, 12% for their TKR and 44% could perceive no difference between the function of their knees[197]. Rougraff *et al* retrospectively compared 120 UKRs to 81 TKRs, finding superior survival in UKR (the end point being any reoperation) and significantly superior combined KSS scores in the UKR group[198].

Author Year	Study design (MINORS)	Prostheses	Knees (start)	Knees (f/u)	f/u (yrs)	Age (yrs)	Male (%)	PROMs	Other outcome	1º PROM pre (μ, range)	1º PROM post (μ, range)	2º PROM pre (μ, range)	2º PROM post (μ, range)	Survival % (95% CI)	MINORS (max 24)
Sun 2012	RCT	Oxford AGC	28 28	28 28	4	60 61	36 32	KSS-Fcn Pain VAS	-	-	80.6 (70-100) 78.9 (70-87)	Not given – reported to be no significant difference post-op		75%* 100%	2/5
Newman 2009	RCT	St Georg Kinematic	52 50	13 17	15	69.6 69.8	35 58	BKS	Survival	54.7 (37-75) 57.2 (31-76)	92 (32-100) 87.5 (48-98)	-	-	89.8 (74.3-100) 78.7 (56.2-100)	3/5
Noticewala 2013	Prosepective cohort	Various	70 128	70 128	2	66.8 67.3	34 37	WOMAC SF-12	-	137.8 132.5	250.0 221.7	30.9 / 50.3 30.2 / 50.0	45.3 / 53.9 40.3 / 50.7	-	17
Sweeney 2013	Retrospective cohort	Oxford Advance	317 425	317 425	0.5	69.0 70.4	44 35	OKS WOMAC	-	18.7 (SD 7.3) 17.7 (SD 7.9)	AMD 0.7 (95% CI -1.3-2.8)	54.2 (15.3) 56.2 (16.6)	AMD 1.5 (95% CI -2.5-5.5)	-	17
Brown 2012	Retrospective cohort	Various	605 2,235	82 lost	>90 days	64.3 65.5	55 33	None	Comps.	-	-	-	-	-	21
Lyons 2011	Retrospective cohort	Various	219 5,606	219 5,606	7	67.7 66.1	53 49	WOMAC SF-12	Survival	48.8 (SD 17) 44.8 (SD 17)	74.0 (21.1) 71.4 (21.7)	32.0 / 54.2 30.2 / 52.7	39.1 / 53.0 37.0 / 52.2	90.4 (88.4-92.4) 94.9 (94.6-95.2)	19
Lombardi 2009	Case-control	Oxford Vanguard	115 115	115 115	6 wks	61 62	38 38	KSS-Fcn KSS-Obj	Speed of recovery	54 (20-100) 49 (-20-100)	63 (45-100) 55 (30-100)	57 (35-95) 11 (0-45)	85 (45-100) 84 (40-100)	-	16
Walton 2006	Retrospective cohort	Oxford Various	183 120	183 120	1	71.5 17.5		OKS Grimby	Return to sport	-	37.8 (SD 9.0) 35.5 (SD 9.7)	-	3.89 (SD 1.3) 2.76 (SD 1.1)	-	15
Manzotti 2007	Case-control	UC-Plus Search	34 34	34 34	4	69.1 70.7	41 41	KSS-Fcn, KSS-Obj	Alignment	49.7 (44-56) 48.2 (44-55)	83.5 (73-100) 78.9 (59-90)	45.1 (39-50) 43.9 (40-49)	80.6 (70-100) 78.9 (70-87)	-	16
Amin 2006	Case-control	Oxford PFC	54 54	52 53	5	68.1 69.3	57 50	KSS-Fcn KSS-Obj	Survival	54 (SD 16.6) 59 (SD 13.5)	85 (79-91) 84 (79-89)	29 (SD 14.1) 32 (SD 12.3)	82 (77-87) 84 (79-89)	88 (79-97) 100 (100-100)	18
Weale 2001	Retrospective cohort	Oxford AGC	31 130	31 130	2.3	62.4 71.3	48 41	OKS	Comps. Survival	-	36.5 (SD 10) 36.5 (SD 11)	-	-	2 revisions* 1 revision	17
Costa 2011	Self-controlled Prospective	EIUS, ZUK Scorpio	34 34	34 34	5	73 73	56 56	KSS-Fcn KSS-Obj	Survival	47 (26-65) 39 (22-58)	96 (61-100) 96 (64-100)	47 (30-70) 46 (25-70)	91 (50-100) 91 (50-100)	85%* 100%	17
Dalury 2009	Self-controlled retrospective	Various	23 23	23 23	3.8	69 68	52 52	KSS-Fcn KSS-Obj	Range of movement						17

Table 1-6: Studies comparing UKR to TKR (current designs)
For each study, UKR is on the upper line and TKR is on the lower. BKS – Bristol Knee Score
***survival figures for the Costa and Sun papers are given as proportion who did not need revision in the time period.**
No formal survival analysis was performed in the study of Weale *et al*. Methodological Index of NOn-Randomised trials is given for each study except the two RCTs – these are assessed on a six point checklist. See Text.

1.9.4. UKR and TKR in National Joint Registries

Whilst NJRs exist in 25 countries worldwide, many are at the very early stages of data collection and others contain too few UKRs to analyse separately. Of the seven large, established NJRs, three (Sweden, Finland and Norway) do not publish separate survival figures for TKR and UKR in their annual reports, although survival from the Finnish and Swedish registries have been published in paper form[199,200]. Of the remaining four, three (England and Wales, Australia and New Zealand) publish separate survival figures per year for TKR and UKR. The remaining register, in Denmark, publishes overall survival figures supplemented by hazard ratios for comparison of UKR and TKR. Italy does not currently have a national registry, but has a large, established registry in the northern region of Emilia-Romagna which publishes separate figures for TKR and UKR. The unadjusted survival figures for TKR and UKR in each registry are displayed in Table 1-8.

In all registries, there is a significantly higher revision rate for UKR. Hazard ratios range from 2.25-3.79. Three registries (England and Wales, Australia and New Zealand) report main reasons for revision (Table 1-7). Reasons for revision vary between registries, but the most frequent reasons for revision are similar in each: aseptic loosening, unexplained pain, bearing dislocation/instability and progression of arthritis. The NJR for England and Wales does not have a specific code for bearing dislocation; surgeons are likely to record bearing dislocations as implant failure, dislocation/subluxation or instability.

Rank	England and Wales		Australia		New Zealand	
	Reason	%	Reason	%	Reason	%
1	Aseptic loosening	24	Aseptic loosening	47	Pain	36
2	Pain	24	Progression	23	Aseptic loosening	34
3	Other (incl. progression)	20	Pain	11	Bearing dislocation	9
4	Instability	6	Infection	4	Progression	7
5	Implant failure	5	Fracture	3	Infection	3

Table 1-7: Top five reasons for revision of UKR in NJRs
Reasons and percentages taken from latest annual report

Two registries collect PROMs from all (England and Wales) or some (New Zealand) of their patients. Neither report comparisons routinely in their annual reports, but extracts of their data have featured in two recently-published journal articles[134,201]. One more study, using postal questionnaires, was performed using patient data from the Norwegian joint registry[202]. The results are displayed in Table 1-9.

Lygre *et al* identified patients from the Norwegian Arthroplasty Register who had received either UKR or TKR for osteoarthritis, sending KOOS and EQ5D questionnaires by post to assess their function[202]. Only prostheses used in at least 100 procedures were included (Genesis, Miller-Galante and Oxford UKRs; AGC, Genesis I, LCS (de Puy) and NexGen (Zimmer) TKRs). Responses were received from 1344 patients (372 UKRs, 972 TKRs). Small but statistically significant differences were detected in 3/5 of the KOOS subscales, adjusted for age, gender and time since surgery. No significant difference was detected in the EQ5D index, nor in the VAS for pain or satisfaction. None of the differences in KOOS subscales met the level considered clinically significant. Analysis of each question of the KOOS revealed a significant difference favouring UKR in four cases, but only one (ability to bend the knee fully) reached clinical significance.

The New Zealand Joint Registry collects PROMs in the form of OKS from a subset of 10% of patients. The paper by Rothwell *et al* reports mean OKS for UKR and TKR, but no statistical comparison is undertaken[134]. The overall, unadjusted mean OKS for UKR was 39.5 points (95% CI 39.2-39.8); for TKR it was 37.7 points (37.5-37.8).

Baker *et al* used data from the NJR for England and Wales to compare PROMs in 505 patients following UKR and 23,393 patients following TKR[201]. Unadjusted postoperative EQ5D and OKS were significantly superior in UKR, but there was no difference in adjusted (for age, gender and pre-operative score) change scores.

Country	Year	Knees (n, %)	Age (μ, SD)	Male (%)	Indication OA (%)	Survival % (95%Confidence Intervals) at different time-points (years post-op)					HR for revision (UKR, 95%CI)
						1	2	5	8	10	
England and Wales	2012	44,081 (8.8) 448,925 (89.8)	64.4 (10.0) 70.0 (9.4)	53 43	99 97	98.8 (98.9-98.7) 99.6 (99.6-99.7)	96.9 (96.7-97.1) 99.1 (99.0-99.1)	92.8 (92.4-93.1) 98.0 (97.7-98.0)	89.2 (88.4-89.9) 97.2 (97.1-97.4)	-	2.63 (2.43-2.85) -3.79 (3.64-3.96)
Australia	2012	36,971 (10.6) 309,673 (88.7)	-	54 44	99 97	97.8 (97.6-97.9) 99.0 (98.9-99.0)	-	91.5 (91.1-91.8) 96.2 (96.1-96.3)	-	84.7 (84.1-85.4) 94.4 (94.3-94.6)	2.59 (2.50-2.69)
New Zealand	2012	6,621 (10.2) 58,289 (89.5)	66.4 (9.6) 68.5 (9.7)	48 48	98 94	98.2 99.3	96.3 98.6	93.3 97.3	90.4 96.3	88.0 95.7	2.72 (2.47-2.99)
Emilia-Romagna, Italy	2010	3,584 (11.7) 27,118 (88.3)	67.4 71.2	31 27	91 93	98.1 (97.6-98.6) 99.2 (99.1-99.3)	95.9 (95.2-96.6) 98.4 (98.2-98.5)	93.0 (92.0-94.0) 96.8 (96.5-97.1)	89.4 (87.7-91.0) 95.6 (95.2-96.0)	-	2.41 (2.10-2.77)
Denmark	2010	3,820 (7.1) 49,671 (91.8)	-	37	93	-	96.8 (96.6-97.0)	95.3 (95.0-95.5)	-	92.6 (92.2-93.1)	2.25 (2.01-2.52)
Finland (Koskinen *et al*)	2008	1,886 48,607	65 (38-91) 70 (31-98)	31 25	100	-	-	-	-	90 (89-90) 73 (70-76)	2.2 (2.0-2.5)
Sweden (Robertsson *et al*)	1999	10,624 15,437	70.8 (7.4) 70.8 (7.1)	31 37	100	-	-	-	-	84.2 88.5	1.47 (no CIs given)

Table 1-8: Outcomes of UKR and TKR in National Joint Registries

For each row, UKR is on the upper line and TKR is on the lower line. If not published, HRs are calculated using the method of Parmar et al[203]. TKR survival figures for England are for cemented TKR. HRs are given to compare UKR with cementless (top figure) and cemented (bottom figure). Denmark does not publish survival figures by prosthesis but does give HR (displayed). Finnish and Swedish data are from published papers and HRs are adjusted. All other figures are unadjusted for case-mix.

Author	Year	Register	UKRs	TKRs	f/u (yrs)	Functional outcomes – adjusted mean differences (positive values favour UKR, asterisk denotes significance, p<0.05)						
						EQ5D	OKS	KOOS-Pain	KOOS-Sympt	KOOS-ADL	KOOS-Sp/Rec	KOOS-QOL
Baker	2012	England and Wales	505	23,393	0.5	0.0 (-0.03-0.01)	0.0 (-0.9-0.9)	-	-	-	-	-
Rothwell	2010	New Zealand	3030	13,627	0.5	-	1.8[a]*					
Lygre	2010	Norway	372	972	5-7	-3.1 (-7.1-1.0)	-	2.1 (-1.1-5.3)	2.7 (0.1-5.3)*	4.1 (0.9-7.4)*	5.4 (1.6-9.3)*	0.7 (-3.0-4.5)

Table 1-9: Studies comparing outcomes of UKR and TKR using registry data

[a]The study by Rothwell *et al* does not attempt to adjust for patient characteristics. The OKS figure is for an unadjusted mean difference.

1.9.5. Assessment of the evidence for UKR

1.9.5.1. Comparative studies of TKR and UKR

Potential bias was assessed for randomised trials using the five-point checklist of Jadad *et al*[204]; non-randomised studies were assessed using the Methodological Index for NOn-Randomised Studies (MINORS)[205]. Both randomised trials are small and give no details of blinding. As a result, they scored 3/5 and 2/5 respectively, and both would be classed as level II evidence.

Of the other comparative studies, only the study of Noticewala *et al*[4] could be classified as Level II. However, the study cohort was small (198 patients) and over 60% of patients eligible for inclusion were excluded due to inadequate data. The precise exclusion criteria and proportion of patients lost to follow-up are not specified.

The remaining ten studies are retrospective cohort studies or case-control studies. Three studies, of Brown *et al*[188], Lyons *et al*[189], and Sweeney *et al*[187], are large studies of institutional databases, which use multiple regression techniques to adjust for covariates including age, gender and pre-operative function. The remainder of the studies are small, retrospective, single-surgeon comparisons or small case-control studies. In many cases the follow-up is very short (none has a mean follow-up of greater than five years). None specify blinded assessment of outcomes; as a result, the best-scoring study for methodological quality (that of Brown *et al*) scored only 21/24 points on the MINORS scale. The remainder scored between 15 and 19 points.

1.9.5.2. Registries and registry-based studies

The joint registry analyses have the benefit of being very large but in most cases, no adjustment is made for baseline differences between the TKR and UKR groups. Systematic differences in baseline values (such as age) suggest that a patient's allocation

to TKR or UKR may have been directly affected (at least in part) by these factors – this is known as confounding by indication. In all cases, implant survival is the primary outcome measure. The three registry-based studies of PROMs seek to address this problem, but each have methodological problems.

The study of Rothwell *et al* was not designed to compare the outcomes of the two procedures, and as such, no adjustment is made for baseline differences, and no statistical analysis is attempted. In addition, the lack of information on pre-operative function suggests substantial unmeasured confounding. The study of Baker *et al* was performed shortly after PROM collection began, and the authors have reported logistical issues with the collection and linkage of data[206]. The analysis used in the study has been criticised by subsequent authors. Particular issues include the use of change scores (raising the possibility of a ceiling effect in well-functioning prostheses), the large number of excluded patients and the lack of balance between the groups in terms of numbers and baseline characteristics[207].

The study of Lygre *et al* was relatively small by the standards of registry-based papers. Again, it did not have any details of pre-operative function and so a level of unmeasured confounding exists. Around a quarter of patients who were sent questionnaires did not return them, which may result in an element of inclusion bias.

1.9.5.3. Non-comparative studies of UKR

Whilst the single-centre series of UKR provide important information about implant safety, they are less useful in providing evidence for the superiority or inferiority of UKR over TKR due to the lack of a control group. As most were from high-volume specialist or designer centres, there is a limit to these studies' external validity. The methodological quality of the studies varies greatly; loss to follow-up was often unacceptably high

(49/124 living patients in the study of Cartier *et al*, for example) or inadequately reported. No study reported an attempt to define an adequate sample size and many studies were very small (this problem was exacerbated by the fact that the study populations were elderly with a large and expected number of deaths). In many cases, the definition of failure was opaque and the statistical methods were often not explicitly stated.

1.9.5.4. Conclusions

Whilst TKR and UKR are both established procedures, the evidence comparing the two consists largely of small and poor-quality comparative studies, and large registry-based studies with variable adjustment for confounders and limited end-points. In order to understand the relative failure rates of TKR and UKR, larger studies are needed with better adjustment for baseline differences between the groups and the problem of confounding by indication needs to be addressed. Ideally, multiple clearly-defined end-points, including PROMs, survival, satisfaction, death and complications, should be assessed by such a study.

1.10. Factors affecting outcome in UKR

Factors predisposing to a good or poor outcome after joint replacement can be divided into three broad areas: surgical factors (such as learning curves and case volume); patient factors (such as age, gender and body mass index); and factors concerning implant design. There is now a large body of evidence in all three areas regarding TKR, but there is much less available evidence regarding UKR specifically[208].

1.10.1. Surgical and unit factors

Two main surgical factors have been demonstrated to affect outcome after UKR: surgical learning curve, and volume of cases performed per year, both by surgeon and by unit.

1.10.1.1. Learning curve

UKR is considered to be a technically demanding procedure with a marked learning curve[209]. Several authors have attempted to quantify this learning curve, either for UKR overall or for specific techniques such as minimally-invasive surgery.

Rees *et al* examined the first 104 cases of minimally-invasive UKR performed in a single centre. They compared range of movement, KSS-Fcn and KSS-Obj for the first ten cases to those from subsequent cases. All outcomes were similar in the 'learners' and 'experienced' groups, except the KSS-Obj, which was significantly worse in the former[210].

Lewold *et al* studied the introduction of a new design of fixed-bearing UKR (Duracon, Howmedica, Rutherford, NJ)[211]. A large series from a high-volume unit (where the surgeons were already familiar with UKR) was compared to four smaller units. The revision rate in the smaller units was significantly higher in the smaller units, with a concentration of failures in the early introduction period. 8/123 implantations in the smaller units were revised. Seven of these were amongst the first ten cases in each unit.

Hamilton *et al* examined the first 445 minimally-invasive UKRs performed at a single unit by four surgeons[212]. They report a drop in revision rate from 8.1% in the first half of all cases to 5.4% in the second. The overall number of revisions was small and so this difference did not reach statistical significance. Of note, the implant used was the Preservation (see Section 1.12) which was subsequently withdrawn due to a high revision rate. Two non-comparative studies, by Song *et al* and Dervin *et al* support the

existence of a learning curve by reporting high rates of failure due to technical error in the early period following introduction of UKR[213,214].

1.10.1.2. Surgeon/unit volume

Separately from the learning curve, several authors have attempted to discern the effect on survival of the number of cases performed per year, by surgeon or unit.

Robertsson *et al* used data from the Swedish Knee Arthroplasty Register to compare the revision rates for UKR in high- and low-volume units[215]. A cut-off of ≥23 cases per year (the number performed by the top quarter of units) was chosen; they report a significant correlation between low use and revision risk.

Curtin *et al* examined the records of 2,848 patients from the US Medicare database to determine the effect of surgeon volume on implant survival[216]. They compared surgeons performing <5 cases per year to those performing 15-40 cases, reporting a relative risk of revision of 1.52 (95% CI 1.10-1.75, p=0.02). The effect was smaller in TKR (the lowest-use group, <40 cases/year, had a relative risk of 1.23 (95%CI 1.19-1.45, p<0.001) compared to the highest-use, ≥125 cases/year). Bini *et al* report a retrospective database analysis (n=1,746, mean follow-up 2.6 years) survival for surgeons performing >12 cases/year, is superior to those performing ≤12 cases (HR 2.18, 95% CI 1.28-3.74, p=0.003)[217].

The New Zealand Joint Registry annual report contains revision rates (per 100 component years) for higher-volume (≥10 cases/year) and lower-volume (<10 cases) surgeons[8]. The revision rates are 1.06 (95% CI 0.90-1.23) and 1.51 (95% CI 1.34-1.70) respectively. Baker *et al* sought to answer the same question using the NJR for England and Wales[91]. They defined low usage as ≤100, and high-usage >100 cases performed during the lifetime of the registry, which at the time was seven years. The same cut-offs, which equate to around 14 cases per year, were applied to surgeon and unit volume. A

significantly higher revision rate was reported for low volume surgeons and units as compared to high-volume. High-volume surgeons in high-volume units had a yearly revision rate of 0.91 revisions per 100 component years (95% CI 0.79-1.04); this is significantly superior to low-volume surgeons in low-volume units, who had a revision rate of 1.87 (95% CI 1.58-2.22), and low-volume surgeons in high-volume units, who had a revision rate of 1.66 (95% CI 1.39-1.98).

1.10.1.3. Technology

In most cases, joint replacements are implanted using a combination of metal 'jigs' to guide saw cuts, and surgical assessment of implant alignment. A number of adjuncts to these traditional methods have been introduced with the aim of reducing the learning curve for joint replacement, decreasing the degree of variability between cases, and improving outcomes overall.

Patient-specific instrumentation (PSI) involves the manufacture of jigs which are matched to the morphology of the patient's native joint, as quantified by pre-operative CT or MRI scans[218]. The use of these instruments allows more accurate restoration of native anatomy, particularly in cases were complex reconstruction is necessary, and, by determining the sizes of implants required prior to surgery, may reduce the amount of inventory required for each case.

Navigation systems allow the accurate positioning of implants relative to consistent anatomical landmarks, with the aim of restoring limb alignment consistently following surgery. Landmarks are identified and marked with optical or magnetic markers, which are registered with a computer during the procedure. The computer tracks the relationship between the static markers and markers placed on cutting jigs; once the jigs are positioned accurately, the cuts are made and the implants inserted using

conventional methods. Navigation can be 'imageless', or performed with the use of a plan based on preoperative CT or MR images. The latter may provide more accurate implantation but with time and cost implications[219].

In robotic systems, the bone resections are made with the assistance of a robotic arm which prevents the surgeon from resecting bone outside an 'envelope' as defined by a pre-operative CT or MR based plan. In the most popular robotic UKR system (MAKO Surgical Inc., Fort Lauderdale, FL), bone resections are made by a burr connected to the robotic arm, which is controlled (with 'virtual walls') by the surgeon. Following resection, conventional implants can be used[220].

Whilst studies of each of these forms of surgical technology have demonstrated benefits in terms of consistency of implant alignment, benefits in terms of outcome have been less clearly demonstrated[221]. The substantial set-up and maintenance costs of each technology have limited their adoption. Research is ongoing into the use of these technologies and they may become more widely used if they are shown to give superior outcomes compared to standard instruments.

1.10.2. Patient factors

Patient characteristics appear to have a greater effect on outcome following knee replacement than either surgical or prosthetic factors[222]. Whilst several large studies examine the effect of patient factors on the outcome of TKR, the literature is more limited for UKR[208].

1.10.2.1. Pre-operative function

The strongest predictor of postoperative function is pre-operative function. Judge *et al* examined patient factors affecting poor PROMs after primary knee replacement (both TKR and UKR) in a group of 1991 patients from a large suburban orthopaedic unit[223].

They reported that for every five points improvement in pre-operative OKS, the odds ratio for achieving a patient-acceptable symptom state following knee replacement was 1.5 (95% CI 1.40-1.66). These findings were supported by the outcomes of the Kinemax Outcomes Study, a prospective international cohort study of 860 patients with a single brand of TKR[224], where patients in the lowest quartile of function pre-operatively (on the basis of the WOMAC score) were four times more likely to have a WOMAC ≤60 at two years (OR 4.12 (95% CI 2.86-6.25)). Conversely, whilst they objectively have poorer PROMs, patients with advanced disease pre-operatively often report high levels of satisfaction[225]. Whilst this finding is likely to be true for UKR as well as TKR, it has never been demonstrated empirically.

1.10.2.2. Age

Youth is an established risk factor for revision in both TKR and UKR. This is partially due to the higher demands that young people place on their knees, and partially due to the higher chance of patients surviving to a point at which their knee fails[226]. However, overall knee function normally declines with age, and young patients appear to have superior outcomes in terms of PROMs. Studies examining the effect of age on UKR outcomes are summarised in Table 1-10.

Author	Year	Ages	Knees	Endpoint	Survival % (95% CI)	Conclusions
Pandit	2011	<60 ≥60	245 755	10 year survival and PROMs (OKS, KSS-Fcn)	97.3 (91.3-100) 95.1 (90.8-99.3)	No effect on survival or OKS. KSS-Fcn superior in <60s (87.8 v. 82.1, p<0.001)
Price	2005	<60 ≥60	52 512	10 year survival and PROMs (HSS score)	91 (78.6-100) 96 (92.8-99.2)	No effect on survival. HSS superior in <60s (94 v 86, p=0.001)
Thompson	2013	<60 ≥60	229	KSS-Fcn	-	KSS-Fcn superior in <60s (93.3 v 77.7, p=0.01)
Matharu	2012	-	459	8 year survival (Cox regression)	93.0 overall No HR given	No effect of age on survival (continuous predictor) using Cox regression (p=0.11)
Kristensen	2013	<60 ≥60	248 447	10.7 year survival	86.5 (78.7-91.7) 82.4 (68.5-90.6)	No effect on survival (p=0.98)
Kuipers	2010	<60 ≥60	437	5 year survival	77.2 (67.8-86.6) 89.4 (84.6-94.2)	Significantly lower survival in <60s (HR 2.2, 95% CI 1.08-4.43, p=0.03)
Bini	2013	<55	332	7 year survival (Cox	HR 4.8 (2.6-9.0)	Significantly lower survival in <55s

		55-65 >65	642 772	regression)	HR 1.9 (1.0-3.7) [ref. group]	compared to >65s (p<0.001)
Sébilo	2013	<70 ≥70	720	10 year survival	76.7 88.3	Significantly lower survival in <70s, p=0.002.
W-Dahl (SKAR)	2010	<55 ≥60	1,050 7,743	10 year survival	76% 91%	Significantly lower survival in <55s, p<0.001
AOANJRR	2012	<55 55-64 65-74 ≥74	5,215 12,305 11,622 7,427	10 year survival	76.3 (74.2-77.6) 83.0 (81.8-84.1) 86.5 (85.5-87.5) 91.2 (90.0-92.2)	Compared to ≥75, lower survival in: 65-74s, HR 1.6 (1.4-1.9), p<0.001 55-64s, HR 2.2 (1.9-2.5), p<0.001 <55s, HR 2.8 (2.4-3.3), p<0.001
NZJR	2012	<55 55-64 65-74 ≥75	894 2,537 2,471 1,486	10 year survival (expressed as revisions per 100 implant years)	1.7 (1.4-2.2) 1.7 (1.5-2.0) 1.0 (0.8-1.2) 0.8 (0.6-1.0)	Significantly lower survival in the younger two age groups compared to the older two age groups

Table 1-10: Studies of the effect of age on outcome in UKR

PROMs are reported by three studies[64,227,228]. Each report PROMs to be superior in patients below 60 years of age, compared with patients 60 or older. The studies of Price *et al* and Pandit *et al* also report survival, which is similar in the two age groups in both studies. A further eight studies examine the effect of age on survival. Case series from Matharu *et al* and Kristensen *et al* report no statistically significant effect of age on the revision rate[183,229]. However, series from Kuipers *et al,* Bini *et al*, and Sébilo *et al*[217,230,231], and the Swedish, Australian and New Zealand NJRs report inferior survival in younger patients[7,8,232]. Studies of TKR have displayed similar findings in terms of PROMs and implant survival[146,226]. Of note, both the Australian and New Zealand registries report a greater age effect with TKR than UKR. Comparing patients <55 and 55-64 with those over 75, the AOANJRR gives hazard ratios of 5.3 (4.6-6.2) and 3.5 (3.0-4.0) respectively, whilst New Zealand gives revision rate ratios of 3.9 (3.3-4.7) and 2.6 (2.2-3.1).

1.10.2.3. Gender

The effect of gender appears to be less important than that of age. Neither Kuipers, Kristensen, Bini nor Matharu discerned any difference between genders in terms of implant survival, Sébilo reports significantly poorer survival in women (87.1% v 79% at ten years, p<0.01)[230]. The AOANJRR reports a slightly higher revision rate for women

(HR 1.1, 95% CI 1.0-1.2), whilst the NJR for England and Wales does not publish a gender comparison, and the New Zealand registry reports no significant difference. This contrasts with the situation in TKR, where male gender is an established risk factor for revision, despite men achieving better functional outcomes than women[208,223,233-236]. This is primarily due to a higher infection rate in men, and the relative rarity of infection as a mode of failure following UKR may account for this difference[237].

Female gender appears to be a risk factor for poor PROMs in TKR. Whilst women have equivalent functional improvement to men, overall scores are lower both pre- and post-operatively[238]. This may be a result of referral patterns – women present later with knee osteoarthritis and are less likely to be referred to surgeons when they do[234,239]. The effect of gender on PROMs following UKR have not been investigated specifically, but the study of Sweeney *et al*[187] suggests that a similar effect may be exhibited in UKR.

1.10.2.4. Obesity

Analysis of the effect of BMI is complicated by the fact that obese patients undergoing knee replacement are more likely to be younger, female, of lower socio-economic status, and to have poorer pre-operative function and more co-morbidities[240]. Obesity appears to be associated with a higher incidence of early complications, particularly infection[127,241]. This is reflected in an increased risk of revision overall: a meta-analysis by Kerkhoffs *et al* reported a hazard ratio of 1.79 (95% CI 1.15-2.78 using a fixed-effects model)[242]. However, BMI does not appear to predict poor PROMs following TKR, either overall or in terms of change scores[127,223,243,244].

Again, the evidence for the effect of BMI on UKR is limited. The studies by Pandit *et al*, Kuipers *et al*, Bini *et al* and Sébilo *et al* report no significant relationship between obesity

and revision rate[64,217,230,231]. As with TKR, there is no evidence that BMI affects outcome in terms of PROMs, but the evidence is limited[64].

1.10.2.5. Other factors

Pre-operative deprivation is a poor prognostic indicator for TKR, in terms of PROMs[223]. Likewise, psychological factors appear to be important predictors of outcomes. Using the anxiety/depression subset of the EQ5D questionnaire, Judge *et al* reported a significant effect of anxiety/depression on six month OKS (multivariable coefficient -0.85 (95% CI -1.68 - -0.03) for moderate anxiety and -2.21 (-4.34 - -0.09) for severe anxiety when compared to patients with no anxiety)[223]. Other authors have determined an effect of other more nebulous psychological traits such as the tendency to catastrophise[209,210]. Unrealistic pre-operative expectations also tend to predict dissatisfaction and poor PROMs after TKR[245]. None of these factors have been investigated for UKR specifically.

1.10.3. Implant factors

In common with TKR, implant factors appear to have a lesser influence on outcomes than patient or surgical factors[222]. Amongst the UKR designs in use today, there are three main design variations: fixed or mobile bearing; metal-backed or monoblock tibial component (in fixed-bearing designs); and cemented or cementless fixation. The latter forms a large part of this thesis and will be covered in more detail in Section 1.12.

Mobile bearings are designed to reduce wear. As wear is a mechanism of late failure, any effect on survival would only be expected in later follow-up. In vivo and retrieval studies have demonstrated very low wear rates for mobile bearings in the long term[246,247]. However, with modern UHMWPE, simulator studies have demonstrated excellent wear characteristics for both fixed and mobile bearings, and both remain in widespread use[248,249]. Clinical studies also prove inconclusive, with some demonstrating

superior kinematics and tibial component survival in mobile-bearing implants[250,251], and some determining no difference in survival or clinical outcome[193]. Mobile bearings do have an additional failure mode, dislocation of the mobile bearing, which is not associated with fixed bearings. Most of these are 'primary' dislocations which result from errors of implantation (such as a failure to address impingement, damage to the medial collateral ligament or femoral component malposition), and which tend to occur early[47]. Treatment is by closed or open bearing relocation (which may also involve removal of osteophytes causing impingement), or revision to a fixed bearing or TKR in recurrent cases. As this is an early mode of failure, it may lead to higher revision rates for mobile-bearing than fixed-bearing UKR in short-term studies. An example of this is in the registry-based study of Lewold *et al*[252], where a large number of early bearing dislocations led to an early revision rate double that of the fixed-bearing Marmor prosthesis. This difference disappeared with longer follow-up[9,47].

Metal-backing produces a stiffer component and results in more even loading of the proximal tibia, which may reduce the incidence of tibial pain and component subsidence[253]. However, in order to maintain an adequate thickness of UHMWPE, metal-backing necessitates the use of a thicker component, resulting in greater resection of bone.

1.10.4. Summary

Whilst there is a large body of evidence detailing the patient- and surgical risk factors for failure of TKR, the evidence is limited in UKR. Most data on patient factors are taken from studies which were not designed to answer these questions directly; often they record trends observed in survival studies or joint registry analyses. Limited statistical analysis is applied to distinguish the effect of the exposure of interest from other confounders. With this caveat, the existing literature provides limited evidence that

youth and female gender may be associated with poorer outcomes in UKR, and that BMI is unlikely to be an important risk factor. There is a need for a large study of the patient factors which predict poor outcome in UKR, along similar lines to the studies of TKR discussed in Section 1.10.2.

Examination of surgical factors has focused on the effect of increasing cases per year on UKR, and has provided convincing evidence of a volume effect in UKR. However, the existing literature has a number of failings. In all cases, the outcome was absolute revision rate, rather than functional outcome, and no study compared TKR to UKR. In all cases, surgeons or units were categorised into 'high' and 'low' volume groups with arbitrary cut-offs. Methods of calculation of volume are also non-standardised, with some studies taking the mean number of cases performed per year, and the most recent study examining the absolute number of cases over an eight year period[91]. For surgeons who are identified as having an unacceptably low volume, it is not clear what (short of abandoning UKR) they can do to improve it. Whilst surgeons have no control over the patients being referred for UKR, they may increase their numbers by broadening their indications for UKR. There is a place for a study examining whether this is viable.

1.11. Fixation in joint replacement

The most common mode of failure of joint replacements is loosening of the bone-implant interface, and the achievement of reliable, long-term bone-implant fixation remains a challenge for those designing and performing joint replacements[6].

1.11.1. Cemented fixation

Since the widespread introduction of joint replacement in the 1960s, the predominant form of fixation has been the use of polymethylmethacrylate (PMMA) bone cement[254].

Cemented fixation remains by far the commonest form of fixation in knee replacement, but the proportions vary between countries. In England and Wales and in Scandinavia, well over 90% of total knee replacements are implanted using cement for both the femoral and tibial components[6,9], however, in Australia, only 54.9% of cases are cemented[7]. This contrasts with the situation in hip replacements, where most implants are now implanted without cement[6,7].

1.11.2. Cementless fixation

Whilst there is now a large body of clinical evidence of the effectiveness of cemented fixation, there remain concerns around various aspects of cement and cementation, and cementless fixation has developed in parallel with that of cemented fixation since the late 1970s.

The development of cementless fixation was precipitated by concerns that, whilst PMMA bone cement produced reliable early fixation, mechanical and biological factors existed which may predispose to failure in the longer term. Radiolucent lines were observed in large numbers in early cemented hip and knee replacements, and large numbers of macrophages and giant cells were observed to be present in the interface in *post mortem* studies[255]. In terms of its mechanical properties, cement was observed to be brittle and prone to destruction in conditions of tension and shear[256]. Other concerns included the observation that loose cement fragments could cause third body wear, that the use of cement introduced an extra interface at which prostheses could fail and the finding of fatigue fractures within cement at late revisions, particularly in heavier patients[257]. 'Cement disease' is a condition where implantation of cement is associated with cardiorespiratory symptoms, and which is thought to be the result of fat or cement emboli formed during implantation[258]. Cement disease is usually associated with total hip replacement in older patients, but has been described during knee replacement[259,260].

It has been suggested that the use of cement may lead to excess mortality following THR, and this may also contribute to the enthusiasm for cementless fixation[135].

Cementless fixation can be achieved through two main means; bone interlock, where the press-fit of the prosthesis into the bone provides primary stability, and osseointegration, where coatings on the surface of the implant encourage bone to bond with the implant. Most current cementless implants use a combination of the two, with interlock producing the primary stability, and osseointegration providing long-term fixation[261].

Early cementless components relied entirely on bone interlock, and it remains an important part of cementless fixation. Osseointegration into coated implants occurs up to twelve weeks following implantation and does not reach full strength until up to three years[261]. During this period, implants need to be held rigidly: even 40μm of micromotion can encourage suboptimal fixation, and if micromotion is as high as 150μm, almost no osseointegration occurs[262]. The main determinant of early stability is the shape of the implant, appropriate sizing and the accuracy of bone preparation. Keels, pegs and screws may be incorporated into prosthetic design to improve early stability[263,264].

Modern cementless prostheses achieve long-term fixation by encouraging integration of the bone with the surface of the implant itself. This can happen through 'ingrowth', into a porous surface, or 'ongrowth', onto a roughened surface. Ingrowth requires pores of between 50 and 400μm, and these can be created by bonding meshes made of metal fibres ('fibre mesh')[265], metal microspheres ('sintered beads')[266], or porous metals ('trabecular metal')[267] to the surface of the prosthesis. For ongrowth, a rough surface is created by either 'grit blasting', using small metal particles to roughen the native surface, or using 'plasma spraying', where molten metal is sprayed onto the implant to create a new roughened layer[261,266].

Calcium hydroxyapatite (HA) is a crystalline form of calcium which makes up the majority of the mineral phase of bone[268]. Furlong and Osborn[269] introduced HA as an osteoconductive coating in hip replacement in 1985, having observed its use in dental applications. It is applied either by plasma spraying or solution deposition, and is often used in conjunction with other coatings such as those outlined above[270]. The addition of HA coating appears to lead to less micromotion than porous surfaces alone in total knee replacement[271-273], and this effect appears to last into the long term in spite of a degree of absorption of the HA coating over time[115].

1.12. Fixation in Unicompartmental Knee Replacement

The use of cement in UKR has mirrored that in TKR. Whilst the very early attempts at both forms of knee replacement were often cementless[43,255], the use of cement became almost universal in both TKR and UKR as both became widely-used procedures in the late 1970s and 1980s[39]. Currently, around 4% of all TKRs implanted in the UK are cementless, and the usage of cementless UKR is so low that it is not reported in either the Australian, Swedish or England and Wales NJR annual reports[6,7,9].

Early attempts at cementless UKR were largely unsuccessful, but this appears to have been due to design factors separate to the method of fixation. A 1993 study of two designs of fixed-bearing cementless UKR demonstrated high rates of polyethylene wear and failure in the first five years following surgery, although these failures could not be attributed to the cementless fixation[274]. Likewise, two further designs, the PCA (Howmedica, Rutherford, NJ) and the LCS/Preservation (De Puy, NJ), demonstrated high failure rates due to their highly-constrained design, regardless of whether they were implanted using cemented or cementless fixation[275-277].

Theoretically, UKR should be more suitable for cementless fixation than TKR. The lack of tibiofemoral constraint ensures that (aside from the effects of friction) all the force transfer through the components is compressive, with minimal shear forces[37]. In contrast, with TKR the use of a constrained tibiofemoral articulation leads to the generation of shear forces at the bone-implant interface (Section 1.4). If there is eccentric loading in TKR, the tibial component may rock and cause tension and failure at the interface; this contrasts with the situation in UKR, where the forces remain compressive.

Aside from the cementless OUKR (see Section 1.6.3), there are currently four cementless implants in use. The Uniglide (see Section 1.5.2) is available in fixed- and mobile-bearing designs and can be implanted with or without cement. There is limited literature currently available, but ten year survival of 97.5% has been reported by the designing centre[278]. The Unix (Stryker, Newbury, UK) is a fixed-bearing, HA-coated cementless implant with a transverse fin and the option to augment fixation with screws. Two clinical studies exist; a designer series reporting 98.4% at a mean follow-up of 9 years, and an independent series reporting survival of 91.2% at ten years[58,177]. In both series, revisions for loosening were very rare. The third cementless UKR currently on the market is the Alpina (Biomet France) which is a fixed bearing, HA-coated implant only available in France. A single series of 159 knees reports survival of 95.7% at five years, with only two reported cases of tibial loosening[279]. Finally, a cementless version of the Genesis implant is available. In the study of Heyse *et al* (described in more detail in Section 1.9.2), 15 year survival was reported at 90% for the cementless tibia (no cementless femora were used), which was no different from cemented prostheses[11]. Whilst the data on these implants is limited, all had very low levels of aseptic loosening, which provides encouragement that cementless UKR may be a viable option.

1.13. Declaration of interests

The focus of this thesis is joint replacement, and in particular, UKR. Research into joint replacement is frequently associated with, funded, or initiated by, the manufacturers of such implants. The department where this work was completed is in part funded by grants from industry, most notably by way of research projects and research fellowships funded by Biomet, Stryker and Zimmer. The principal supervisor of this thesis receives royalties from Biomet as a designer of the Oxford Knee.

The author of this thesis was initially employed by the Nuffield Orthopaedic Centre NHS Trust in a research fellowship post which was funded by Biomet. The employment costs of the second and third years of this project, together with all other costs of the project, were met by charitable funds from Arthritis Research UK and the Royal College of Surgeons of England. None of the funding bodies, either industrial or charitable, had any input into the conduct of this work or the decision to seek publication.

1.14. Scope and structure of thesis

As stated in Section 1.1, the aim of this thesis is to compare the failure rates in UKR and TKR, and to delineate modifiable factors to improve the revision rate of UKR. This thesis will be structured as follows.

In Chapter 3, the failure rates of UKR and TKR are compared in matched patients from the National Joint Registry for England and Wales. This represents the largest and most detailed comparison of UKR and TKR performed to date. In light of the findings of Section 1.9.5, UKR and TKR are compared in terms of failure (including death, reoperation and readmission, in addition to implant survival), and patient-reported outcomes. Multiple covariates are included in the analysis using data from the NHS

PROMs and Hospital Episode Statistics databases. Patients receiving each implant are closely matched using propensity score techniques. This is designed to address the issue of confounding by indication.

Chapter 4 and Chapter 5 concern modifiable risk factors for failure and poor functional outcome in UKR, using the linked dataset used in Chapter 3. In Chapter 4, the linked HES, NJR and PROM datasets are analysed to determine the predictors of revision and poor functional outcome following UKR, in terms of patient and surgical factors. In Chapter 5, the effect of surgical and unit volume on survival and functional outcomes is determined. As the principal mechanism by which surgical volume can be increased is by broadening indications for UKR, a further analysis is performed to determine how much indications can be broadened before the effect of operating on less suitable patients outweighs the positive effect of higher surgical volumes.

The second part of the thesis concerns implant factors, primarily the effect of the introduction of a new design of implant. As the majority of revisions in NJRs are performed for loosening (Table 1-7 on page 17), the introduction of a new, cementless implant is intended to make the fixation of UKR more reliable in less experienced hands.

Chapter 6 reports an RCT comparing cementless OUKR to the widely-used cemented version in terms of fixation and patient-reported outcome. To establish the safety of the cementless device and to quantify rare complications, a large, multicentre study of the cementless device was performed; the results of this study are described in 6.1. A small number of cases in this series raised concerns about fixation; these are described in more detail in Chapter 8, alongside a mechanical and histological study of the bone-implant interface in the cementless OUKR.

In the final experimental chapter, Chapter 9, the effect of the introduction of the cementless OUKR is examined by further analysis of NJR data. Using the same matching techniques that were used in Chapter 3, the survival and functional outcome of the cementless implant is compared to that of the cemented implant in matched patients.

Chapter 2 Data and statistical methods

2.1. Introduction

The studies contained within this thesis use data from several sources. In this Chapter, the datasets are described, and the methods used in the initial processing and cleaning of the datasets are described. The large datasets described in Sections 2.2-2.4 are analysed in Chapters 3-6 and 9. Each Chapter has a specific analysis plan and the statistical methods used for the analyses are described in the relevant Chapter. The other data sources (Sections 2.5 and 2.6) are used in the studies in Chapters 7 and 8. Throughout this thesis, all data cleaning and statistical analysis was performed using Stata IC v.12.1 for Windows (Stata Corp., College Station TX), unless otherwise stated.

2.2. The National Joint Registry for England and Wales

2.2.1. Background

The National Joint Registry for England and Wales (NJR) was founded in 2002 and the first data were collected the following year. It describes its purpose as being "to collect high quality and relevant data about joint replacement surgery in order to provide an early warning of issues relating to patient safety"[122].

The NJR now contains data from over one million joint replacements and the first patients within the database are now reaching their tenth post-operative year[6]. Data are communicated in several ways. The principal method of reporting of NJR data is in the form of an annual report; component-level data are released separately to implant manufacturers, and surgeons may access their own data in real-time via a website

(www.njrclinicianfeedback.org.uk). Data may be released on application for the purposes of research; these requests are considered by the NJR research sub-committee.

2.2.2. Data collection

Data are collected on standardised forms; specific forms exist for hip and knee replacements and for primary and revision operations. Patients give their consent for data collection pre-operatively via a separate form (forms are reproduced in Appendix 3). Staff at each hospital enter the data contained in these forms onto the central NJR database via a web portal. Data are collected for all NHS or private sector joint replacements performed in England and Wales. Since 2013, Northern Ireland has been included (and the name has changed to the NJR for England, Wales and Northern Ireland). As the date of extract of the data used here is August 2012, only cases from England and Wales are included.

2.2.3. Data extract

Release of data for the purposes of this study was approved by the NJR Research Sub-committee. Two separate extracts were produced: one containing all records of primary knee replacements (TKR, UKR and patellofemoral replacement) with linked mortality and revision data. The second extract contained only Oxford UKRs and AGC TKRs. The second extract contained component-level data including serial numbers to allow detailed analysis of implant factors; permission was given by the manufacturer of both implants (Biomet) for the data to be used for this purpose. Both extracts were from the start of data collection by the NJR in January 2003 until 28th August 2012.

2.2.4. Data cleaning and initial processing

The main extract contained records for 552,015 knees. Prior to data cleaning, several variables within the dataset contained missing or implausible values. The baseline

descriptive statistics for the un-processed NJR dataset are given in Table 2-1. Data were imported into Stata and coded. All cases without operation data were removed as were all cases performed for a diagnosis other than osteoarthritis and all cases described as 'complex primary' knee replacements, and all patellofemoral or hinged/linked knee replacements.

		TKR	UKR	PFJR	Hinged/Linked
N (missing=109)		500,935	42,698	7,172	1,101
Mean age (range)		70.2 (-1.5-102.4)	64.4 (18.8-95.8)	61.0 (21.1-93.8)	72.1 (21.5-98)
Gender (male, n, %)		213,657 (42.7)	22,419 (52.5)	1,702 (23.7)	317 (28.8)
Mean BMI (range)		14.6 (-1-581)	15.7 (0-493)	14.2 (0-317)	13.4 (0-425)
ASA (n, %)	1	66,657 (13.3)	10,599 (24.8)	1,882 (26.2)	95 (8.6)
	2	357,332 (71.3)	28,649 (67.1)	4,636 (64.6)	663 (60.2)
	3	74,933 (15.0)	3,385 (7.9)	643 (9.0)	326 (29.6)
	4+	2,013 (0.4)	65 (0.2)	11 (0.2)	17 (1.5)
Unit type (n, %)	NHS (England)	336,318 (67.1)	25,161 (58.9)	4,523 (63.1)	890 (80.8)
	NHS (Wales)	25,441 (5.1)	1,789 (4.2)	526 (7.3)	63 (5.7)
	Private	114,118 (22.8)	13,919 (32.6)	1,948 (27.2)	113 (10.3)
	ISTC	25,057 (5.0)	1,829 (4.3)	175 (2.4)	35 (3.2)
Indication (n, %)	Osteoarthritis	486,003 (97.0)	42,247 (98.9)	6,949 (96.9)	843 (76.6)
	Rheumatoid arthritis	9,680 (1.9)	55 (0.1)	23 (0.3)	90 (8.2)
	Other inflammatory	3,080 (0.6)	36 (0.1)	13 (0.2)	22 (1.9)
	Previous trauma	2,592 (0.5)	126 (0.3)	46 (0.6)	97 (8.8)
	Avascular necrosis	1,718 (0.3)	267 (0.6)	7 (0.1)	31 (2.8)
	Previous infection	349 (0.1)	8 (0.0)	3 (0.0)	12 (1.1)
Year of Surgery (n, %)	2003	12,400 (2.5)	991 (2.3)	129 (1.8)	15 (1.4)
	2004	25,175 (5.0)	2,105 (4.9)	264 (3.7)	27 (2.5)
	2005	38,585 (7.7)	2,706 (6.3)	406 (5.7)	59 (5.4)
	2006	44,975 (9.0)	3,812 (8.9)	519 (7.2)	75 (6.8)
	2007	60,398 (12.1)	5,063 (11.9)	872 (12.2)	125 (11.4)
	2008	66,683 (13.3)	5,859 (13.7)	1,043 (14.5)	144 (13.1)
	2009	68,088 (13.6)	5,977 (14.0)	1,096 (15.3)	170 (15.4)
	2010	70,367 (14.1)	6,109 (14.3)	1,080 (15.1)	189 (17.2)
	2011	71,721 (14.3)	6,158 (14.4)	1,112 (15.5)	178 (16.2)
	2012 (to August)	42,543 (8.5)	3,918 (9.2)	651 (9.1)	119 (10.8)

Table 2-1: Baseline characteristics of NJR extract prior to data cleaning

2.2.4.1. Data cleanaing

All variables were examined for missing or improbable data. In most cases, the data available were complete and plausible. Patients below the age of 18 and those with missing data were removed (five patients). Body Mass Index (BMI) was the least complete dataset and needed extensive cleaning. In the initial dataset, 20,441/552,015 values were missing (3.7%), and a further 281,387 were coded as 0 (51.0%). A further 1493 patients had a BMI recorded as less than 16 or greater than 60; the maximum value being 581. The decision was made to exclude all values above 60 and below 16.

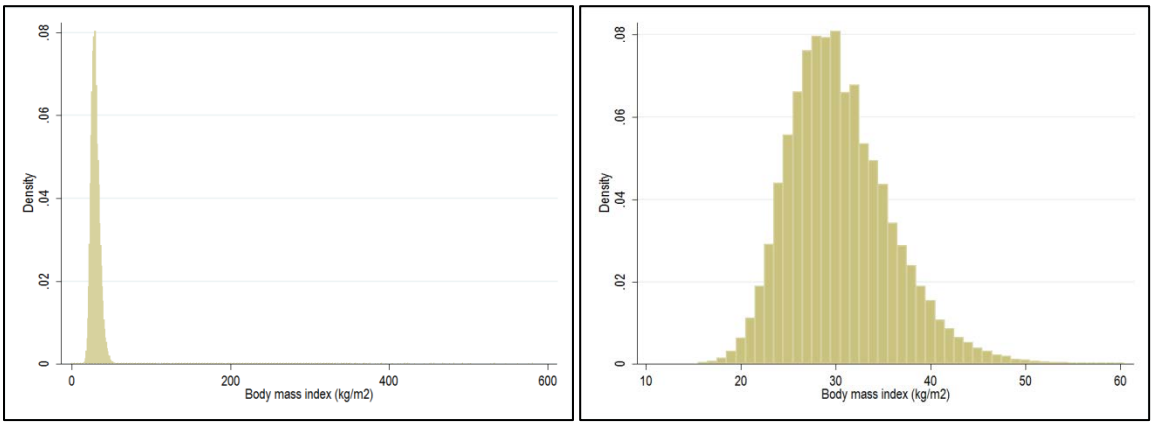


Figure 2-1: Distribution of BMI data pre- and post-cleaning

The full, cleaned dataset contained the records of 505,643 TKRs and UKRs, and 9,098 linked revisions. Subsets of this dataset were used for each study and are described and tabulated in each Section. The proportion of missing data varied between studies.

2.2.4.2. Missing data: Multiple Imputation

Given the normal distribution of the data shown in Figure 2-1, data are taken to be missing at random, although this cannot be proven definitively. In each Chapter, the effect of the missing BMI data was explored. For each comparison, the analysis excluding BMI was compared to analysis of the complete-case dataset and a dataset with missing BMI values completed using Multiple Imputation (MI). If the effect of BMI was

not statistically significant, or the sensitivity analyses demonstrated that inclusion of BMI made no material difference to the outcome of the comparison, BMI was excluded from the estimates. The exception to this is the study in Chapter 4; this study was designed specifically to assess the factors contributing to failure and the imputed BMI data were included in the main analysis.

In MI, multiple copies of the entire dataset are made and, in each, the values of the missing data points are predicted from the distribution of the complete data. To reflect the uncertainty of the prediction, a degree of variation is introduced into the imputation process; hence, for each copy of the data, the imputed values differ. The statistical test of interest is then applied to the imputed datasets. As each set differs, the estimates produced by the statistical tests will differ; the software produces an overall estimate by taking an average of the results of each dataset[280]. Analyses were performed using the MI suite of commands in Stata[281].

2.2.4.3. Linkage

In the analyses presented in Chapters 3 to 5, the NJR datasets were linked to datasets from the Hospital Episode Statistics and Patient-Reported Outcome Measure databases. When linkage was made, the NJR was treated as the 'master' in terms of primary surgical and demographic data. Descriptive analyses of the linked NJR/HES and NJR/PROM datasets are presented in Chapter 3. The process of linkage to HES and PROM datasets is covered in Sections 2.3 and 2.4 respectively.

		TKR	UKR
N (missing=0)		463,657	41,986
Age (mean, range)		70.3 (18.1-102.4)	64.4 (18.8-64.4)
Gender (male, n, %)		199,542 (43.0)	22,081 (52.6)
BMI missing (n, %)		246,206 (53.1)	21,456 (51.1)
BMI (mean, range)		30.6 (16-60)	29.9 (16-60)
ASA (n, %)	1	59,436 (12.8)	10,414 (24.8)
	2	334,188 (72.1)	28,174 (67.1)
	3	68,254 (14.7)	3,334 (7.9)
	4+	1,779 (0.4)	64 (0.2)
Unit type (n, %)	NHS (England)	308,734 (66.6)	24,762 (59.0)
	NHS (Wales)	24,247 (5.2)	1,748 (4.2)
	Private	105,893 (22.8)	13,672 (32.6)
	ISTC	24,783 (5.4)	1,804 (4.3)
Indication (n, %)	Osteoarthritis	463,657 (100)	41,986 (100)
	Rheumatoid arthritis	0 (0)	0 (0)
	Other inflammatory	0 (0)	0 (0)
	Previous trauma	0 (0)	0 (0)
	Avascular necrosis	0 (0)	0 (0)
	Previous infection	0 (0)	0 (0)
Year of Surgery (n, %)	2003	77 (0.02)	984 (2.34)
	2004	17,595 (3.8)	2,063 (4.9)
	2005	36,246 (7.8)	2,665 (6.4)
	2006	42,275 (9.1)	3,744 (8.9)
	2007	57,001 (12.3)	4,978 (11.9)
	2008	64,636 (13.9)	5,774 (13.8)
	2009	66,177 (14.3)	5,873 (14.0)
	2010	68.331 (14.7)	5,991 (14.3)
	2011	69,880 (15.1)	6,043 (14.4)
	2012 (to August)	41,439 (8.9)	3,871 (9.22)

Table 2-2: Baseline characteristics of cleaned NJR extract

2.3. Hospital Episode Statistics

2.3.1. Background and data collection

Hospital Episode Statistics (HES) are data collected on every emergency department attendance, inpatient stay and outpatient appointment in the NHS in England. Private patients treated in NHS hospitals or Independent Sector Treatment Centres (ISTCs), and

NHS procedures carried out in private hospitals are included. The trust responsible for the patient contributes information to the HES database, usually collated by coding teams within the trust, using data from patient notes and discharge summaries. Data have been collected since 1989, and are currently collected by the Health and Social Care Information Centre (HSCIC). Data are provided by hospitals to the HSCIC and include diagnosis and procedure codes (up to 20 diagnoses and 24 procedures), length of stay, and mode of admission and discharge. Until 2006, data on admission to critical care were included in the main database but these records are now kept separately. HES data are collected on the episode level, and so each patient may have many HES records.

2.3.2. Data extract

To preserve anonymity of the patients within the NJR, patients in the HES database were matched to those in the NJR by the HSCIC Linkage Service. They used patient identifiers to identify matching patients and each HES record was supplied with an NJR identifier to allow matching. The extract contained all inpatient stays for financial years 2002-3 until 2012-13, for patients contained in the original NJR extract. Patients were identified using a pre-defined hierarchy of NHS number, date of birth, gender and postcode in a stepwise process as displayed in Table 2-3. 519,097/552015 (94%) patients within the NJR extract had at least one HES episode. The HES extract contained 3,900,546 records.

Step	Records	NHS	DoB	Sex	Postcode
1	492,715	Exact	Exact	Exact	Exact
2	25,390	Exact	Exact	Exact	
3	302	Exact	Partial	Exact	Exact
4	58	Exact	Partial	Exact	
5	66	Exact			Exact
6	533		Exact	Exact	Exact
7	18		Exact	Exact	Exact
8	15	Exact			

Table 2-3: Process of matching NJR patients to HES records

2.3.3. Data linkage

As discussed in Section 2.3.2, each HES record was labelled with unique NJR identifiers, but all records pertaining to each patient were included, regardless of whether they were related to the primary surgery recorded in the NJR. As a result, even after receiving the data, linkage was required to identify the HES records representing the primary surgery in the NJR, any revision operations within the NJR, and any readmissions, re-operations or revisions related to the primary surgery but not recorded in the NJR. For matching, the cleaned extract of 505,643 TKRs and UKRs was used.

Initially, primary surgery was matched using operation codes and dates of surgery. For each record, a marker was placed if any of the 24 operations could plausibly represent primary surgery (using the procedure codes stipulated by the NJR). The second step was to identify if the date of the identified procedure matched the date given in the corresponding NJR record (+/- one day). Of the 505,643 records, 345,490 (68%) primary operations were linked to HES records. Of the records lost, most were Welsh (as Wales is not covered by HES) or operations carried out in private hospitals and privately funded (the 36,529 matched records from private hospitals are patients funded by the NHS to have their surgery in private units). Of operations performed in NHS hospitals or ISTCs, 308,961/360,083 (86%) were matched to a HES record.

The second stage was the identification of revision operations. In 2011, the NJR identified around 3,500 revision operations in HES that were not recorded within the NJR as a result of incomplete recording. They contacted all trusts where these revisions took place to confirm that they were, in fact, revisions. Whilst only 66.5% of trusts responded, within these trusts, 78.5% of HES revisions were confirmed as being revisions by NJR definitions. As a result, in addition to those revisions recorded in the NJR (5,812 for which primary records were matched to HES records), HES revisions

matching the anatomical site of the primary operation (and dated after the primary NJR operation) were identified using similar techniques to those used to identify primaries. This identified a further 3,128 revisions.

Following this, re-operations were identified using procedure codes in a similar fashion. Re-operations included open operations (such as debridements for infection or ligament repairs), arthroscopic operations (excision of loose bodies or menisci in UKR, washouts for infection), and closed operations (such as manipulation under anaesthetic for stiffness). 11,944 re-operations were identified.

2.4. Patient-Reported Outcome Measures

2.4.1. Background

Whilst data on the complications of surgery have been collected for some time, the collection of data regarding the quality of outcomes was not performed until the Darzi review of 2008[282]. One of the key recommendations of this report was the collection of Patient-Reported Outcome Measure (PROM) data from commonly-performed operations. PROMs are currently collected for four operations (hip replacement, knee replacement, groin hernia repair and varicose vein surgery); collection started in April 2009.

2.4.2. Data collection

Data are collected by staff within participating NHS trusts. For each operation, a generic and procedure-specific questionnaire are completed pre-operatively and at six months post-operatively (the EQ5D, EQ5D VAS and, in the case of knee replacement, OKS). Pre-operatively, patients assess their general health state and report if they suffer from a number of conditions such as diabetes or heart disease; postoperatively, patients report

their overall satisfaction with the procedure and report whether they feel that their symptoms have improved, deteriorated or stayed the same as a result of their surgery.

2.4.3. Data extract

Following the HES-NJR linkage described in Section 2.3.2, corresponding PROM records were identified using HES identification codes. An extract of 214,503 records was produced by the HSCIC.

2.4.4. Data linkage

205,943 of the 214,503 extracted records could be linked to the cleaned NJR dataset on the basis of NJR identifiers. Only 98,555 cases were linked on the basis of operation date. Cases were removed if either pre- or post-operative questionnaires were not complete, or if the questionnaires were not completed within the accepted timescale (pre-operative questionnaire no more than 90 days pre-operatively, postoperative questionnaire between six months and one year postoperatively). 69,749 knees were therefore available for analysis (65,547 TKRs and 4,202 UKRs).

2.5. Oxford Orthopaedic Research Database

2.5.1. Background

The Oxford Orthopaedic Research Database (OORD) was used for the randomised trial in Chapter 6 and the Oxford parts of the multi-centre study in 6.1. Data have been collected since the introduction of the Phase 3 OUKR in 1998. Originally data were collected and stored on paper but electronic data recording began in 2002 and all data collected between 1998 and 2002 have subsequently been transferred to the electronic database.

2.5.2. Data collection

Data are collected prospectively on all patients operated by, or under the care of, two consultant surgeons at the Nuffield Orthopaedic Centre in Oxford (Prof. DW Murray and Mr CAF Dodd). Surgical details, including findings, surgical technique and implant information, are entered from a form completed by the surgeon at the time of surgery (see Appendix 3). Pre-operative and post-operative PROMs (OKS, KSS-Fcn, KSS-Obj and Tegner Activity Scale) are collected by a research physiotherapist, separate from the surgical team. The database (and the outcome assessment system associated with it) serves two purposes; firstly, it is used for the routine collection and analysis of outcome data on the OUKR. Secondly, it is used to collect and store data for specific studies, such as those contained within this thesis. Postoperative data are collected routinely at 1, 5, 7, 10 and 15 years. Supplemental follow-up appointments are introduced (and supplemental data may be collected) if necessary for specific studies.

2.6. Other data sources

2.6.1. Musgrave Park Hospital, Belfast

The Outcomes Unit at Musgrave Park Hospital in Belfast contributed data for the multicentre study in 6.1. Data are collected from all patients operated upon by a single surgeon (Mr D Beverland), by a team of outcomes nurses. Data and radiographs are stored as hard copies and data is entered into a bespoke database system. For the purposes of the multicentre study, pre- and post-operative OKS were recorded, along with complications, revisions and re-operations. Operative details were collected using the same standardised form used at Oxford. Radiographs were either conveyed digitally to Oxford for interpretation or, in a small number of cases which were not available digitally, examined during a visit to Musgrave Park.

2.6.2. Christchurch, New Zealand

Four units in Christchurch supplied data for the multi-centre study. Outcomes staff in each unit collected data and these were collated centrally at the University of Otago by a trial co-ordinator. Again, the same standardised form was used to record operative data, and the same outcomes were recorded as in Belfast. All radiographs were sent to Oxford for interpretation.

2.7. Personal contribution to data collection and analysis

As described in Section 2.2, a large proportion of the data in this work was provided by the NJR for England and Wales and other national databases, and was provided following requests to each body. In order to avoid the use of identifiable data, limited linkage was provided by the Health and Social Care Information Centre: each PROM and HES record was labelled with pseudonymised NJR identification numbers. Procedure-level linkage was conducted by the author and is described in the relevant methods sections of this thesis.

The data for the studies of the cementless OUKR (Chapters 6 and 7) were collected by individuals separate from the surgical team to avoid the potential for bias. Raw clinical and radiological data were passed to the author for analysis.

All analyses, of locally- and nationally-collected data were performed by the author of this thesis.

Results, Part One: Mechanisms of failure in TKR and UKR

Chapter 3 Comparison of outcomes following TKR and UKR

3.1. Introduction

Despite the widespread use of TKR and UKR, the evidence supporting the use of one procedure over the other is limited (see Section 1.9.5). The two RCTs which approach this question are small and have methodological flaws; they also suffer from a high likelihood of sampling bias as they were performed in high-volume units in a very limited sample of patients. The observational studies and joint registries vary in quality and susceptibility to bias, and are affected by a high incidence of confounding by indication: they have limited or no adjustment for the patient characteristics predisposing to treatment by either modality.

Another problem with the literature as it stands concerns outcome measures. Whilst some studies examine patient-reported outcome measures, differences in baseline PROMs render these comparisons challenging. Presentation of postoperative scores with inadequate adjustment for differences in pre-operative scores gives an artificially favourable result to UKR (due to the large effect pre-operative scores have on post-operative scores)[223]. Use of change scores (i.e., post-operative score minus pre-operative score) gives an artificially unfavourable result in UKR due to regression to the mean[283].

In most cases, implant survival is the primary outcome measure. Whilst it is a widely-used end-point, it has important limitations, as described in Section 1.8.1. In order to determine the merits of each procedure accurately, multiple outcome measures should be used, including PROMs, re-operations aside from revision, complications and

[*] Part of this chapter ("Adverse outcomes of total and unicompartmental knee replacement: a study of 101,330 matched patients from the National Joint Registry for England and Wales") was published in the *Lancet* in July 2014.

mortality. Confounding by indication must be addressed, and baseline differences in demographics and PROMs must be adjusted for.

The aim of this chapter is to undertake a comprehensive comparison of the rates of adverse outcomes after TKR and UKR, using a large dataset from the National Joint Registry for England and Wales, together with linked datasets from the Hospital Episode Statistics and PROMs databases. Multiple outcomes will be studied, including PROMs, complications, readmission, revision, reoperation and death. In order to address the problem of confounding by indication, patients have been matched using propensity scoring techniques, which are described in Section 3.3.1.

3.2. Methods

3.2.1. Data sources

The three sources of data for this study, along with details of data collection, processing and linkage, are described in Chapter 2. Whilst data has been collected for the NJR since 2003, PROM data has only been collected since 2009; as a result, this study is in two parts. The first part uses NJR/HES linked data to examine failure rates of UKR and TKR, and the second uses NJR/PROMs linked data to examine the patient-reported outcomes of each procedure. Where data were provided by more than one source, the NJR was taken as the most reliable. The variables used in each dataset are displayed in Table 3-1.

	NJR	HES	PROMs
Patient factors	Age*	Age	Age
	Gender*	Gender	Gender
	BMI	Co-morbidities*	Pre-operative OKS
	ASA grade	Deprivation	Pre-operative EQ5D
			Co-morbidities
			Admission from home
Surgical factors	Operation type*	Operation type	Operation type
	Unit type*	Unit type	
	Surgeon volume		
	Surgeon grade		
	Implant details		
	Thromboprophylaxis		
Outcomes	Death*	Medical complications	OKS
	Surgical complications*	Critical care	EQ5D
	Revision*	Length of stay	Satisfaction
	Revision details	Readmission	Patient-reported complications
		Reoperation	Patient-reported readmission
			Death

Table 3-1: Sources of data
Asterisks denote the preferred source if data are available from more than one source

3.2.2. Exposures

For both parts of the study patients undergoing primary UKR were compared to matched patients undergoing primary TKR. As detailed component-level data was unavailable, both lateral and medial UKR were included in the UKR group. Analyses were restricted to patients undergoing primary knee replacement for osteoarthritis. Patients undergoing patellofemoral replacements or hinged/linked knee replacements were excluded. Other exclusions were knee replacements labelled as 'complex primaries', primary operations involving augmentation and stems (implying a complex deformity), and patients under the age of 18.

3.2.3. Outcomes

3.2.3.1. Failure rates and complications

The failure rates of TKR and UKR were compared by six metrics: rate of revision, rate of revision/reoperation, rate of readmission, length of stay, complications of surgery and mortality (at 30 and 90 days, 1, 4 and 8 years).

Revisions included patients identified as having undergone revision in the NJR data, together with ipsilateral revision operations identified from the HES database (see Section 2.3). Re-operations were identified from the HES data and included MUA, arthroscopic surgery, debridement for infection and operations for wound problems (when identified as being associated with the ipsilateral knee). Length of stay was derived from the HES database and represented the number of days from admission to discharge. Complications of surgery are recorded at the time of primary surgery within the NJR and include fracture, ligament avulsion and tendon damage (see the data collection form, Appendix 3).

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) were compared for the two procedures. Complex revisions were defined as revisions to hinged components or components with stems or wedges, or two-stage procedures.

3.2.3.2. Patient-reported outcomes

The primary outcome measures for this analysis were the six-month OKS and EQ5D. Secondary outcome measures included patient-reported satisfaction, complications, readmission and re-operations.

The EQ5D comprises five questions concerning mobility, self-care, activities of daily living, pain and anxiety/depression, each with three possible answers. These answers can be presented separately or as a weighted overall index rated from 1 (perfect health) to -0.594, the worst possible state[284], with an additional question regarding overall health, reported on a visual analogue scale (VAS). More details regarding the collection of these data are given in Chapter 2.

The OKS has twelve items relating to knee pain and function, each ranging from 0-4, and presented as an overall score on an ordinal scale between 0-48 (more details in Section 1.8.2)[285]. Various cut-offs have been proposed to indicate success or failure of surgery. The Kalairajah groups corresponding to excellent (>41 points), good (34-41), fair (27-33) or poor (<27) have become widely used[134,286]. An OKS of ≥30 at six months following surgery represents a patient acceptable symptom state (PASS), indicating satisfaction with surgery[223].

Other information collected includes self-reported general health and disability, whether the patient is admitted from home or care, and if they suffer from any of a panel of conditions such as heart disease, diabetes and stroke. At six months, the OKS and EQ5D are collected, and patients are asked to report any complications and re-admissions, to report whether they are better or worse than pre-operatively and to report their overall satisfaction with the procedure.

3.2.4. Confounders

The NJR dataset contains data on confounders including patient factors (age, gender, American Society of Anaesthesiologists (ASA) score, and Body Mass Index (BMI)); surgeon/unit factors (cases performed per year, unit type (public/private hospital or Independent Sector Treatment Centre (ISTC)), grade of operating surgeon), and technical

factors (such as cemented or cementless fixation). HES contains detailed comorbidity information (the Charlson co-morbidity index[287]) and markers of deprivation. Deprivation is assessed using the Index of Multiple Deprivation (IMD), a governmental assessment of the level of deprivation in small geographical areas (known as lower super output areas, LSOAs) in England[288]. The IMD assesses 37 indicators, which are divided up into seven domains (income, employment, health and disability, education, barriers to housing and services, living environment, and crime). On the basis of these indicators, all 32,482 areas are ranked; for the purposes of this study IMD was grouped by national quintiles, higher quintiles being less deprived.

For patients in the PROM dataset there are additional confounders including self-rated disability, pre-operative PROMs, and self-reported history of a number of conditions.

Confounders were selected for the analysis if they were expected to affect outcome, regardless of whether they were considered to influence treatment allocation[289].

3.2.5. Statistical analysis

3.2.5.1. Propensity score matching

In order to remove the confounding effect of differences in baseline characteristics, and to reduce the potential for confounding by indication, propensity score matching was used to generate matched cohorts for comparison[290]. This involved estimating the effects of each confounder on choice of intervention using logistic regression. Using the estimates produced by the model, a score was generated representing the probability of each knee receiving UKR; three TKR cases were matched to every one UKR case on the basis of this propensity score. As the populations, confounders and outcomes differed between the two parts of the study, both score calculation and matching were performed separately for each part.

Confounders used in the propensity score calculations are presented in Table 3-2 and Table 3-3. Body Mass Index had a large proportion of missing data, and as such, it was not included in either propensity score analysis; see 'sensitivity analyses', below.

Following matching, the balanced nature of the groups allows statistical analyses to be performed without needing to adjust for baseline characteristics. Therefore, univariable regression models were used as appropriate to each outcome. Cox regression was used to examine survival outcomes (revision, reoperation and mortality). Continuous outcomes (length of stay, PROMs) and binary outcomes (incidence of complications) were examined using linear and logistic regression respectively. Individual EQ5D domains were examined using ordered logistic regression. Re-operation rate (within the first year) was examined using a zero-inflated Poisson model.

3.2.5.2. Diagnostics and sensitivity analyses

Given the high proportion of missing data in the BMI dataset, it was not included in the propensity score calculation. As a sensitivity analysis, the analysis was repeated with complete case data (with and without the introduction of BMI as a covariate). As the dropping of cases without BMI data would lead to imbalance of the groups, a third analysis was performed of the whole dataset with BMI completed using multiple imputation (see Section 2.2.4). Results are given in Section 3.3.4.

Following the propensity-score matching, balance diagnostics were performed. The baseline values of each variable in the two groups were compared to ensure that the groups were well-matched on each variable. Balance diagnostics were performed using the user-written 'pbalchk' command in Stata.

The principal assumption of the Cox model is that that of proportionality of hazards: that the relationship between the survival curves for each stratum of the exposure variable is the same throughout the entire time-period studied. This was tested graphically using Schoenfeld's residuals.

For each individual failing (in this case, being revised) at a given time-point, for each variable (including the exposure of interest – in this case, operation type – and all covariates), a value is calculated for the difference between the observed and model-predicted value for each variable: this is the Schoenfeld residual. These values are plotted against time on a scatter plot. If the hazards are proportional, the Schoenfeld residuals will have a random pattern when plotted against time. If there is a non-random pattern, then the hazards are said to be non-proportional.

For the purposes of this analysis, if non-proportional hazards were detected, the survival analysis was broken up into sections in which the hazards were proportional. Details are given in the relevant results section.

Stata IC v.12.1 was used for all statistical analysis, except matching, which was performed using 'R' (R Foundation for Statistical Computing, Vienna, Austria).

3.3. Results

3.3.1. Matching

A pool of 345,490 HES/NJR-linked records (319,228 TKRs and 26,262 UKRs) were available for matching. Of these, 58,863 had complete records in the PROM database (55,208 TKRs and 3,655 UKRs).

On the basis of the propensity scores, it was possible to match 25,358/26,262 (96.6%) of the UKRs in the overall pool to TKRs. As matching was performed on a ratio of three TKRs to each UKR, there were 101,432 knees, of which 76,074 were TKRs. These patients formed the study group for the comparison of failure rates. For the comparison of patient-reported outcomes, 3,519/3,655 (96.2%) of patients with PROM data could be matched to TKRs. Therefore, the second study group comprised a total of 14,076 patients. Pre- and post-matching baseline variables are displayed in Table 3-2 (for the failure comparison cohort) and Table 3-3 (for the PROM comparison cohort).

Distribution of propensity scores pre-and post-matching are demonstrated in Figure 3-1. These kernel density plots are for the PROMs cohort; similar plots were examined for the complications cohort. Formal balance diagnostics were performed and satisfactory balance was displayed between groups (Table 3-2 and Table 3-3).

		Crude			Matched		
		TKR	UKR	Sig.	TKR	UKR	Sig.
Number of patients		315,767	25,982	-	75,996	25,334	-
Mean age at surgery (SD)		70.4 (9.1)	64.3 (9.7)	<0.001	64.7 (9.3)	64.7 (9.4)	1.000
Gender (male)		135,515 (42.9%)	13,547 (52.1%)	<0.001	39,573 (51.8%)	13,106 (51.8%)	0.349
Unit type	Public Hospital	269,857 (85.5%)	22,085 (85.4%)	0.044	64,179 (84.5%)	21,544 (85.1%)	0.017
	Independent hospital	33,542 (10.6%)	2,872 (11.1%)	0.030	9,141 (11.9%)	2,801 (11.1%)	<0.001
	ISTC	12,368 (3.9%)	1,025 (4.1%)	0.822	2,705 (3.6%)	987 (3.9%)	0.005
ASA score	1	36,461 (11.6%)	5,885 (22.7%)	<0.001	16,050 (21.1%)	5,463 (21.6%)	0.134
	2	228,079 (72.2%)	17,725 (68.2%)	<0.001	53,268 (70.1%)	17,507 (69.1%)	0.003
	3+	51,227 (16.22%)	2,372 (15.7%)	<0.001	6,678 (8.8%)	2,364 (9.3%)	0.009
Cases performed by consultant		231,151 (73.2%)	22,255 (85.7%)	<0.001	64,998 (85.5%)	21,628 (85.4%)	0.540
Cases/yr per consultant (SD)		73.9 (52.5)	85.7 (56.6)	<0.001	84.7 (58.8)	84.7 (55.4)	0.522
Fixation	Cemented	285,749 (90.5%)	23,407 (90.1%)	0.033	68,776 (90.5%)	22,822 (90.1%)	0.052
	Cementless	26,135 (8.3%)	1,944 (7.5%)	<0.001	5,684 (7.5%)	1,912 (7.6%)	0.723
	Hybrid	3,883 (1.2%)	631 (2.43%)	<0.001	1,536 (2.0%)	600 (2.4%)	<0.001
Thromboprophylaxis – Chemical	Heparin (inc. LMWH)	209,221 (66.3%)	15,816 (60.9%)	<0.001	48,546 (63.9%)	15,438 (60.9%)	<0.001
	Aspirin	34,668 (11.0%)	3,924 (15.1%)	<0.001	9,519 (12.5%)	3,858 (15.2%)	<0.001
	Warfarin	3,447 (1.1%)	211 (0.8%)	<0.001	727 (1.0%)	208 (0.8%)	0.051
	Direct Thrombin Inhib.	12,487 (4.0%)	1,101 (4.2%)	0.025	2,654 (3.5%)	1,050 (4.1%)	<0.001
	Other	23,410 (7.4%)	1,927 (7.4%)	0.986	5,205 (6.8%)	1,830 (7.2%)	0.042
	None/unspecified	32,514 (10.3%)	3,003 (11.6%)	0.003	9,345 (12.3%)	2,950 (11.6%)	0.006
Thromboprophylaxis – Mechanical	TEDS	203,878 (64.6%)	16,772 (64.6%)	0.965	49,246 (64.8)	16,323 (64.4)	0.286
	Int. calf compression	40,297 (12.8%)	3,641 (14.0%)	0.001	16,686 (22.0%)	5,653 (22.3%)	0.235
	Other	31,716 (10.1%)	2451 (9.4%)	<0.001	1,012 (1.33%)	266 (1.05%)	0.001
	None/unspecified	39,876 (12.6%)	3,118 (12.0%)	<0.001	9,052 (11.9%)	3,092 (12.2%)	0.212
IMD (quintiles)	1	48,598 (15.4%)	2,951 (11.4%)	<0.001	8,744 (11.5%)	2,915 (11.5%)	0.999
	2	59,609 (18.9%)	4,361 (16.8%)	<0.001	12,247 (16.1%)	4,291 (16.9%)	0.002
	3	70,398 (22.3%)	5,791 (22.3%)	0.983	16,723 (22.0%)	5,666 (22.4%)	0.232
	4	71,870 (22.8%)	6,179 (23.8%)	<0.001	19,070 (25.1%)	5,986 (23.6%)	<0.001
	5	65,292 (20.7%)	6,700 (25.7%)	<0.001	19,212 (25.3%)	6,476 (25.6%)	0.371
Ethnicity	Undefined	38,832 (12.3%)	3,654 (14.1%)	<0.001	9,983 (13.1%)	3,593 (14.2%)	<0.001
	White	263,333 (83.4%)	21,506 (82.8%)	0.010	63,547 (83.6%)	20,934 (82.6%)	<0.001
	Asian	8,587 (2.7%)	515 (2.0%)	0.647	1,643 (2.2%)	511 (2.0%)	0.166
	Black	2,992 (1.0%)	120 (0.5%)	<0.001	471 (0.6%)	116 (0.5%)	0.003
	Other	2,023 (0.7%)	187 (0.7%)	<0.001	352 (0.5%)	180 (0.7%)	<0.001
Comorbidities (Charlson)	None	240,663 (76.2%)	20,865 (80.3%)	<0.001	60,935 (80.2%)	20,291 (80.1%)	0.761
	Mild	60,152 (19.1%)	4,298 (16.5%)	<0.001	12,560 (16.5%)	4,233 (16.7%)	0.501
	Moderate	11,389 (3.6%)	642 (2.5%)	<0.001	1,988 (2.6%)	635 (2.5%)	0.342
	Severe	3,563 (1.1%)	177 (0.7%)	<0.001	513 (0.7%)	175 (0.7%)	0.792

Table 3-2: Baseline variables pre- and post-matching for failure rate comparison

		Crude			Matched		
		TKR	UKR	Sig.	TKR	UKR	Sig.
Number of patients		55,208	3,655	-	10,557	3,519	-
Mean age at surgery (SD)		69.5 (8.8)	63.9 (9.2)	<0.001	64.4 (8.6)	64.4 (8.2)	0.404
Gender (male)		24,945 (45.2%)	1,951 (53.4%)	<0.001	5,584 (53.0%)	1,869 (53.1%)	0.086
Unit type	Public hospital	41,992 (76.1%)	2,737 (74.9%)	0.050	7,815 (74.0%)	2,636 (74.9%)	0.369
	Private hospital	10,573 (19.2%)	728 (19.9%)	0.185	2,285 (21.6%)	699 (19.9%)	0.072
	ISTC	2,643 (4.8%)	190 (5.2%)	0.147	457 (4.3%)	184 (5.2%)	0.073
ASA	1	6094 (11.0)	859 (23.5)	<0.001	2,214 (21.0)	769 (21.9)	0.241
	2	41733 (75.6)	2524 (69.1)	<0.001	7,664 (72.6)	2,478 (70.4)	0.132
	3+	7381 (13.4)	272 (7.5)	<0.001	679 (6.5)	272 (7.8)	0.293
Cases performed by consultant		43024 (77.9)	3,207 (87.7)	<0.001	9,238 (87.5)	3,075 (87.4)	0.566
Cases/yr per consultant (SD)		77.9 (53.3)	92.8 (58.8)	<0.001	91.1 (60.3)	90.9 (56.8)	0.080
Fixation	cemented	50,605 (91.7)	3,201 (87.6)	<0.001	9,517 (90.2)	3,084 (87.6)	0.123
	cementless	4,183 (7.6)	369 (10.1)	<0.001	941 (8.9)	354 (10.1)	0.748
	hybrid	420 (0.8)	85 (2.3)	<0.001	99 (0.9)	81 (2.3)	<0.001
Mean days since surgery (SD)		579.8 (312.9)	620.1 (299.9)	<0.001	616.1 (308.5)	621.9 (300.4)	0.028
Pre-op EQ5D		0.430 (0.304)	0.484 (0.289)	<0.001	0.482 (0.291)	0.481 (0.289)	0.412
EQ5D anxiety score		1.38 (0.54)	1.34 (0.53)	<0.001	1.34 (0.53)	1.34 (0.53)	0.316
EQ5D VAS		69.0 (19.3)	71.3 (19.1)	<0.001	71.2 (18.8)	71.1 (19.2)	0.733
Pre-op OKS		19.5 (7.6)	21.9 (7.6)	<0.001	21.7 (7.7)	21.8 (7.6)	0.292
Admitted from own home		55,018 (99.7)	3,642 (99.6)	0.458	10,518 (99.6)	3,508 (99.6)	0.600
Patient-reported disability		31,977 (57.9)	1,491 (40.8)	<0.001	4,444 (42.1)	1,478 (42.0)	0.672
Patient-reported co-morbidities	Heart disease	5,743 (10.4)	261 (7.1)	<0.001	781 (7.4)	260 (7.4)	0.662
	High BP	26,392 (47.8)	1,441 (39.4)	<0.001	4,197 (39.8)	1,426 (40.5)	0.806
	Stoke	838 (1.5)	36 (1.0)	0.003	110 (1.0)	35 (1.0)	0.599
	Circulation problems	3,900 (7.1)	125 (3.4)	<0.001	381 (3.61)	125 (3.6)	0.571
	Lung disease	4,152 (7.5)	248 (6.8)	0.076	728 (6.9)	242 (6.9)	0.979
	Diabetes	6,647 (12.0)	322 (8.8)	<0.001	984 (9.3)	321 (9.1)	0.543
	Kidney disease	911 (1.7)	36 (1.0)	0.004	110 (1.0)	26 (1.0)	0.994
	Nervous disease	441 (0.8)	23 (0.6)	0.403	71 (0.7)	23 (0.7)	0.457
	Liver disease	263 (0.5)	11 (0.3)	0.169	41 (0.4)	11 (0.3)	0.664
	Cancer	2,503 (4.5)	119 (3.3)	<0.001	328 (3.2)	119 (3.4)	0.856
	Depression	3,913 (7.1)	257 (7.0)	0.501	744 (7.1)	242 (6.9)	0.506

Table 3-3: Baseline variables pre- and post-matching for PROMs cohort

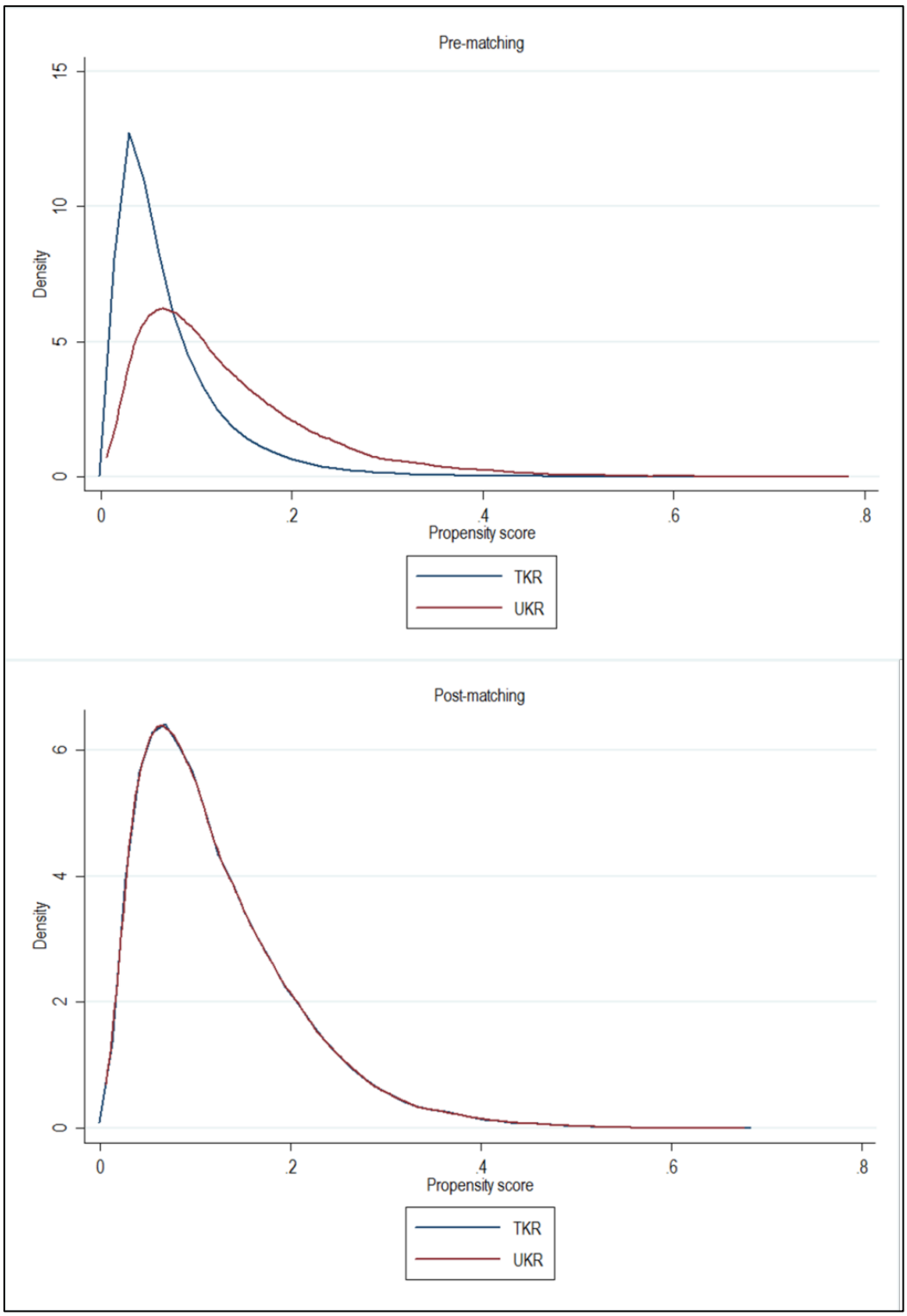


Figure 3-1: Propensity scores pre- and post-matching

3.3.2. Comparison of failures and complications

At eight years, the unadjusted hazard ratio for revision in UKR was 2.59 (95% CI 2.45-2.73) compared to TKR. When non-revision re-operations were included, this effect was attenuated but still significant (HR 1.64, 95% CI 1.57-1.71). Unadjusted hazard ratios for mortality at 30 and 90 days were 0.14 (0.07-0.29) and 0.28 (0.19-0.41) respectively. At eight years, the hazard ratio was 0.52 (95%CI 0.48-0.55). Complications and readmissions were more common in TKR.

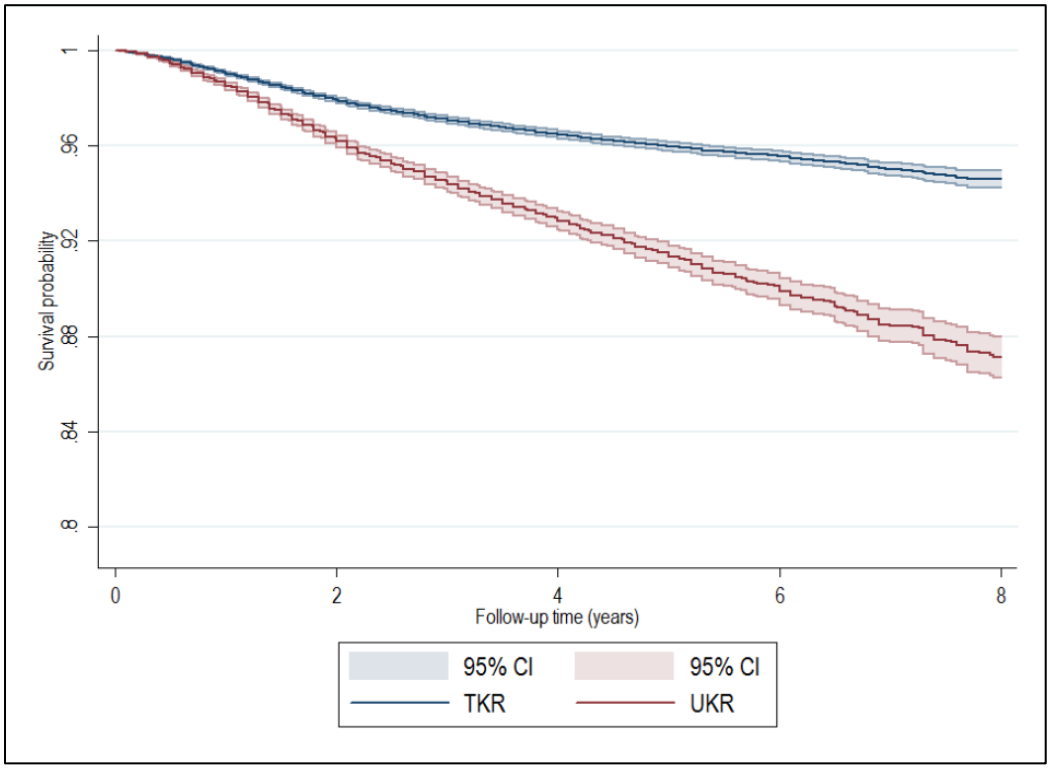


Figure 3-2: Revision rates of TKR and UKR

In matched patients, revision remained more common in UKR patients (HR 2.11, 95%CI 1.98-2.25, Table 3-4 and Figure 3-2). Inclusion of all re-operations reduced the overall survival figures and attenuated the difference between TKR and UKR. At eight years, implant survival was 87.3% (95% CI 86.7-87.8) for TKR and 80.4% (95% CI 79.4-81.4) for UKR (HR 1.37, 95% CI 1.31-1.44). The survival hazard for reoperation varied over time. There were more re-operations for TKR than UKR in the first three months before the

TKR hazard became shallower and the hazards crossed at around 15 months (Figure 3-3). To allow for the deviation from proportionality of hazards, a break was introduced at three months: from 0-3 months, the revision/reoperation rate was significantly higher for TKR (HR 0.46, 95%CIs, 0.38-0.56); subsequently there was a significantly higher risk of reoperation for UKR (HR 3.33; 95% CI 2.73-4.04. Full details are given in Table 3-4.

Outcome	Time-point	Survival (TKR)	Survival (UKR)	Cox HR	NNT
Revision	4 years	96·4 (96·2-96·5)	92·7 (92·3-93·1)	1·96 (1·82-2·10)	30·0 (26·1-34·7)
	8 years	94·6 (94·2-94·9)	87·0 (86·2-87·9)	2·11 (1·97-2·25)	17·6 (15·6-19·9)
Revision/ reoperation	0-3 months	87·2 (86·7-87·8)	80·4 (79·4-81·4)	0·46 (0·38-0·56)	14·7 (13·2-16·6)
	3 months - 8 years			3·33 (2·73-4·04)	
Death	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)

Table 3-4: Crude and matched survival models at eight years. Hazard ratios <1 favour UKR.

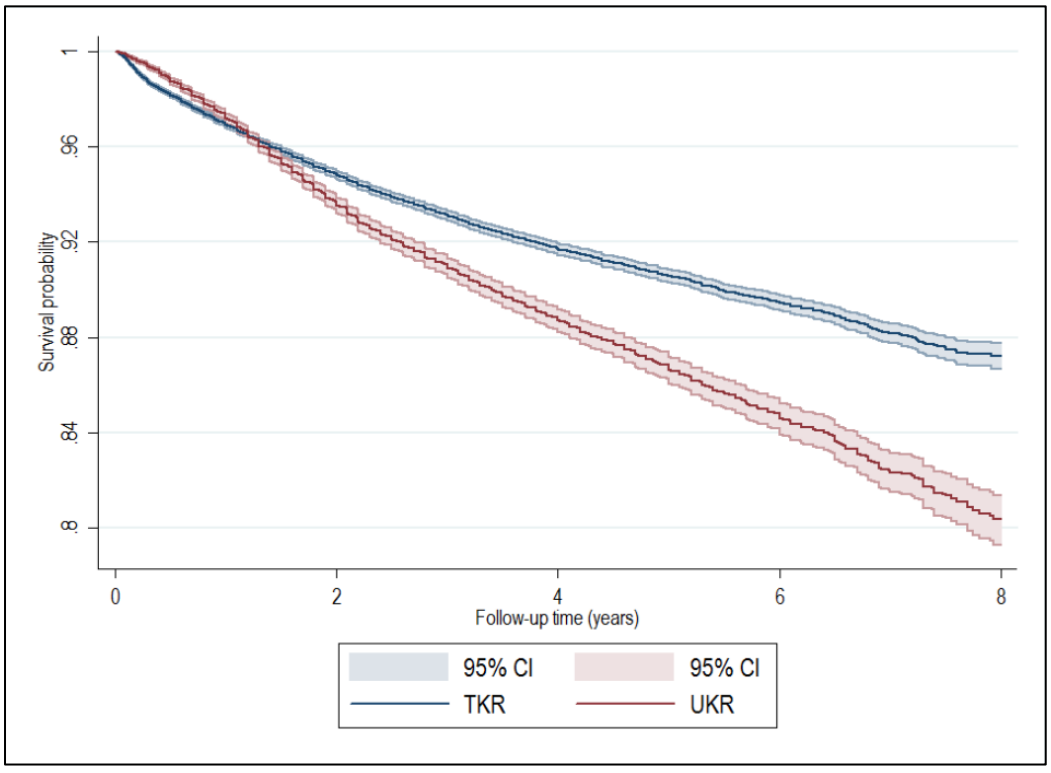


Figure 3-3: Revision/reoperation rates of TKR and UKR

At eight years, 20,223/315.767 (6.4%) of patients who had undergone TKR, and 895/25,087 (3.4%) patients who had undergone UKR had died. Unadjusted mortality rates at eight years for TKR and UKR were 19.1% and 10.8% respectively. Adjusted mortality was significantly higher for TKR at all time-points. At 30 days, 90/76,074 patients (0.24%) had died in the TKR group compared with 7/25,358 (0.06%) in the UKR group. Hazard ratios were 0.23 (0.11-0.50) and 0.46 (0.31-0.69) at 30 and 90 days. Hazard ratios at one, four and eight years were 0.70 (0.58-0.84), 0.75 (0.68-0.82) and 0.85 (0.79-0.92) respectively (Figure 3-4). Whilst the hazard ratio decreased over time, the absolute difference in death rates increased to 1.1% (95% CI 0.7-1.4%) at four years, before decreasing to 0.7% (95% CI -0.5-1.9) at eight years.

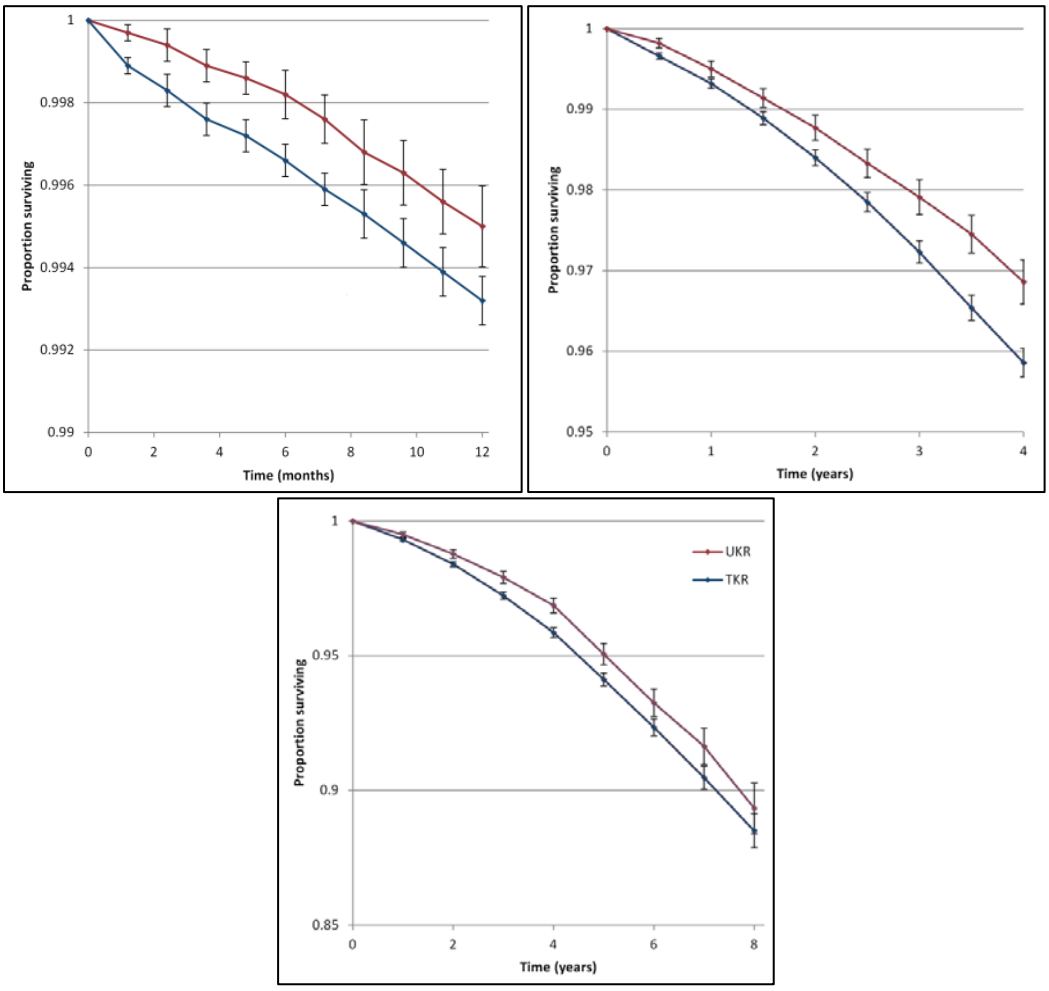


Figure 3-4: Death rates at one, four and eight years following TKR and UKR

Mean length of stay was 1.38 days shorter for UKR (95% CI 1.33-1.43); readmission within the first year was significantly less likely in UKR (incidence rate ratio 0.65, 95% CI 0.58-0.72). Intra-operative complications, blood transfusion, thromboembolism, stroke and myocardial infarction were significantly less likely in UKR (Table 3-5).

	Crude comparisons		Propensity matched comparisons	
	Odds ratio	Significance	Odds ratio	Significance
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)	<0.001
Thromboembolism	0.42 (0.34-0.52)	<0.001	0.49 (0.39-0.62)	<0.001
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

Table 3-5: Crude and matched logistic models for complications. Odds ratios <1 favour UKR

Reasons for revision differed in TKR and UKR (Table 3-6). Whilst aseptic loosening was the commonest reason for revision following either operation, significantly more TKRs were revised for infection and stiffness. Progression of arthritis and bearing dislocation are modes of failure which are almost exclusive to UKR and as a result, the odds ratio for revision by either greatly favours TKR. Unexplained pain, aseptic loosening, malalignment, wear, peri-prosthetic fracture and other, unspecified reasons for revision are significantly more common in UKR.

Main revision reason	TKR			UKR			Hazard Ratio (95% CI)	Significance
	Rank	N	%	Rank	N	%		
Loosening/lysis	1=	351	25.1	1	385	30.1	3.17 (2.75-3.67)	<0.001
Infection	1=	351	25.1	7	61	4.8	0.50 (0.38-0.66)	<0.001
Pain	3	152	10.9	2	264	20.6	5.08 (4.16-6.21)	<0.001
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)	<0.001
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)	<0.001
Dislocation/Dissociation	8	30	2.2	5	92	7.2	10.01 (6.52-15.38)	<0.001
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)	<0.001
Peri-prosthetic Fracture	11	15	1.1	10	22	1.7	4.24 (2.19-8.18)	<0.001
Implant fracture	12	5	0.4	12	3	0.2	1.68 (0.40-7.05)	0.478

Table 3-6: Reasons for revision in UKR and TKR.
Percentages represent the percentage of all revisions that are for the reason given. Hazard ratios represent the overall risk of being revised for each reason at eight years. Hazard ratios <1 favour UKR.

Whilst the majority of revisions in TKR required augmentation or constraint, the majority of revisions recorded for UKR in the NJR were conversions to a 'primary' TKR. These conversion-type operations accounted for all the difference in the revision rate between UKR and TKR. The probability of partial revisions (including secondary patellar resurfacing in TKR, and bearing exchange in UKR) was similar for TKR and UKR, as were complex revisions (Table 3-7).

	TKR			UKR			Hazard ratio (95% CI)	Significance
	N	% of revisions	% of all cases	N	% of revisions	% of all cases		
Bearing/patella	259	18.6	0.34%	81	6.3	0.32%	0.90 (0.70-1.16)	0.430
Revision to 'Primary' TKR	247	17.7	0.33%	854	66.8	3.37%	10.07 (8.74-11.62)	<0.001
Complex revision	890	63.8	1.17%	344	26.9	1.4%	1.12 (0.99-1.27)	0.068

Table 3-7: Type of revision operation (revisions recorded in NJR).
Percentages are given as percentage of revised cases, and as percentage of total patient population entering the study. Hazard ratios <1 favour UKR.

3.3.3. Comparison of patient-reported outcomes

Overall the OKS increased from a mean of 19.6 points (95% CI 19.6-19.7) to 35.1 (95% CI 35.0-35.2). Before matching, the unadjusted postoperative score was 34.9 points (95% CI 34.9-35.1) for TKR and 37.7 (95% CI 37.4-38.0) for UKR (p<0.001).

	TKR	UKR	Adjusted mean difference	Significance
6 month OKS	36.1	37.7	1.57 (1.21-1.94)	<0.001
6 month EQ5D	0.751	0.772	0.021 (0.011-0.030)	<0.001
6 month VAS	71.2	71.1	0.26 (-0.43-0.94)	0.351

Table 3-8: Patient-reported outcome measures (matched patients)

Following matching, the six month OKS was 36.1 (95% CI 35.9-36.3) for TKR and 37.7 (95% CI 37.6-38.0) for UKR (p<0.001). The EQ5D index was 0.751 (95% CI 0.747-0.756) for TKR and 0.772 (95% CI 0.764-0.780) for UKR (p<0.001). Details are given in Table 3-8. Each domain of the EQ5D was examined individually; all except the anxiety/depression domain were significantly better in UKR (Table 3-9). There was no significant difference between the groups in terms of EQ5D VAS.

Domain	Difficulty level	TKR	UKR	Significance
Mobility	None	6,104 (58)	2,174 (62)	<0.001
	Moderate	4,447 (42)	1,344 (38)	
	Severe	6 (0.06)	1 (0.03)	
Self-care	None	9,103 (85)	3,108 (88)	<0.001
	Moderate	1,525 (14)	406 (11)	
	Severe	19 (0.2)	5 (0.1)	
Ability to undertake usual activities	None	5,296 (50)	1,949 (55)	<0.001
	Moderate	4,929 (47)	1,480 (42)	
	Severe	332 (3)	90 (3)	
Pain / discomfort	None	3,944 (37)	1,524 (43)	<0.001
	Moderate	6,094 (58)	1,819 (52)	
	Severe	519 (5)	176 (5)	
Anxiety / depression	None	8,553 (81)	2.851 (81)	0.981
	Moderate	1,795 (17)	595 (17)	
	Severe	209 (2)	73 (2)	

Table 3-9: Comparison of individual EQ5D domains
Numbers in each difficulty group; percentages are given in parentheses

The distribution of scores within the two groups is demonstrated in Figure 3-5. Similar proportions of patients undergoing TKR and UKR attained the very worst scores (OKS<20). However, significantly more UKRs than TKRs achieved the very best scores: an excellent Kalairajah score (OKS>41) was more common in UKR than TKR (odds ratio 1.59 (95% CI 1.47-1.73), p<0.001). Scores rated as 'good' (OKS 34-41), 'fair'(OKS 27-33) and 'poor' (OKS <27) were more common in TKR (Table 3-10).

kalairajah	TKR	UKR	Total	OR (95% CI)	p
Excellent (>41 points)	3,714 (35.18%)	1,604 (45.58%)	5,318	1.59 (1.47-1.73)	<0.001
Good (34-41)	3,462 (32.78%)	994 (28.25%)	4,456	0.81 (0.74-0.88)	<0.001
Fair (27-33)	1,635 (15.49%)	408 (11.59%)	2,043	0.72 (0.64-0.81)	<0.001
Poor (<27)	1,746 (16.54%)	513 (14.58%)	2,259	0.87 (0.77-0.98)	0.021
Total	10,557	3,519	14,076		

Table 3-10: Post-operative OKS, grouped by Kalairajah score

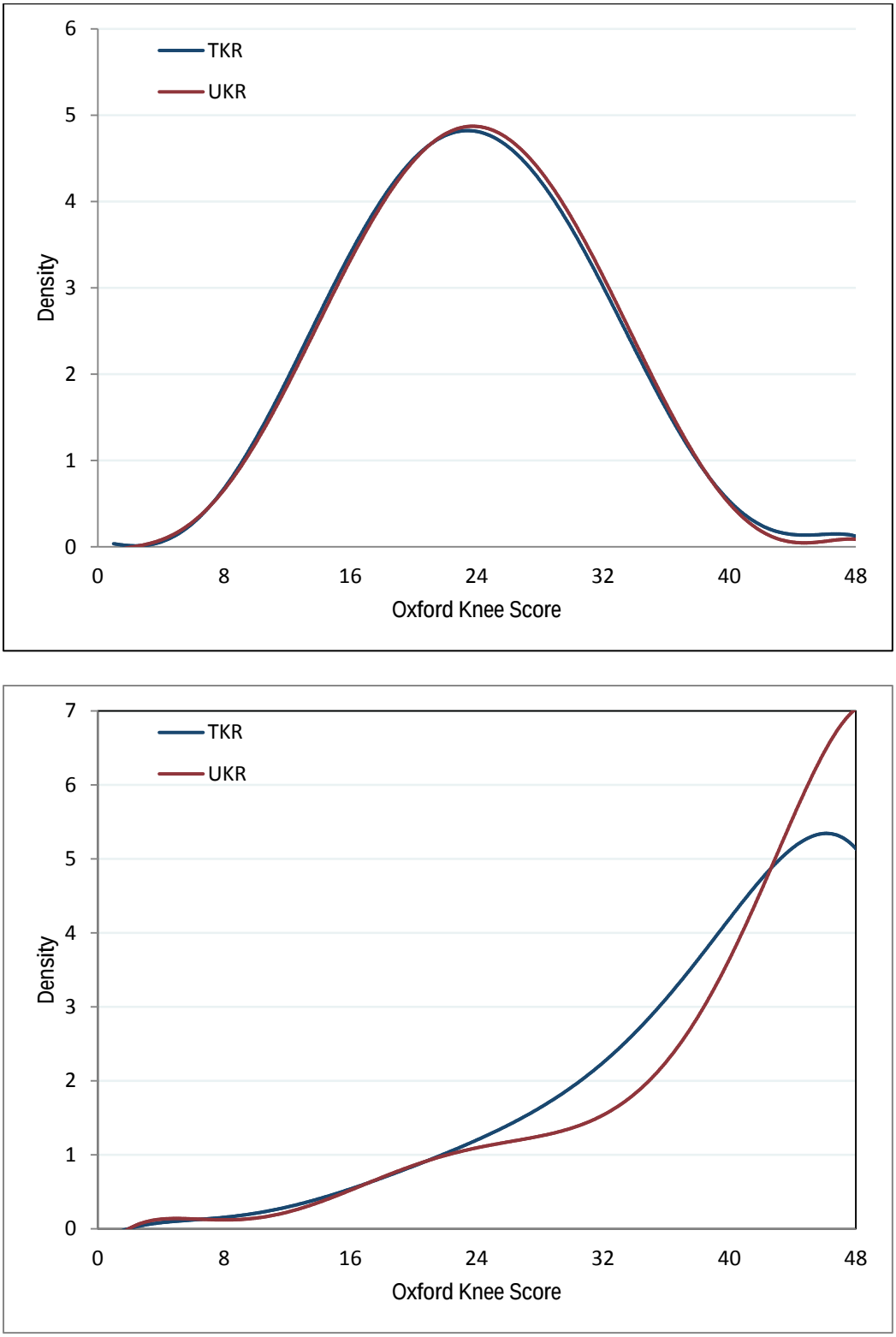


Figure 3-5: Kernel density plots demonstrating OKS score distributions
Top: Pre-operative scores; bottom: Six month scores

Patient-reported complications, re-operation and satisfaction are summarised in Table 3-11. Bleeding, wound problems and drug reactions were significantly more common

following TKR. Patients' reports of complications and admission agree with the data from HES reported in Section 3.3.2. Patients were significantly more likely to report complications and readmission in the six months following TKR, but reoperation rates were comparable between the groups. Patients were more likely to report excellent satisfaction levels following UKR (OR 1.27, 95% CI 1.17-1.39, p<0.001). Around 89% of patients reported that they were better after the procedure than before, regardless of whether they had undergone TKR or UKR.

		TKR (%)	UKR (%)	OR (95%CI)	Significance
Complications	Drug reaction	1,358 (13.7)	368 (11.0)	0.78 (0.69-0.88)	<0.001
	Urinary	996 (10.3)	318 (9.6)	0.93 (0.81-1.06)	0.254
	Bleeding	770 (8.0)	194 (6.0)	0.76 (0.62-0.86)	<0.001
	Wound	1,203 (12.3)	238 (7.3)	0.56 (0.48-0.65)	<0.001
	Readmitted	978 (9.3)	256 (7.3)	0.77 (0.67-0.89)	<0.001
	Reoperation	350 (3.3)	99 (2.8)	0.84 (0.67-1.06)	0.14
Satisfaction	Excellent	2,493 (23.7)	994 (28.3)	1.27 (1.17-1.39)	<0.001
	Very Good	3,905 (37.1)	1,241 (35.4)	0.93 (0.86-1.01)	0.067
	Good	2,510 (23.9)	718 (20.5)	0.82 (0.75-0.90)	<0.001
	Fair	1,220 (11.6)	424 (12.1)	1.04 (0.93-1.18)	0.429
	Poor	395 (3.8)	130 (3.7)	0.99 (0.81-1.21)	0.899
Improvement	Much better	7,627 (72.3)	2,599 (73.9)	1.08 (1.00-1.19)	0.06
	A little better	1,702 (16.1)	518 (14.7)	0.90 (0.81-1.00	0.049
	Same	496 (4.7)	187 (5.4)	1.15 (0.97-1.37)	0.108
	A little worse	436 (4.1)	118 (3.4)	0.81 (0.65-0.99)	0.041
	much worse	268 (2.5)	85 (2.4)	0.95 (0.74-1.22)	0.687

Table 3-11: Other patient-reported outcomes (satisfaction, improvement, complications and readmissions)

3.3.4. Sensitivity analyses

For each cohort, the primary outcomes were re-examined using complete-case data (with and without BMI), and whole cohort data with BMI completed using multiple imputation (details in Section 3.2.5.2). In this Section, Cox regression was used for the survival analyses (rather than competing risks regression) as competing risks regression was not possible with imputed data. Whilst BMI had a statistically significant effect in

each estimate, the effect size was small. As a result, effect sizes and statistical significance of the estimates were similar. Given that BMI had a small effect and doubts about whether the data are missing at random (see Section 2.2.4), BMI is excluded from the analyses displayed above. Details of the sensitivity analyses are contained in Table 3-12.

Comparison	Main analysis	Complete case (excl. BMI)	Complete case (with BMI)	Imputed BMI dataset
Revision	2.11 (1.97-2.25)	1.85 (1.65-2.06)	1.87 (1.68-2.10)	2.12 (2.00-2.27)
Revision / Reoperation	1.40 (1.31-1.44)	1.24 (1.14-1.34)	1.26 (1.16-1.36)	1.38 (1.31-1.45)
Death (8 year)	0.87 (0.80-0.94)	0.88 (0.76-1.02)	0.86 (0.74-0.99)	0.86 (0.80-0.93)
6 month OKS	1.58 (1.21-.194)	1.43 (0.95-1.90)	1.14 (0.67-1.61)	1.42 (1.06-1.77)

Table 3-12: Sensitivity analyses
Figures are hazard ratios for the survival analyses and coefficients for the OKS comparison.
95% confidence intervals are given in parentheses)

3.4. Discussion

3.4.1. Summary of results

This study has demonstrated that, in matched patients, around 40% more patients undergoing UKR go on to undergo further surgery in the first eight postoperative years than those undergoing TKR and twice as many patients undergo revision in the same time period.

However, patients undergoing TKR are twice as likely to suffer a venous thromboembolism, myocardial infarction or deep infection requiring further surgery, three times as likely to suffer a stroke, and four times as likely to need a blood transfusion. Patients undergoing TKR are around four times more likely to die in the first 30 days following surgery, and around 15% more likely to die in the first eight postoperative years. Complications were higher whether reported by the patient or recorded in the HES database. Inpatient stays are longer, and readmissions are more likely, after TKR when compared to UKR. Aseptic loosening was the commonest reason

for revision in both TKR and UKR, but was more common in UKR. Aside from loosening, revisions of TKRs are more likely to be for stiffness or infection, whilst revisions of UKR are likely to be for unexplained pain, arthritis progression or unspecified 'other' reasons. Most revisions of UKR are to a 'primary' TKR, whilst most revisions of TKR require augmentation.

UKR resulted in significantly better outcomes at six months, in terms of joint-specific outcome and health-related quality of life. This difference was particularly striking in terms of the highest scores: patients undergoing UKR had an odds ratio of 1.59 for attaining an 'excellent' score. As a corollary, 'good', 'fair' and 'poor' scores were more common in TKR.

Prior to matching, there were significant differences in the characteristics of patients being offered UKR and TKR. Patients undergoing UKR were younger (the mean age being 64.3 years, compared to 70.4 years in TKR), healthier (mean ASA and Charlson indices were both lower in UKR) and more likely to be male (whilst only 43% of patients undergoing TKR were male, this figure was 52% in UKR). Following matching, balance was achieved; the fact that UKR survival was superior in this study compared to data from NJR reports suggests that some of the covariates corrected by the matching process are of prognostic importance. These factors will be explored in more detail in Chapter 4.

3.4.2. Strengths and limitations of this study

The strengths of this study include the large study population. The use of an unselected, registry-based sample leads to high external validity. The use of data from the NJR, HES and PROM databases allows adjustment for a very large set of potential confounders. Using propensity score techniques to match on multiple confounders (including patient demographics, comorbidities and pre-operative functional status) overcomes the

difficulties experienced by previous authors in analysing comparable patients; baseline matching obviates the need for the comparison of change scores or the adjustment for baseline variables within the final regression model.

Limitations include the follow-up, which was short for PROMs (although six months was selected for the national PROM programme as functional scores are seen to plateau after around 6 months[201]), and, at eight years, at best medium term for the survival analyses. Whilst the cohorts were matched on multiple variables, data on severity of disease, surgical technique and detailed information on brands and models of implant were not available; this raises the possibility of unmeasured confounding. Notably, the dataset used has inadequate information to distinguish between medial and lateral UKR (although the revision rate for each have been demonstrated to be similar in a previous study of the same dataset[291]). It is impossible to determine the precise clinical and radiological criteria for each procedure – severity of disease is adjusted-for using pre-operative PROMs. Matching on stage of disease is best conducted using an RCT design; such a study is currently recruiting[292]. The selection of patients via propensity score matching raises questions about the generalizability of the findings; however, fewer than 5% of the UKRs were excluded as unmatchable and this is unlikely to be a substantial problem. Limitations of this chapter in the context of the work as a whole are discussed further in Chapter 10.

3.4.3. Conclusions and further work

This study represents the largest, most comprehensive comparison of functional outcomes and failure rates in TKR and UKR. The findings of superior outcomes and lower morbidity and mortality with UKR suggest that UKR is a valuable option in end-stage single-compartment osteoarthritis. However, there remain significant differences between the two procedures in terms of revision and reoperation rates.

The next two chapters of this thesis concern the factors affecting the revision rate of UKR. In Chapter 4, patient and surgical factors predisposing to revision will be considered and modifiable risk-factors for revision in UKR identified. In Chapter 5, the effect of surgical caseload and usage will be considered and recommendations for optimal surgical practice in UKR will be made.

In common with previous reports from NJRs, this study has identified aseptic loosening as the commonest cause for revision in UKR. The cementless UKR, considered in the second part of this thesis, is designed with the aim of addressing the problem of aseptic loosening. The studies in Chapters 6-9 are intended to discern whether this aim is achieved.

Chapter 4 Determinants of revision and functional outcome following UKR

4.1. Introduction

Chapter 3 of this thesis has demonstrated significant differences between the practice of TKR and UKR. Chapter 3 has highlighted specific factors related to patient selection: for instance, younger, healthier patients are more likely to be offered UKR. Examination of NJR annual reports reveals that surgical practice also varies between the two procedures, with surgeons performing substantially fewer UKRs each year than TKRs[97]. When the differences in patient factors are addressed during the matching process, a substantial change is noted in the hazard ratio for revision compared to TKR. Whilst the annual reports of NJRs give hazard ratios between 2.5 and 3.5 (see Section 1.9.4), the hazard ratio for revision in the matched analysis performed in Chapter 3 is only 2.11; inclusion of non-revision re-operations brings this hazard ratio below 2. This effect suggests that there may be specific patient characteristics which predispose to good outcomes following UKR; identification of these factors may lead to better patient selection and better outcomes overall.

As outlined in Section 1.10, the factors predicting revision, satisfaction and poor functional outcome in TKR have been extensively studied[190,200,201,209,211,271-275]. However, these factors remain relatively unexplored in UKR[208,223,224,233,235,293-297]. Amongst other factors, youth and male gender appear to predict revision in TKR[208], whilst female gender, anxiety or depression and deprivation appear to predispose to a poor functional

[*] A version of this chapter ("Determinants of revision and functional outcome following unicompartmental knee replacement") was published in *Osteoarthritis and Cartilage* in July 2014.

outcome and dissatisfaction with surgery[223,296,297]. There is conflicting evidence about the importance of body mass index, with some studies suggesting that it affects survival, complications, and patient-reported outcome[293,296], and others reporting no effect[223,244]. The extent to which these factors affect the outcome of UKR is uncertain. As was explored in Section 1.10, there has been no previous comprehensive study exploring the factors predicting outcome in UKR. This is in spite of the fact that UKR has been a widely-used and much-studied procedure over more than thirty years.

As a result of this, practice with respect to UKR varies widely between centres and surgeons. Debate continues as to whether patients should be selected for UKR on the basis of age, BMI, or activity level, amongst other factors[64,80]. The aim of this chapter is to delineate the determinants of outcome following UKR, using the linked HES/NJR and NJR/PROM cohorts described in Chapter 2 and analysed in Chapter 3.

4.2. Patients and Methods

4.2.1. Data sources

This study uses the HES/NJR and HES/PROM/NJR linked datasets described previously. All patients in the NJR extract who underwent UKR between 2003 and August 2012 were identified (n=41,986). Using unique patient identifiers, these patients were linked to corresponding HES records. Given the smaller patient population covered by HES, 25,982 of the 41,986 cases recorded in the NJR could be linked (62%); these patients formed the study group. 3,862 of the 25,982 records (14.9%) in the HES/NJR-linked dataset could be linked to complete (i.e., pre- and post-operative) PROM records. As PROMs have been collected for a shorter time-period than the other two databases, patients with PROMs comprise a small subgroup of the total.

4.2.2. Outcomes of interest

There were three primary outcome measures: revision, patient-reported outcome and satisfaction. Revision was defined as the removal, exchange or addition of any of the components and was assessed using survival analysis techniques (see 'statistical methods', below). Patient-reported outcome was assessed using the OKS, which is described fully in Section 1.8.2[285]. For the purposes of this study, the OKS was examined in two ways; firstly, as a continuous outcome, and secondly, as a binary outcome representing patients whose OKS was worse after surgery than before. This was intended to identify patients who experienced very poor outcomes but who did not (either through frailty or patient choice) receive revision surgery (see Section 1.8.1). Finally, satisfaction was rated on the basis of the question: "How would you describe the results of your operation?", answered on a five-point ordinal scale from 1 (poor) to 5 (excellent).

4.2.3. Exposures

Exposures can be divided into patient and surgical factors. Patient factors included patient demographics (age, gender, ethnicity); and health state (Body mass index (BMI), Charlson co-morbidity index and American Society of Anaesthesiologists (ASA) grade). Pre-operative function was assessed using the OKS and EQ5D. As in the previous chapter, the patient-reported general health state and whether or not the patient reported a disability were also recorded.

Ethnicity was recorded as reported by the patient on admission; it is recorded using the classifications used in census reports, and there are 17 possible categories. As some of these categories become too small to analyse meaningfully, these have been merged into six broader categories. These are: White (including White British, White Irish and other; Mixed Ethnicity; Asian (including Indian, Pakistani, Bangladeshi and other); Black

(Carribean, African and other); Other (including Chinese); and Not Given. This categorisation has been used in other studies of the NHS PROMs database[298]. Deprivation was again assessed using the IMD.

Surgical factors included unit type (whilst all the cases in this cohort were publically funded, they may have been performed in public or private hospitals, or in independent-sector treatment centres); unit size (expressed as the number of UKRs performed in the unit per year); and use of thromboprophylaxis (chemical or mechanical).

Categorisation of continuous variables was avoided wherever possible; the exception was made for non-linear predictors with established groupings (such as BMI). As discussed in Chapter 2, the BMI dataset displayed a large proportion of missing data. As in Chapter 2, multiple imputation was used to complete the missing values. The same methodology for MI was used as described in Section 3.2.5.2. The aim of this study is to determine the importance of each predictor of failure; as a result, unlike in Chapter 3, it was decided *a priori* to include the imputed BMI data in the main analysis.

4.2.4. Statistical analysis

4.2.4.1. Descriptive statistics

Descriptive statistics were performed and continuous predictors were presented as means, standard deviations and ranges. Categorical predictors were presented as numbers in each category and percentages.

4.2.4.2. Model specification

Predictors of implant survival were examined using Cox regression. Univariable hazard ratios and confidence intervals were produced to determine the overall effect of each predictor on risk of revision. A multivariable Cox model was fitted to determine the relative effect sizes of the predictors of interest. Clustering by surgeon was accounted for

by using cluster-robust standard errors. Survival analyses were censored at eight years as in the previous chapter. As in the previous chapter, Schoenfeld's residuals were examined to confirm proportionality of hazards

For the examination of continuous PROM outcomes, analysis of covariance (ANCOVA) was used. The use of an ANCOVA model allows the examination of the effect of predictors on the OKS whilst accounting for baseline differences in OKS between patients[283]. Again, both univariable and multivariable models were constructed. Clustering by surgeon was accounted-for using a two-level random intercept model. As the multivariable model used imputed data, explained variation was assessed by calculating the adjusted R^2 using the method described by Harel[299].

For the binary PROM outcome (improvement / no change in OKS versus deterioration), logistic regression was used; again, predictors were examined in univariable and multivariable models and clustering was accounted for using a two-level random intercept model. Ordered logistic regression was used to examine the effect of each of the predictors on satisfaction.

4.2.4.3. Regression diagnostics

The linearity of the effect of each exposure was assessed using two techniques. For survival analyses, fractional polynomial plots were produced to characterise the survival hazard[300]. For PROM (linear regression) analyses, scatterplots were produced and smoothed curves fitted using locally-weighted scatterplot smoothing (LOWESS[301]); scatter points were supressed in these graphs for clarity (examples of both types of plot are given in Figure 4-2). If predictors were found to be non-linear, they were categorised or linear splines were fitted. In the case of predictors with established categories (such as BMI), categorisation was used; otherwise, linear splines were fitted to break the hazard

down into roughly linear subsections; these were then entered separately into the model. Interactions were examined using the interaction commands within Stata. In the case of a continuous-continuous interaction with a non-linear predictor, fractional polynomials were fitted and interactions detected using the user-written 'mfpigen' command[302].

Colinearity was assessed by checking the variance inflation factor after running each model. Normality of residuals was assessed by plotting standardised normal probability-probability plots. Heteroskedasticity (where the variance of the residuals is non-constant) was examined using graphical examination of residuals. If heteroskedasticity was demonstrated, robust standard errors were used with the sandwich variance estimator. As before, analyses were performed using Stata IC v12.1.

4.3. Results

Overall implant survival was 91.8% (95% CI 91.3-92.3) at five years and 89.1% (95% CI 88.3-89.9) at eight years. OKS increased from 21.9 (SD 7.6) points pre-operatively to 37.5 (SD 9.5) points at six months. EQ5D index increased from a mean score of 0.480 (SD 0.290) pre-operatively to 0.770 (0.250) at six months. 84.3% of patients had good, very good or excellent levels of satisfaction. Adverse outcomes were rare: 5.5% of patients had worse OKS at six months than beforehand and 3.8% reported poor satisfaction. Descriptive statistics are displayed in Table 4-1; outcomes are given in Table 4-2.

4.3.1. Regression diagnostics

No evidence of colinearity was demonstrated for any of the models. The distribution of residuals was not demonstrated to deviate significantly from normality (Figure 4-1). Heteroskedasticity was demonstrated in the continuous OKS comparison and robust standard errors were employed with the sandwich variance estimator to account for this.

Linearity of predictors is considered in the following Sections; example linearity graphs are given in Figure 4-2.

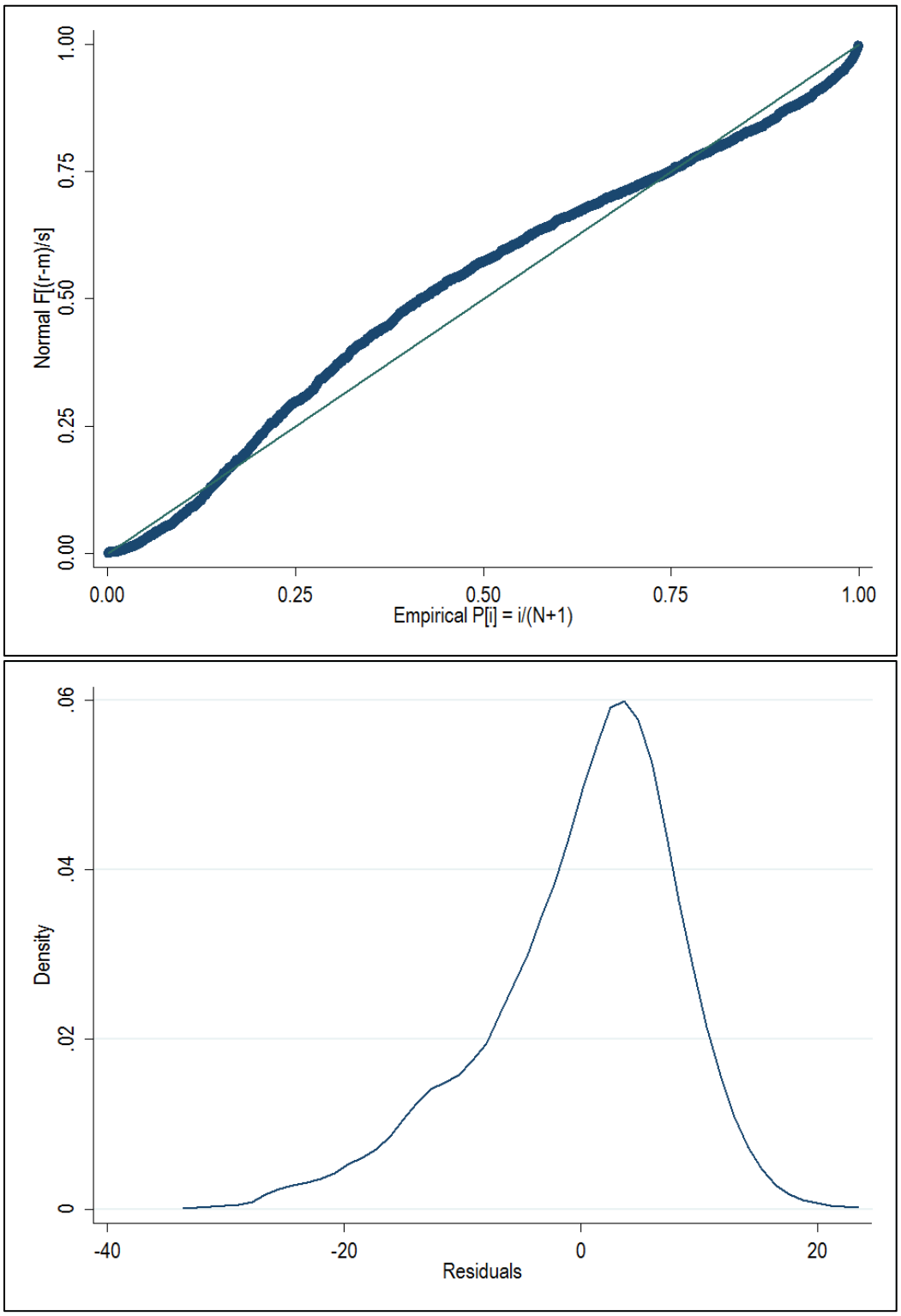


Figure 4-1: Estimation of normality of residuals
Probability-probability plot (top) and kernel density plot of resuduals (bottom) demonstrate only a minor deviation from normality.

NJR Variables	Mean (SD, Range)
Age	64.3 (9.7, 21.7-95.8)
BMI; 13,441 (52%) missing	30.2 (5.0, 16-60)
Unit size	49.4 (60.9, 1-317)

HES/PROM variables	Mean (SD, Range)
Pre-operative OKS	21.9 (7.6, 0-43)
Pre-operative EQ5D	0.480 (0.290, -0.426-1)

Variable		N (%)
Gender (male)		13,547 (52.1)
ASA grade	1	5,885 (22.7)
	2	17,725 (68.2)
	3+	2,372 (9.1)
Ethnicity	Not Given	3,654 (14.1)
	White	21,506 (82.8)
	Mixed race	54 (0.2)
	Asian	515 (2.0)
	Black	120 (0.5)
	Other	133 (0.5)
Unit type	NHS Hospital	22,085 (85.0)
	Private hospital	2,872 (11.1)
	ISTC	1,025 (4.0)
Consultant performed		22,255 (85.7)
Mechanical thrombo-prophylaxis	TEDs	16,772 (64.6)
	Foot pumps	5,820 (22.4)
	Other	272 (1.1)
	None	3,118 (12.0)
Chemical thrombo-prophylaxis	Heparin / LMWH	15,816 (60.9)
	Aspirin	3,924 (15.1)
	Warfarin	211 (0.8)
	DTI	1,101 (4.2)
	Other	1,927 (7.4)
	None	3,003 (11.6)
Implant fixation (cemented)		23,209 (90.0)

Variable		N (%)
Charlson co-morbidity index	None	20,865 (80.3)
	Mild	4,298 (16.5)
	Moderate	642 (2.5)
	Severe	177 (0.7)
IMD (Quintiles)	1 (most deprived)	2,951 (11.4)
	2	4,361 (16.8)
	3	5,791 (22.3)
	4	6,179 (23.8)
	5 (least deprived)	6,700 (25.8)
Number with PROMs		3,429 (13.2)
Pre-op EQ5D anxiety / depression	None	2,331 (68.0)
	Moderate	1,002 (29.2)
	Extreme	96 (2.8)
Self-reported health	Excellent	133 (4.9)
	Very good	894 (33.0)
	Good	1,209 (44.7)
	Fair	413 (15.3)
	Poor	58 (2.1)
Self-reported disability		1,347 (41.2)

Table 4-1: Baseline variables

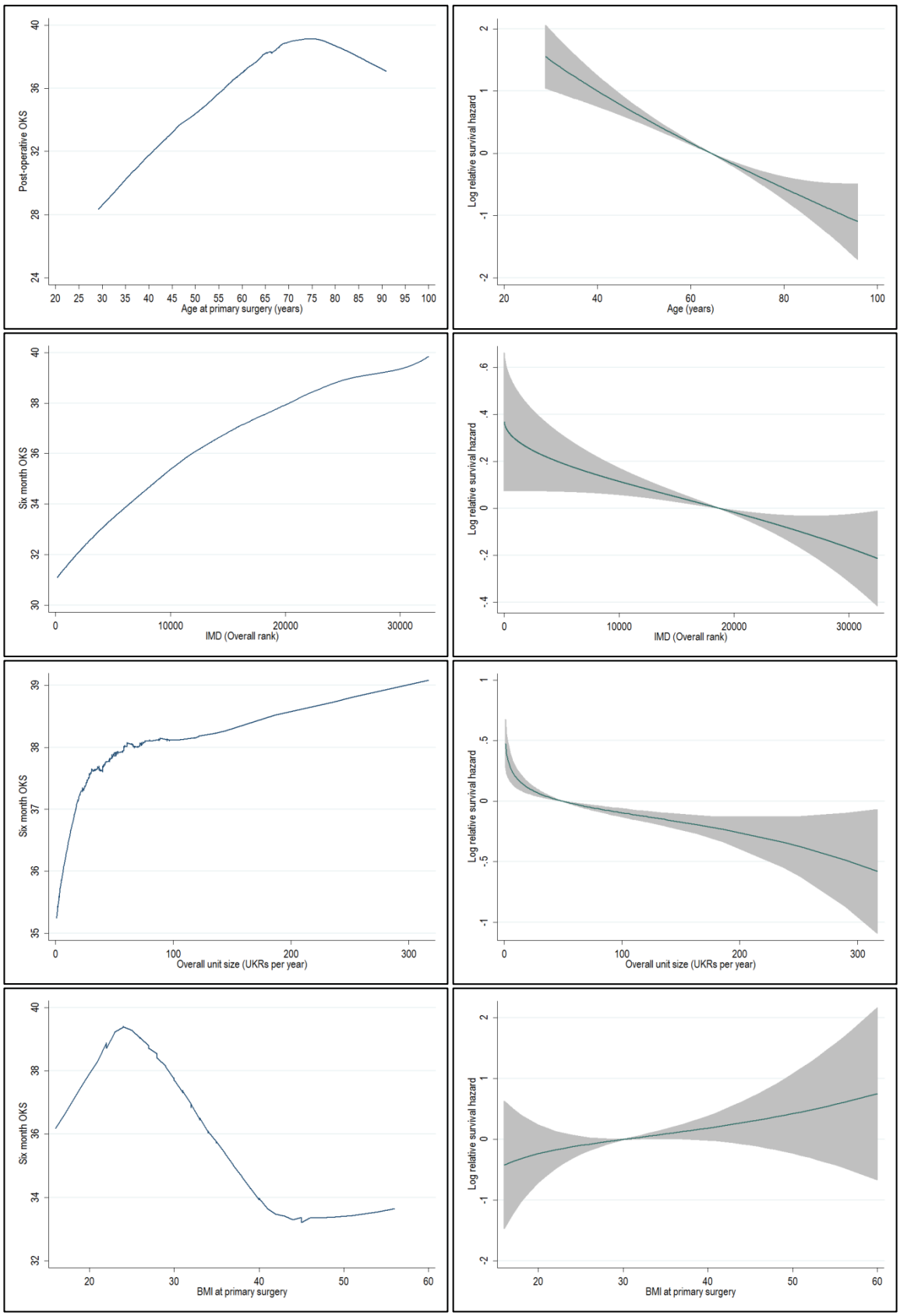


Figure 4-2: Assessment of linearity: example plots
Variables are assessed for the PROM comparison using LOWESS plots (left) and for the survival comparison using fractional polynomial plots (right). For survival, age, IMD and BMI are considered to be linear; for PROMs, only IMD (of these plots) is considered to be linear. The remainder of these variables are categorised (BMI) or fitted using linear splines for the purposes of analysis.

Outcome		
Eight- year implant survival (95% CI)		89.1 (88.3-89.9)
OKS, mean (SD)		37.5 (9.5)
EQ5D, mean (SD)		0.770 (0.250)
Improvement, N (%)	Better	3,204 (93.4)
	Same	37 (1.1)
	Worse	188 (5.48)
Satisfaction, N (%).	Excellent	930 (27.1)
	Very Good	1223 (35.7)
	Good	725 (21.1)
	Fair	410 (12.0)
	Poor	128 (3.7)
	Not given	13 (0.4)

Table 4-2: Overall outcomes

4.3.2. Factors affecting implant survival

Univariable and multivariable survival models are displayed in Table 4-3. Implant survival was better in older patients, men, and those with no co-morbidities (compared to those with moderate co-morbidities). Revision was less likely if the procedure was performed in a unit undertaking high numbers of cases per year and if it was performed by a consultant rather than a trainee. The effect of unit size on revision risk was non-linear, reducing markedly up to 40 cases/year but being relatively constant beyond that point. There was a strong trend towards inferior survival in independent-sector treatment centres compared to NHS hospitals, and in areas with higher levels of deprivation, but both had only borderline significance. Neither BMI, ethnicity, nor choice of thromboprophylaxis had any effect on implant survival following UKR. Survival was equivalent whether cemented or cementless UKR was used.

Variable		Univariable		Multivariable	
		HR (± 95 CI)	Significance	HR (± 95 CI)	Significance
Age		0.96 (0.96-0.97)	<0.01	0.96 (0.96-0.97)	<0.01
Gender (male)		0.83 (0.74-0.94)	<0.01	0.86 (0.76-0.96)	0.01
ASA (per one grade increase)		0.94 (0.85-1.05)	0.27	1.06 (0.95-1.20)	0.30
BMI (n=13,501)		1.02 (1.00-1.04)	0.05	1.01 (0.98-1.03)	0.59
Ethnic group - white		Reference			
Not Given		0.86 (0.72-1.02)	0.09	0.86 (0.72-1.02)	0.08
Mixed race		0.42 (0.07-2.65)	0.36	0.34 (0.05-2.24)	0.26
Asian		0.94 (0.60-1.46)	0.77	0.81 (0.52-1.25)	0.34
Black		1.39 (0.71-2.72)	0.33	1.02 (0.50-2.06)	0.96
Other		0.39 (0.09-1.61)	0.19	0.39 (0.09-1.61)	0.19
Unit type – NHS hospital		Reference			
Independent hospital		1.07 (0.88-1.30)	0.51	1.07 (0.87-1.30)	0.53
ISTC		1.10 (0.78-1.55)	0.59	1.43 (0.99-2.05)	0.05
Consultant performed		0.91 (0.77-1.07)	0.24	0.78 (0.67-0.91)	<0.01
Mechanical thrombo-prophylaxis	TEDS	Reference			
	Foot pumps	1.02 (0.84-1.23)	0.87	0.98 (0.81-1.19)	0.82
	Other	1.32 (0.80-2.18)	0.27	1.24 (0.77-2.01)	0.37
	None	1.04 (0.85-1.27)	0.70	1.01 (0.83-1.22)	0.94
Chemical thrombo-prophylaxis	Heparin/LMWH	Reference			
	Aspirin	0.98 (0.79-1.22)	0.85	1.11 (0.90-1.37)	0.34
	Warfarin	0.61 (0.30-1.26)	0.18	0.71 (0.35-1.44)	0.34
	DTI	0.56 (0.30-1.04)	0.07	0.55 (0.30-1.01)	0.06
	Other	0.86 (0.63-1.18)	0.36	0.81 (0.59-1.11)	0.19
	None	1.15 (0.93-1.43)	0.20	1.22 (0.98-1.51)	0.08
Fixation		0.99 (0.77-1.26)	0.91	1.02 (0.79-1.31)	0.89
Charlson - No comorbidities		Reference			
Mild comorbidities		1.09 (0.94-1.27)	0.26	1.12 (0.96-1.30)	0.16
Moderate comorbidities		1.36 (0.95-1.95)	0.09	1.49 (1.04-2.12)	0.03
Severe comorbidities		1.21 (0.62-2.35)	0.58	1.40 (0.72-2.72)	0.33
IMD (per quintile)		0.91 (0.87-0.96)	<0.01	0.96 (0.91-1.00)	0.07
Unit size (per ten cases)	Up to 40 cases/yr	0.97 (0.96-0.99)	<0.01	0.92 (0.86-0.97)	0.01
	Above 40 cases/yr			0.99 (0.97-1.01	0.32

Table 4-3: Survival models

4.3.3. Factors affecting patient-reported outcome measures and satisfaction

PROM and satisfaction models are displayed in Table 4-4. For the multivariable linear regression model, the adjusted R^2 is 0.24. As has been previously demonstrated in other forms of joint replacement, pre-operative OKS had a strong positive effect on six-month OKS. Age strongly affected both pre-and post-operative OKS in a non-linear fashion. For both pre- and post-operative OKS, scores peaked at around 75 years of age (Figure 4-3).

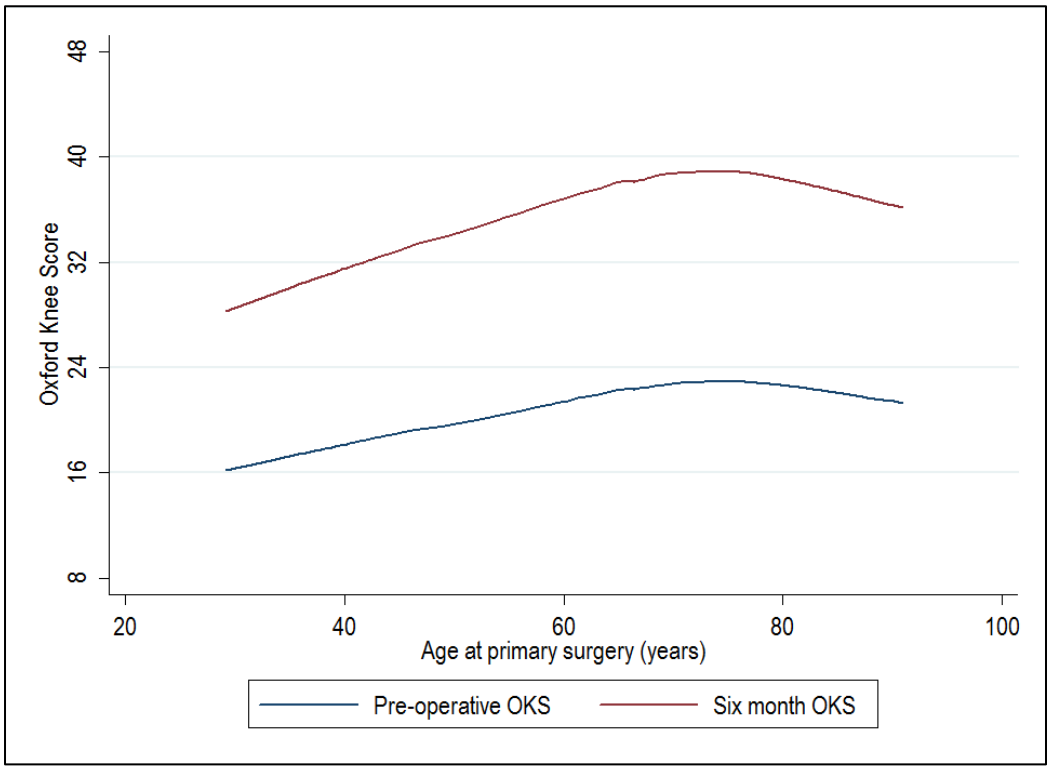


Figure 4-3: The effect of age on pre-operative and six-month OKS

As such, two linear splines were fitted, one up to 75 years and one beyond 75 years. Up to the age of 75, age had a significant positive effect on six-month OKS (0.14 points per year, $p<0.001$). Above 75, scores reduced but this did not reach statistical significance. As this was an ANCOVA model, these findings were adjusted for the observed baseline differences in OKS. In addition, older patients were less likely to have worse scores at six months than pre-operatively, and were more likely to be satisfied.

Variable		OKS model (continuous)		OKS model (binary)		Satisfaction	
		Co-efficient (± 95 CI)	Sig.	Odds ratio (± 95 CI)	Sig.	Odds ratio (± 95 CI)	Sig.
Age (per year)	18-75	0.14 (0.09-0.20)	<0.001	0.96 (0.94-0.98)	<0.001	1.02 (1.01-1.03)	<0.001
	≥75	-0.18 (-0.63-0.07)	0.162				
Gender		0.19 (-0.63-1.02)	0.650	1.06 (0.74-1.53)	0.744	1.01 (0.86-1.18)	0.924
ASA grade		-0.53 (-1.35 - 0.29)	0.206	1.00 (0.70-1.44)	0.998	0.88 (0.77-1.02)	0.088
BMI (Ref: normal)	Underweight	4.42 (-5.06-13.91)	0.360	1.00 (0.96-1.05)	0.923	1.00 (0.98-1.02)	0.979
	Overweight	-0.03 (-1.47 – 1.42)	0.972				
	Obese	-1.04 (-2.50 – 0.41)	0.160				
Ethnicity (Ref: White)	Un-defined	0.24 (-1.08 – 1.57)	0.717	0.90 (0.46-1.75)	0.750	1.05 (0.84-1.32)	0.654
	Mixed race	-0.60 (-7.33 – 6.12)	0.860	-	-	0.65 (0.32-1.33)	0.239
	Asian	-9.77 (-14.26 - -5.27)	<0.001	1.42 (0.43-4.64)	0.564	0.41 (0.21-0.79)	0.007
	Black	-10.79 (-19.19 - -2.75)	0.009	3.65 (0.68-19.56)	0.131	0.53 (0.29-0.99)	0.048
	Other	-1.92 (-6.56 – 2.72)	0.428	-	-	0.82 (0.47-1.44)	0.494
Unit type (Ref: NHS)	Private hospital	0.48 (-0.76 – 1.72)	0.448	0.78 (0.43-1.41)	0.412	1.16 (0.90-1.49)	0.265
	ISTC	1.09 (-0.91 – 3.09)	0.286	0.26 (0.03-1.99)	0.193	1.27 (0.91-1.78)	0.154
Consultant performed		0.99 (-0.25 - 2.22)	0.116	0.56 (0.35-0.91)	0.018	1.40 (1.13-1.74)	0.002
Mechanical thrombo-prophylaxis (Ref: TEDS)	Foot pumps	0.88 (-0.22 – 1.98)	0.117	1.01 (0.65-1.58)	0.951	1.10 (0.89-1.36)	0.362
	Other	-1.29 (-7.22 – 4.63)	0.668	0.74 (0.09-5.86)	0.773	0.71 (0.35-1.46)	0.358
	None	-1.48 (-3.37 – 0.41)	0.125	1.31 (0.68-2.53)	0.426	0.89 (0.67-1.18)	0.423
Chemical thrombo-prophylaxis (Ref: Heparin / LMWH)	Aspirin	-1.61 (-2.54 – 0.25)	0.108	1.78 (1.02-3.12)	0.043	0.75 (0.55-1.01)	0.058
	Warfarin	-3.18 (-9.92 – 3.57)	0.356	1.17 (0.23-6.01)	0.854	1.01 (0.41-2.45)	0.988
	DTI	0.40 (-1.19 – 1.99)	0.624	0.80 (0.36-1.77)	0.584	0.82 (0.63-1.05)	0.120
	Other	-0.44 (-1.69 – 0.81)	0.486	0.77 (0.42-1.38)	0.375	0.93 (0.74-1.16)	0.509
	None	0.93 (-1.04 – 2.90)	0.356	0.83 (0.36-1.92)	0.663	1.00 (0.72-1.37)	0.985
Implant fixation		-0.56 (-1.78 - 0.65)	0.365	1.21 (0.67-2.18)	0.530	0.81 (0.65-1.02)	0.068
Charlson co-morbidity index (Ref: None)	Mild	-0.71 (-1.79 - 0.37)	0.198	1.01 (0.63-1.61)	0.962	1.07 (0.88-1.29)	0.498
	Moderate	0.41 (-2.18 – 3.00)	0.756	2.95 (1.23-7.05)	0.015	1.21 (0.66-2.22)	0.540
	Severe	5.86 (-0.81 – 12.53)	0.085	1.72 (0.20-15.01)	0.624	2.19 (0.77-6.19)	0.140
IMD (Quintiles)		0.93 (0.60-1.27)	<0.001	0.76 (0.66-0.88)	<0.001	1.07 (1.01-1.15)	0.029
Unit size (per 10 cases)	0-40 cases	0.32 (-0.05 – 0.70)	0.088	0.98 (0.95-1.02)	0.354	1.01 (1.00-1.03)	0.032
	≥40 cases	0.00 (-0.07 – 0.12	0.570				
Pre-operative OKS		0.24 (0.18 - 0.30)	<0.001	1.10 (1.07-1.13)	<0.001	1.00 (0.99-1.01)	0.807
Pre-op EQ5D anxiety / dep. (Ref: None)	Moderate	-0.60 (-1.57-0.36)	0.221	1.29 (0.86-1.94)	0.220	0.97 (0.81-1.15)	0.708
	Extreme	-3.32 (-6.16 - -0.47)	0.023	1.63 (0.52-5.11)	0.404	0.92 (0.55-1.54)	0.752
Self-reported health		-1.70 (-2.24 - -1.16)	<0.001	1.30 (1.03-1.65)	0.027	0.58 (0.52-0.65)	<0.001
Self-reported disability		-2.33 (-3.24 – 1.41)	<0.001	1.92 (1.30-2.86)	<0.001	0.82 (0.70 – 0.96)	0.012

Table 4-4: Patient-reported outcome and satisfaction models
Values are omitted for the binary OKS model where none of the group deteriorated

When studying the effects of age and pre-operative OKS level on OKS, an interaction was detected. Young patients with poor pre-operative scores appeared to fare particularly poorly: whilst poorly-functioning patients (ie, those with a pre-operative OKS ≤ 15) above the age of 65 can expect to gain 22.5 points on their pre-operative OKS (95% CI 21.3-23.8), those below the age of 65 can only expect to gain 18.8 points (95% CI 17.7-19.8). The effect of age is much reduced (albeit still statistically significant) in patients with better pre-operative OKS (Figure 4-4).

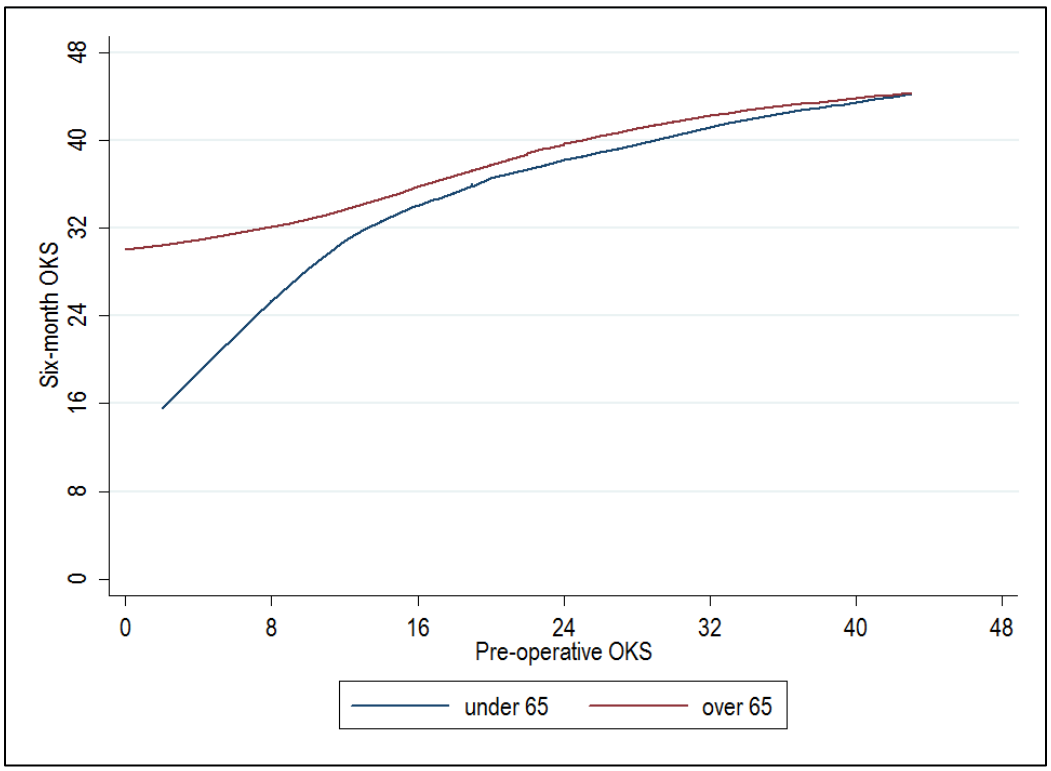


Figure 4-4: Pre-operative OKS plotted against post-operative OKS by age subgroups

To explore this further, the model was stratified into patients with poor pre-operative OKS (≤15 points) and those with better pre-operative OKS (>15); these results are given in Table 4-5. The stratification was not observed to affect the effect sizes or significance levels for any of the other variables studied and the overall model presented (in Table 4-4) is not stratified by preoperative OKS. No further interactions were detected.

		Coeficient (95% CI)	Significance
Pre-op OKS≤15	Age (18-75)	0.27 (0.14-0.40)	<0.001
	Age (>75)	-0.42 (-1.05 – 0.20)	0.186
Pre-op OKS>15	Age (18-75)	0.09 (0.04-0.15)	0.002
	Age (>75)	-0.07 (-0.34 – 0.19)	0.6

Table 4-5: Interaction of age and pre-operative OKS

Ethnicity appeared to affect outcome, with black and Asian patients reporting significantly worse OKS and satisfaction. Patients were less likely to deteriorate and more likely to be satisfied if their operation was performed by a consultant rather than a trainee; whilst there was a trend to higher overall scores in consultant-performed cases, this was not statistically significant. Unit size did not have as great an effect on patient-reported outcome as it did on implant survival. The effect of unit size on six-month OKS was again non-linear; OKS improved by 0.32 points for every ten cases up to 40, before becoming essentially constant above 40 cases. Only borderline significance was achieved in either section. There was a small but statistically significant increase in satisfaction if the case was performed in a higher-volume unit.

Those with co-morbidities (measured by the Charlson index) were more likely to have worse scores at six months than pre-operatively; patients who reported poor health prior to surgery or who described themselves as having a disability, had worse outcomes by all three metrics. Overall, thromboprophylaxis did not exert a great effect on patient-reported outcome, with the exception of patients taking aspirin, who were more likely to report deterioration in their OKS, as well as having a trend to lower overall OKS and satisfaction.

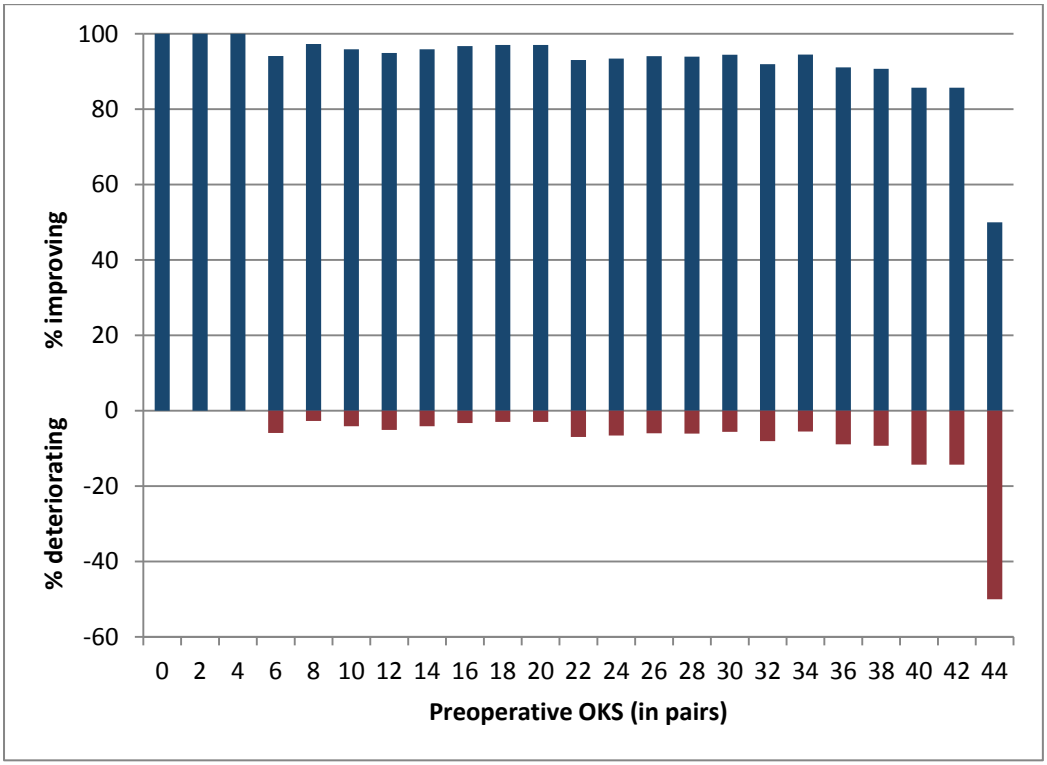


Figure 4-5: Relationship between pre-operative OKS and risk of deterioration
Pre-operative OKS has been grouped in pairs for clarity

Better pre-operative OKS predicted better post-operative OKS, but patients with higher pre-op scores had a higher chance of having a worse six month score than they had beforehand (Figure 4-5). Very few patients underwent UKR with an OKS of more than 35 points pre-operatively, but these patients (n=120) had a 15.8% chance of being worse post-operatively than pre-operatively; the chance of deterioration was only 5.1% in patients with a pre-operative OKS of 35 points or fewer. Patients with extreme anxiety or depression (as measured using the EQ5D) had significantly worse scores overall compared to those with no anxiety/depression, but were no more likely to deteriorate or to be dissatisfied. Neither BMI, ASA grade, unit type, nor implant fixation had any effect on outcome by any measure.

4.3.4. Sensitivity analysis: BMI

As in the previous chapter, missing data for BMI were completed using multiple imputation. As this chapter specifically examined the importance of each predictor variable, BMI was included in its imputed state (whilst it was omitted from the propensity score calculation in Chapter 3 and examined as a sensitivity analysis). The process of MI has been discussed in detail elsewhere (Chapter 2). In order to determine whether errors had occurred in the MI process, the BMI effect was again examined as univariable, complete-case and imputed datasets; no important differences were noted between the effect sizes within each analysis (Table 4-6), and the imputed dataset was used in the full analysis.

Analysis		Univariable	Multivariable (complete case)	Multivariable (imputed)
Survival, hazard ratio		1.02 (1.00-1.04), p=0.05	1.00 (0.99-1.02), p=0.66	1.01 (0.98-1.03), p=0.59
OKS (continuous), coefficient	Underweight	1.40 (-8.50-11.30), p=0.78	4.34 (-5.14-13.83), p=0.37	4.42 (-5.06-13.91), p=0.36
	Normal	Reference	Reference	Reference
	Overweight	-0.03 (-1.27-1.21), p=0.96	-0.24 (-1.47-1.42), p=0.97	-0.03 (-1.47 – 1.42), p=0.97
	Obese	-1.50 (-2.74 - -0.26), p=0.02	-1.13 (-2.59-0.33), p=0.13	-1.04 (-2.50 – 0.41), p=0.16
OKS (binary), odds ratio		1.02 (0.98-1.06), p=0.31	1.00 (0.95-1.04), p=0.89	1.00 (0.96-1.05), p=0.92
Satisfaction, odds ratio		0.97 (0.96-0.99), p<0.001	1.00 (0.98-1.02), p=0.99	1.00 (0.98-1.02), p=0.98

Table 4-6: BMI model comparison

4.4. Discussion

The overall results of this study have supported the findings reported in Chapter 3, that UKR is a highly effective intervention in relieving the symptoms of end-stage osteoarthritis. However, some groups of patients have been demonstrated to fare significantly better than others and important risk factors, in terms of patient selection and surgical practice, have been identified.

As in previous studies of TKR, pre-operative function has been demonstrated to be a strong predictor of post-operative function[223,224]. However, patients with poor pre-operative functional status are just as likely to be satisfied with their surgery despite reporting poorer overall scores. Patients with higher pre-operative OKS values are also at higher risk of being worse off following surgery than they were beforehand. This may simply be an issue of measurement: patients with high pre-operative PROMs may make gains undetectable by the OKS[150]. This is supported by the finding that overall six-month OKS and satisfaction level are just as great with patients with the highest pre-operative OKS as those with lower values. However, caution should be exercised when offering any form of joint replacement to patients with very high pre-operative function.

Age has been demonstrated to have a significant positive effect on outcome by each metric studied, following adjustment for baseline differences in OKS. Whilst OKS tends to deteriorate with age in the general population[145], this study has demonstrated that young patients undergoing UKR tend to have lower baseline OKS levels than older patients receiving the same operation, which may represent a higher threshold for offering joint replacement to younger patients. However, even following adjustment for these differences, older patients have been shown to derive the greatest benefit from UKR, as well as having lower revision rates than younger patients. These findings,

together with the lower rates of perioperative morbidity and mortality associated with UKR[5,188], suggest that older patients may be particularly suitable for UKR. This is contrary to current practice – at present, UKR is more likely to be offered to younger patients: whilst UKR comprises nearly 20% of all knee replacements performed in patients in their fifties, it only comprises 5% of knee replacements in octogenarians[97]. Of particular concern would appear to be younger patients with very poor pre-operative PROMs, who appear to fare particularly poorly in terms of OKS gain.

In England and Wales, men are more likely than women to be offered UKR: 58% of TKRs are performed in women, whilst the equivalent figure is only 46% in UKR[97]. On the basis of this study, men and women achieve very similar patient-reported outcomes and satisfaction levels. However, there is a small but statistically significant difference in eight-year survival, with men less likely to undergo revision than women. This contrasts with the situation in TKR, where male gender is an established risk factor for revision, despite men achieving better functional outcomes than women[208,223,233,235]. A large part of the effect in TKR is due to a higher infection rate in men[233], and the relative rarity of infection as a mode of failure following UKR may account for this difference[97,237]. It is not clear from this study whether the small observed effect of gender on survival in UKR is due to problems caused by the fact that women are generally smaller than men (and hence the implants used are smaller and implantation may be more technically demanding), or to some factor intrinsic to female gender. One potential reason may be the higher incidence of inflammatory arthropathies in women; UKRs implanted in patients with undiagnosed inflammatory arthritis are at higher risk of revision secondary to degeneration of un-replaced parts of the knee. However, given the small margin of difference in survival, and the equivalent patient-reported outcomes, this study does not provide evidence for restriction of access to UKR on the basis of gender.

This study provides no evidence for restricting UKR on the basis of any of the other patient factors examined. Neither BMI nor ASA score have been demonstrated to influence outcome by any metric. Whilst deprivation, morbidity, and anxiety/depression pre-dispose to a poor outcome (in terms of implant survival, PROMs and satisfaction), all are also established risk factors for a poor outcome following TKR[223,295,297,303]. Likewise, whilst Black and Asian patients have been demonstrated to have poorer outcomes in terms of patient-reported outcome and satisfaction, these differences are similar to those reported in TKR[294]. The reasons for these differences are complicated and may be related to differences in social support, expectations (for instance, placing more importance on the ability to kneel or sit cross-legged), pain perception and access to joint replacement[304]. Black and Asian patients may be more likely to present later in the disease process and therefore have more severe disease prior to joint replacement[298]. This is supported by the data presented here, which demonstrate that Black and Asian patients had significantly worse OKS prior to surgery than their White counterparts. In addition, patients of different ethnicities may present with different patterns of arthritis, which may affect suitability for UKR[23]. The conclusions that can be drawn from this study in this regard are limited by the small number of patients in the two ethic groups which demonstrate significantly poorer outcomes (Black and Asian, which comprise 2.5% of the study population collectively).

In terms of surgical factors, patients are less likely to be revised, less likely to deteriorate clinically and more likely to be satisfied if a consultant rather than a trainee performs their UKR. Revision is less likely if surgery takes place in a high-volume unit and patients undergoing surgery in such units report greater satisfaction. A similar effect on survival has been demonstrated in previous studies of both TKR and UKR[91,215,305]. For every ten case increase (up to 40 cases per year), the hazard ratio for revision is 0.92; the

effect is much reduced above this level. This effect may represent improved surgical or post-surgical care in units with greater experience of UKR, or it may simply reflect the surgeons in the unit performing a greater number of cases each and hence gaining greater experience and expertise[91,215]. The effect of differences in usage are explored further in Chapter 5, and further discussion is beyond the scope of this chapter.

Whilst joint registries consistently report poorer survival in TKR when it is performed using cementless implants (as discussed in Section 1.11.2), this study demonstrates no such effect in UKR[97]. This supports the view, expounded in Section 1.12, that UKR may be more suitable for cementless fixation than TKR; cementless fixation will form the focus of the second Part of this thesis. Whilst implant survival was unaffected, patients taking aspirin for thromboprophylaxis had a greater chance of deterioration with a trend to lower overall OKS and satisfaction. This may simply be an indicator of higher levels of pre-existing morbidity in patients receiving aspirin, but warrants further investigation.

4.4.1. Findings in context

The literature on predictors of failure in UKR is limited and is covered in detail in Section 1.10. This study supports that of Pandit *et al,* in finding no effect of BMI on outcome; however, this study reports superior PROMs in older people, which was not found in that study[64]. Thompson *et al* reported a higher revision rate in women, which agrees with this study, however, they report superior PROMs in younger patients[228]. As in this study, the study of Sebillo *et al*, reported significantly superior survival in older patients and men, but reported no difference in overall patient-reported outcome or satisfaction for either group, and no effect of BMI[230]. Case series from Matharu *et al* (459 UKRs) and Kristensen *et al* (695) and Price *et al* (564) report no statistically significant effect of age or gender on the revision rate[183,227,229]. Kuipers *et al* again report no effect of

BMI, but they report a higher risk of revision in younger patients, contrary to the findings presented here[231].

4.4.2. Strengths and limitations

The strengths of this study include the size of the sample studied: this study represents the largest and most comprehensive examination of risk factors for failure in UKR yet performed. The use of linked datasets from the NJR, HES and PROMs databases has facilitated the examination of a large number of predictors. The fact that this study used an unselected registry sample with multiple surgeons and implants suggests that these findings may be generalised to the population as a whole.

Limitations include the lack of information concerning pre-operative disease state, which represents a source of unmeasured confounding[306]. Detailed prosthesis information was not available; however, as discussed in Section 1.6, the majority of the UKRs performed in England and Wales are of a single design, and prosthesis choice has not been demonstrated to exert a significant effect on outcome after UKR in previous studies[91,230]. The large amount of missing BMI data limits the conclusions that can be drawn regarding BMI. However, BMI was not found to exert an appreciable effect on outcome in either the complete-case (see Section 4.3.4) or the imputed datasets. Patient-reported outcome was only available in the short-term; however, patient-reported outcomes have been demonstrated to stabilise after the first six months following surgery, and longer-term results have been presented in the form of revision rates[307].

4.4.3. Conclusions

This study has identified important surgical and patient factors predisposing to good or poor results after UKR. Of note, older patients, who are the patients least likely to be offered UKR, are those who appear to derive the greatest benefit and have the lowest

revision rates. Particular caution should be exercised in younger patients with very low pre-operative functional scores. No evidence has been found for the use of narrow indications for UKR in terms of BMI or ASA, and many other prognostic factors are common to both UKR and TKR.

One important predictor of outcome is surgical volume. In this chapter, superior outcomes have been demonstrated for patients operated upon by consultant surgeons in high-volume units, supporting the assertions made by previous studies that the outcome of UKR is particularly dependent on surgical experience. In Chapter 5, the effect of surgeon (rather than unit) caseload will be explored in detail, together with the reasons for the effects observed.

Chapter 5 The effect of patterns of usage on outcome following UKR

5.1. Introduction

Whilst UKR has been demonstrated by previous chapters to be an effective intervention with important benefits over TKR, the revision rate for UKR remains unacceptably high in comparison to TKR. In Chapter 4, important patient and surgical factors have been identified which may represent targets for improving the revision rate. Amongst these is surgical caseload, which will be investigated in more detail in this chapter. Previous authors have demonstrated a relationship between implant survival and surgical case-load, both within units and for individual surgeons (Section 1.10.1.2).

However, surgical caseload is not a predictor of outcome in and of itself; rather, it is the expression of other predictors. The most obvious of these is surgical skill (on the principle that 'practice makes perfect'); however, low-volume surgeons have published excellent results for UKR[308], and likewise, surgeons who have very high-volume TKR practices have failed to attain results even comparable to those reported by the NJR[309]. Other factors may include revision threshold (surgeons who believe that UKR is a procedure with very limited indications may be more ready to revise it to a TKR than those who strongly believe in UKR)[128], and errors in patient selection for UKR. It is also unclear whether this caseload effect extends to patient-reported outcomes as well as revision. A similar caseload effect has been described in TKR, but the magnitude of this effect has not been compared to that in UKR[305,310,311].

An additional problem is how to achieve the required number of cases, given that the number and nature of patients presenting for knee replacement each year is beyond the control of the operating surgeon. When the population of patients presenting to

surgeons for knee replacement remains the same, the principal mechanism of increasing the number of patients undergoing UKR is to broaden the indications. However, the indications for UKR are controversial (as discussed in Section 1.5.3).

Surgeons are reluctant to increase their indications beyond those traditionally accepted for fear of increasing their revision rate by operating on patients less likely to do well. As discussed in Section 1.10, the traditional, narrow, indications for UKR have been challenged by newer research, and units performing large numbers do so with much broader indications, offering UKR to up to 50% of patients[64,65]. It is unclear to what extent the indications may be broadened, before the positive effect of improving outcomes through increased volumes is outweighed by the negative effect of selecting inappropriate patients.

This chapter has four aims:

1. To determine the effect of caseload on outcome, both in terms of implant survival and patient-reported outcome, and to identify thresholds for high, medium and low volume on the basis of this effect.
2. To determine whether differences in patient selection explain the differences in outcome between high, medium and low-volume surgeons.
3. To compare patient-reported outcomes, revision and reoperation rates of UKRs performed by high- medium- and low-volume surgeons with matched patients undergoing TKR.
4. To study the effect of broadening indications, to determine whether outcomes can be preserved whilst offering UKR to a broader population of patients.

5.2. Methods

5.2.1. Data sources

The analyses in this chapter are again based on the NJR, HES and PROMs datasets first encountered in Chapter 3. Different parts of this extract were used for each of the analyses performed.

5.2.1.1. Descriptive analysis of caseload (aim 1) and usage (aim 4) effects

The effect of surgical caseload on survival of UKR and TKR was examined using the extract of 552,015 patients from the NJR for England and Wales. In addition to the inclusion and exclusion criteria used in Chapters 3 and 4, cases from 2003 and 2012 were excluded. This was because the dataset for each of these years was incomplete, and so caseload could not be accurately assessed for these years. Likewise, linkage to HES and PROMs datasets was not attempted for this analysis, as it was necessary to include those patients who would have been excluded by linkage (predominantly those undergoing their surgery in the private sector) in the caseload calculation. The study group comprised 459,280 cases, of which 37,131 (8.1%) were UKRs.

Having defined the caseload for each surgeon using the larger dataset, the analysis of patient-reported outcome was performed using a subset of these patients who could be linked to corresponding records in the PROM database. As previously outlined, operations not performed under the auspices of the NHS, and those performed outside England, are not included in the PROM database. Using unique patient identifiers, PROM records were linked to corresponding NJR records. PROM records were excluded if they corresponded to operations in the 2012 calendar year, or if any of the pre- or post-operative questionnaires were missing or had been taken either too early (>6 months prior to surgery or <6 months following surgery) or too late (more than one year

following surgery). As such, 50,088/459,280 cases (10.9%) were linked to a PROM record; 3,279 of the 50,088 linked cases were UKRs (8.8%).

5.2.1.2. Analysis of patient factors (aims 2 and 3)

For the analysis of patient factors, and for the matched analysis, NJR cases were linked to corresponding HES records. In common with the PROM dataset, this led to the exclusion of patients from the NJR who underwent their surgery in private units and those from Wales. This leads to the loss of some patients from the analysis (and hence HES linkage was not undertaken for the descriptive analysis); however, for patients who can be linked, a large amount of extra information is available, allowing close matching of patients. Information obtainable from HES includes detailed socioeconomic and co-morbidity data, perioperative complications and non-revision re-operations.

5.2.2. Exposures and outcomes

Caseload and volume figures were calculated using the unique surgeon identifiers contained in the NJR record. Using this identifier, the number of UKRs for each surgeon was calculated for each calendar year from 2004 to 2011. Each patient was allocated a value for surgeon caseload, which represented the number of cases performed in the year of surgery by the surgeon in charge. For the descriptive analyses on the surgeon level, a mean number of cases per year was calculated for each surgeon. Only years in which the surgeon performed UKR were counted; this prevents an artificial reduction in apparent surgical caseload in surgeons who started contributing in later years of the NJR, or who retired or abandoned UKR in later years. An equivalent figure for TKR caseload was calculated for each surgeon.

Mean TKR and UKR caseloads may be described on the surgeon level or the patient level. Surgeon-level mean caseload is the mean number of cases per year, per surgeon in

the NJR. Patient-level caseload is the mean surgeon caseload per case performed in the NJR. Caseload is higher on the patient-level than it is on the surgeon-level as higher-volume surgeons perform more cases by definition. In the example given in Table 5-1, the mean surgeon-level caseload is (3+2+1+1)/4=1.75; the mean patient-level caseload is (3+3+3+2+2+1+1)/7=2.1.

Patient	Surgeon	Cases per year
1	1	3
2	1	3
3	1	3
4	2	2
5	2	2
6	3	1
7	4	1

Table 5-1: Caseload calculation example

Surgical usage was calculated as $\frac{UKRs\ in\ the\ year\ of\ surgery}{UKRs\ in\ year+TKRs\ in\ year}$ and expressed as the percentage of the total represented by UKR.

Two outcomes, implant survival and patient reported outcome, were explored in the descriptive analysis. Implant survival was calculated per surgeon, per year, and expressed as a patient-time incidence rate (revisions per 100 implant years)[6]. For the survival comparisons in volume groups, a Kaplan-Meier estimate of survival was produced. Survival analysis was censored at eight years; this reflects the small numbers included in the NJR during its early years. Three PROMs were collected: the OKS[137,285]; the EQ5D[312]; and the EQ5D general health Visual Analogue Scale (VAS, 0-100).

5.2.3. Analysis

5.2.3.1. Descriptive analysis of caseload effect

For the first, descriptive analysis, the effect of surgical caseload on revision rate and patient-reported outcome was characterised using scatter-plots, and curves were fitted using LOWESS, as previously used in Section 3.2.5.2[301]. Again, the scatter points were suppressed in the plots presented. As these plots demonstrated a non-linear effect of UKR caseload on survival hazard and six month OKS, three linear splines were fitted, corresponding to roughly linear segments observed on the plots. Once the splines were fitted, implant survival and PROMs in each spline section were compared using Cox and linear regression respectively.

5.2.3.2. Analysis of patient factors

Surgical caseload was divided into three groups corresponding to each spline section, representing cases performed by low, medium and high volume surgeons. The patient characteristics in each volume group were compared using linear and logistic regression and multivariable regression was performed to determine whether the difference in patient-factors between the groups explained the difference in outcomes between the groups.

5.2.3.3. Comparison of matched TKR and UKR patients in volume groups

Matching was performed using propensity score methods as outlined in Chapter 3. Propensity scores were estimated using a logistic model (the outcome being allocation to either TKR or UKR). Again, patients were matched at a ratio of three TKRs to one UKR, within a calliper of 0.02 standard deviations of the logit of the propensity score[313]. The logistic model used to create the propensity scores included patient factors (age, gender, co-morbidities, deprivation indices), surgical factors (cementless or cemented fixation, thromboprophylaxis), and surgeon/unit factors (length of follow-up, NHS or private

unit). Patients were matched on overall practice size (ie, number of TKRs+UKRs performed each year). Matching was repeated for the PROM comparison, for which patients were also matched on pre-operative OKS and EQ5D.

5.2.3.4. UKR usage comparison (aim 4).

As with the descriptive analysis in Section 5.2.3.1, the form of the relationship between usage and survival was characterised using LOWESS plots. Cox regression was used to estimate the effect of usage in univariable and multivariable analyses. Again, non-linear relationships were fitted using linear splines to provide a quantitative estimate of the effect on survival at different values of the predictor. Finally, Kaplan-Meier analysis was used to determine the survival that can be achieved using 'optimal' usage (as suggested by this study) and to compare it to the low usage levels considered 'ideal' by previous authors (i.e., ≤5%); more details are given in Section 1.10.2).

As described in Section 1.6.1, the majority of the UKRs performed in England and Wales are OUKRs. Unlike some other implants, the OUKR is specifically recommended to be used with broad indications (whist other implants specify more limited indications[314,315]). As this implant accounts for a high proportion of cases, and has specific attributes which may change the effect of the variable of interest, a sub-group analysis was performed, restricted to the patients receiving this specific implant.

Once the 'optimal' usage group was defined, another propensity-score matched comparison was undertaken, comparing TKR to UKRs in the 'optimal' usage group, both in terms of revision, and revision/reoperation.

As with previous chapters, statistical analyses were performed using Stata IC v.12.1.

5.3. Results

1,272/2,589 (49%) of the knee replacement surgeons listed in the NJR had performed at least one UKR between 2004-2012 (Figure 5-1); the mean surgeon-level caseload was 5.4 (SD 9.3). 313/1,272 (25%) of UKR surgeons had a mean caseload of only one UKR/year in the years that they performed UKR; this was the commonest mean UKR caseload. The mean patient-level caseload was 24.8 (SD 25.0).

2,536/2,589 surgeons (98%) had performed at least one TKR; the mean number of TKRs per year was 33.6 (SD 32.5) on the surgeon level and 70.5 (SD 49.6) on the patient level. 8.3% of all knee replacements were UKRs; the mean usage of UKRs was 5.9% (SD 12.7). When restricted to surgeons performing both TKR and UKR, the usage of UKRs was 11.0% (SD 13.4). The baseline characteristics of the patients in this study are displayed in Table 5-2.

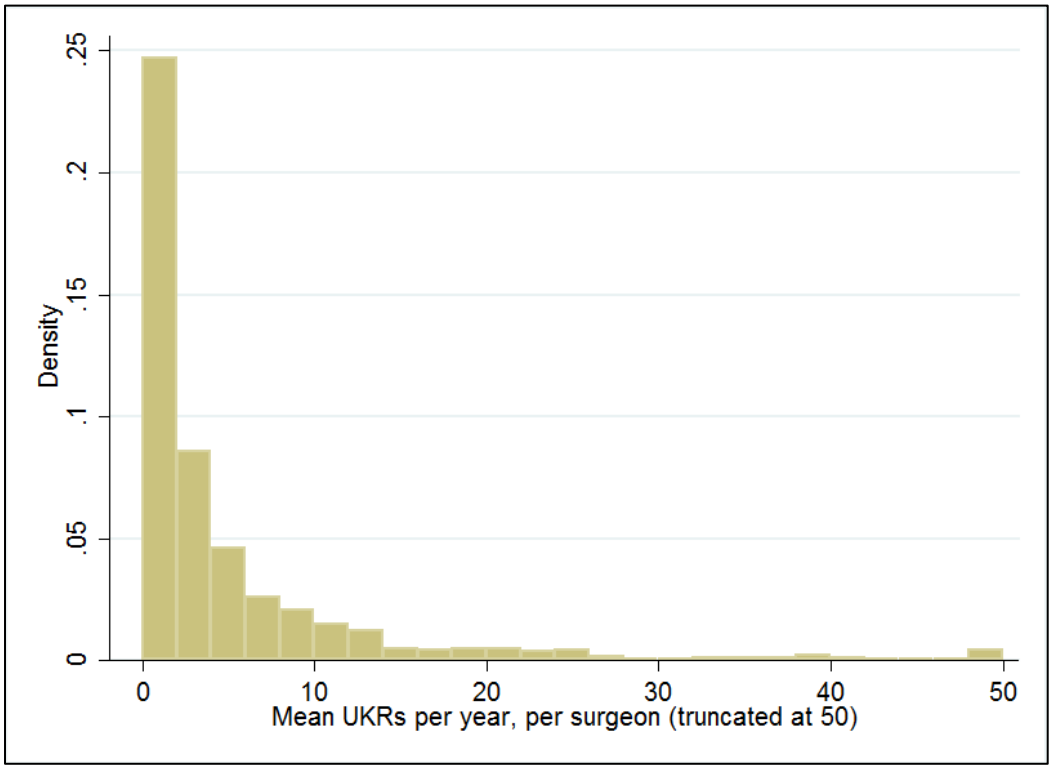


Figure 5-1: Distribution of UKR caseload amongst surgeons in England and Wales

		TKR	UKR		
			1-10 cases/yr	11-29 cases/yr	**≥30 cases/yr**
N (%)		422,149	12,025	14,139	10,967
Mean age at surgery (SD)		70.4 (9.1)	63.2 (9.4)	64.5 (9.4)	65.7 (10.0)
Gender, N males (%)		181,857 (43.1)	6,329 (52.6)	7,416 (52.5)	5,706 (52.0)
ASA	1	55,515 (13.2)	3,305 (27.5)	3,330 (23.6)	2,455 (22.4)
	2	303,176 (71.8)	7,781 (64.7)	9,722 (68.8)	7,514 (68.5)
	3+	63,458 (15.0)	939 (7.8)	1,087 (7.7	998 (9.1)
BMI (52.7% missing)		30.6 (5.5)	30.0 (5.0)	30.0 (5.0)	29.8 (5.2)
Unit type	Public	304,357 (72.1)	8,220 (68.4)	9,259 (65.5)	6,250 (57.0)
	Private	94,983 (22.5)	3,541 (29.5)	4,296 (30.4)	4,035 (36.8)
	ISTC	22,809 (5.4)	264 (2.2)	584 (4.1)	682 (6.2)
N with HES linkage (%)		285,234 (67.6)	7,566 (62.9)	8,903 (63.0)	6,381 (58.2)
Charlson	0	219,230 (76.9)	6,152 (81.3)	7,195 (80.8)	5,041 (79.0)
	1	53,427 (18.7)	1,200 (15.9)	1,439 (16.2)	1,129 (17.7)
	2+	12,577 (4.4)	214 (2.8)	269 (3.0)	211 (3.3)
Mean IMD rank (SD)		17,194 (8917.6)	17,857.8 (8845.3)	18,505 (8681.3)	19,718.8 (8643.3)
Ethnicity	White	236,775(83.0)	6,255 (82.7)	7,339 (82.4)	5,313 (83.3)
	Asian	7,627 (2.7)	139 (1.8)	175 (2.0)	143 (2.2)
	Black	2,675 (0.9)	50 (0.7)	26 (0.3)	30 (0.5)
	Mixed race	542 (0.2)	16 (0.2)	22 (0.3)	11 (0.2)
	Other	1,226 (0.4)	39 (0.5)	33 (0.4)	46 (0.7)
	Undefined	36,389 (12.8)	1,067 (14.1)	1,308 (14.7)	838 (13.1)
N with PROM linkage (%)		46,809 (88.9)	968 (8.1)	1,243 (8.8)	1,068 (9.7)
Pre-op OKS		19.5 (7.6)	21.0 (7.3)	22.2 (7.6)	22.2 (7.8)
Pre-op EQ5D		0.430 (0.304)	0.453 (0.29)	0.490 (0.29)	0.499 (0.29)
Pre-op VAS		69.1 (19.3)	70.1 (19.4)	71.3 (18.9)	72.2 (19.1)
Pre-op EQ5D anxiety	None	30,449 (65.1)	645 (66.6)	865 (69.6)	756 (70.8)
	Moderate	19,964 (32.0)	295 (30.5)	348 (28.0)	287 (26.9)
	Severe	1,396 (3.0)	28 (2.9)	30 (2.4)	25 (2.3)

Table 5-2 Patient characteristics for TKR (overall) and UKR (by volume group).

5.3.1. Descriptive analysis

Overall unadjusted implant survival was 97.1% (95% Confidence Interval 97.0-97.2) for TKR, and 89.8% (95% CI 89.1-90.4) for UKR. For both TKR and UKR, increasing caseload was associated with improved implant survival. However, the magnitude of this effect was much greater for UKR (Figure 5-2). With UKR, there is an initial steep drop in revision rate, before the curve becomes shallower (around 10 cases per year) before

reaching a plateau at around 30. Between 0-10 cases per year, the mean revision rate was 2.52 per 100 implant years (equating to an eight-year survival of 87.9%; 95% CI 86.9-88.8%); this fell to 1.40 if between 10 and 30 cases per year were performed (90.1%, 95% CI 89.0-91.2). If 30 or more cases were performed per year, the revision rate was 0.98 (92.4, 95% CI 90.9-93.6).

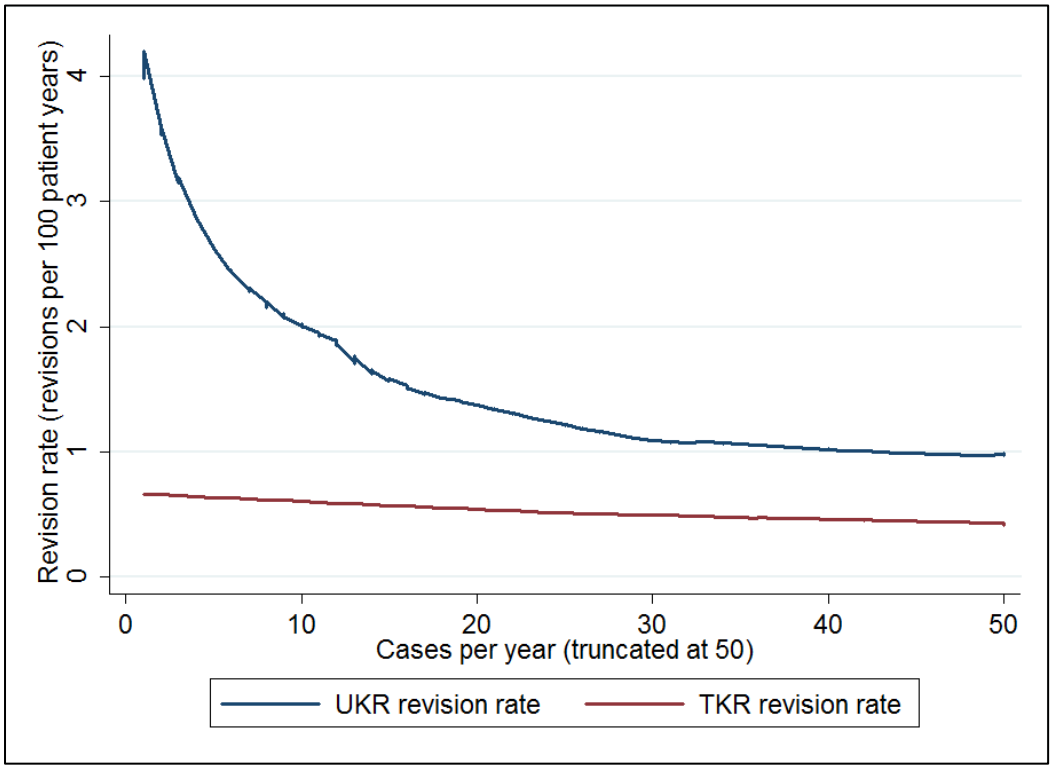


Figure 5-2: The effect of increasing caseload on UKR and TKR survival (caseload truncated at 50 cases for clarity)

Linear splines were fitted to the curve, with knots placed at 10 and 30 cases per year. Hazard ratio for revision was 0.86 (95% CI 0.61-0.88) per 5-case increase in annual caseload between 1 and 10 cases, 0.90 (95% CI 0.74-0.87) between 10 and 29 cases, and 1.00 (95% CI 0.96-1.04) if 30 or more cases are performed per year. By contrast, in TKR, the effect of volume is effectively linear. The hazard ratio for revision is 0.99 (95% CI 0.98-0.99) for every 5-case increase in caseload. Unadjusted Kaplan-Meier curves for high, medium and low volume UKR and TKR overall are given in Figure 5-3.

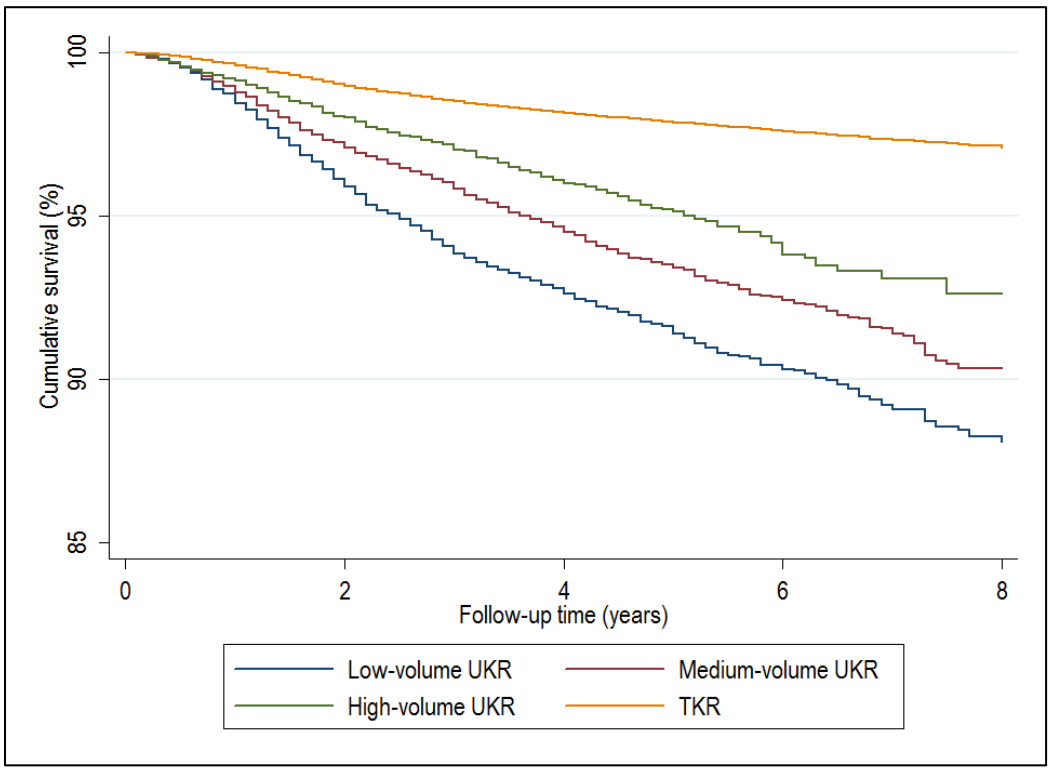


Figure 5-3: Survival hazards in three UKR volume groups, and in TKR overall (unadjusted for patient characteristics)

The effect of caseload on six month OKS was assessed, adjusted for pre-operative OKS. In UKR, there was a steep increase in OKS from 1-10 cases per year, which became more shallow from 10-70 cases, and stabilised above 70 cases (Figure 5-4). The effect of caseload on OKS following TKR was less marked, but there was an effectively linear increase in OKS between 0 and 210 cases, before declining above 210 cases (Table 5-3).

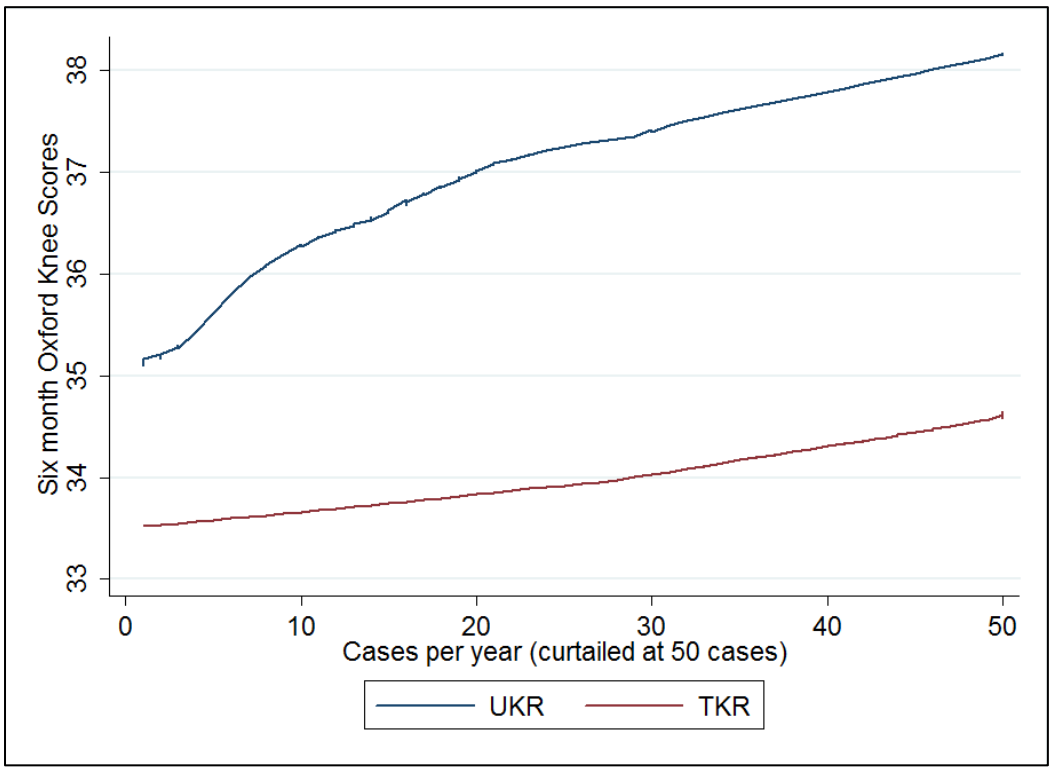


Figure 5-4: Effect of caseload on six month OKS (comparison of TKR and UKR, limited to 50 cases per year)

TKR		UKR	
Spline section	HR per 5 cases (95% CI)	Spline section	HR per 5 cases (95% CI)
Overall	0.99 (0.98-0.99)	0-10 cases	0.86 (0.78-0.94)
		10-30 cases	0.98 (0.86-0.93)
		>=30 cases	1.00 (0.98-1.02)

TKR		UKR	
Spline section	Coefficient per 5 cases (95% CI)	Spline section	Coefficient per 5 cases (95% CI)
0-210 cases	0.02 (0.01-0.03)	0-10 cases	0.93 (0.29-1.58)
		10-70 cases	0.19 (0.08-0.27)
>=210 cases	-0.01 (-0.11 - -0.03)	>= 70 cases	-0.16 (-0.40-0.10)

Table 5-3: Regression models for caseload comparison (Survival, above and patient-reported outcome, below)

5.3.2. Patient characteristics

There are marked differences between the patient factors in each volume group. Higher volume surgeons operated on older patients, with more co-morbidities, but a lower level of deprivation. Pre-operative OKS was slightly higher on average in the higher volume surgical groups, and patients had a lower level of anxiety/depression as recorded by the EQ5D. Details of the patient characteristics in each group are given in Table 5-2.

Reasons for revision differed between groups. Surgeons in the lower caseload groups were more likely to revise for aseptic loosening, pain, or malalignment (Table 5-4).

5.3.3. Comparison of matched patients

Propensity score techniques were used to match UKRs to TKRs on a 1:3 ratio. Matching was successful with over 95% of UKRs being matched in each round of matching. Marked differences in the hazard ratio for revision and reoperation were observed between the volume groups. For revision (as defined by the NJR), the hazard ratio reduced from 3.19 (95% CI 2.84-3.58) in the low-volume group to 2.58 (2.28-2.93) in the medium, and 1.96 (1.66-2.32) in the high-volume group. When revisions and re-operations from the HES database were included, the hazard ratios reduced further, being 1.61 (1.50-1.73) in the low volume group and 1.32 (1.22-1.43) in the medium volume group. In the high-volume group, the revision/reoperation rates for UKR and TKR were similar (HR 1.10, 95% CI 0.99-1.22).

Marked differences were present between the groups in terms of six month OKS. In the high-volume and medium volume groups, there was a statistically significant difference in OKS favouring UKR (2.2 points and 1.4 points respectively). In the low-volume group, there was no difference observed between the groups. Full details are given in Table 5-5.

	0-10 cases			11-29 cases			>=30 cases		
	N	% of revised	% of cases	N	%	% of cases	N	% of revised	% of cases
Aseptic loosening	281	32.4%	2.3%	181	24.5%	1.3%	111	29.8%	1.0%
Unexplained Pain	195	22.5%	1.6%	168	22.7%	1.2%	53	14.2%	0.5%
Disease progression	89	10.3%	0.7%	95	12.9%	0.7%	50	13.4%	0.5%
Other	88	10.1%	0.7%	82	11.1%	0.6%	46	12.4%	0.4%
Malalignment	60	6.9%	0.5%	34	4.6%	0.2%	17	4.6%	0.2%
Dislocation	50	5.8%	0.4%	60	8.1%	0.4%	41	11.0%	0.4%
Infection	39	4.5%	0.3%	38	5.1%	0.3%	21	5.6%	0.2%
Instability	36	4.1%	0.3%	35	4.7%	0.2%	14	3.8%	0.1%
Wear	14	1.6%	0.1%	16	2.2%	0.1%	7	1.9%	0.1%
Stiffness	9	1.0%	0.1%	8	1.1%	0.1%	3	0.8%	0.0%
Periprosthetic fracture	7	0.8%	0.1%	19	2.6%	0.1%	9	2.4%	0.1%
Implant fracture	0	0.0%	0.0%	3	0.4%	0.0%	0	0.0%	0.0%

Table 5-4: Reasons for revision following UKR (by caseload group)

	Low volume		Medium volume		High volume	
	TKR	UKR	TKR	UKR	TKR	UKR
Matching pool with HES linkage	285,234	8,367	285,234	8,903	285,234	6,316
Matched	24,603	8,201	26,388	8,796	18,672	6,224
% Matched	8.6%	98.0%	9.3%	98.8%	6.5%	98.5%
Survival (NJR revisions only)	95.8 (95.3-96.3)	87.2 (85.8-88.4)	96.2 (95.7-96.6)	89.8 (88.3-91.0)	96.2 (95.4-96.8)	91.2 (88.8-93.1)
Revision HR	3.19 (2.84-3.58), p<0.001		2.58 (2.28-2.93), p<0.001		1.96 (1.66-2.32), p<0.001	
Survival (Revision/reoperation)	86.4 (85.6-87.2)	77.5 (75.8-79.1)	87.2 (86.4-88.0)	81.2 (79.4-82.8)	88.3 (87.1-89.3)	83.1 (79.9-85.8)
Revision/reoperation HR	1.61 (1.50-1.73), p<0.001		1.32 (1.22-1.43), p<0.001		1.10 (0.99-1.22), p=0.086	
Matching pool with PROMs	46,809	860	46,809	1,081	46,809	934
Matched	2,460	820	3,114	1,038	2,679	893
% Matched	5.3%	95.3%	6.7%	96.0%	5.7%	95.6%
Mean OKS (95% CI)	35.2 (34.8-35.6)	35.8 (35.1-36.5)	36.2 (35.9-36.6)	37.7 (37.1-38.2)	36.4 (36.1-36.8)	38.6 (38.0-39.1)
Coefficient	0.61 (-0.18-1.41), p=0.131		1.43 (0.77-2.09), p<0.001		2.16 (1.48-2.85), p<0.001	

Table 5-5: Matched survival comparisons

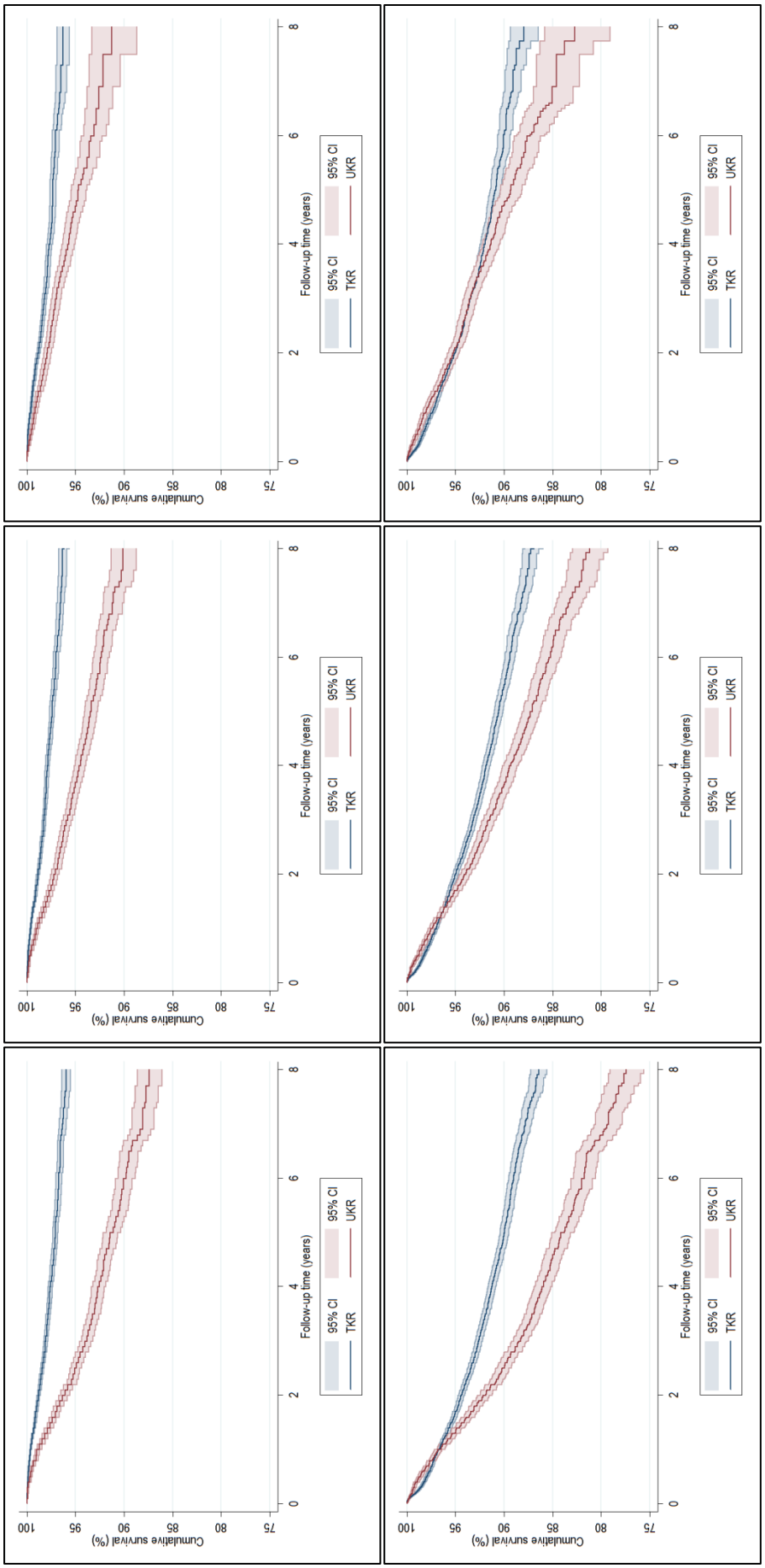


Figure 5-5: Matched survival comparisons in volume groups
Top row: revision (as per NJR definition); bottom row: revision/reoperation (as per HES data).
From left to right: low, medium and high volume groups

5.3.4. UKR usage effect

The relationship between usage and revision rate was again non-linear (Figure 5-6). In both the univariable and multivariable analyses, the lowest risk of revision was for those surgeons performing between 40 and 60% UKRs; this was considered the 'optimal' range. From 0-20%, there was a statistically significant decline in revision risk; above 65%, there was a slight increase. Linear splines were fitted with knots placed at 20% and 65% (Table 5-6).

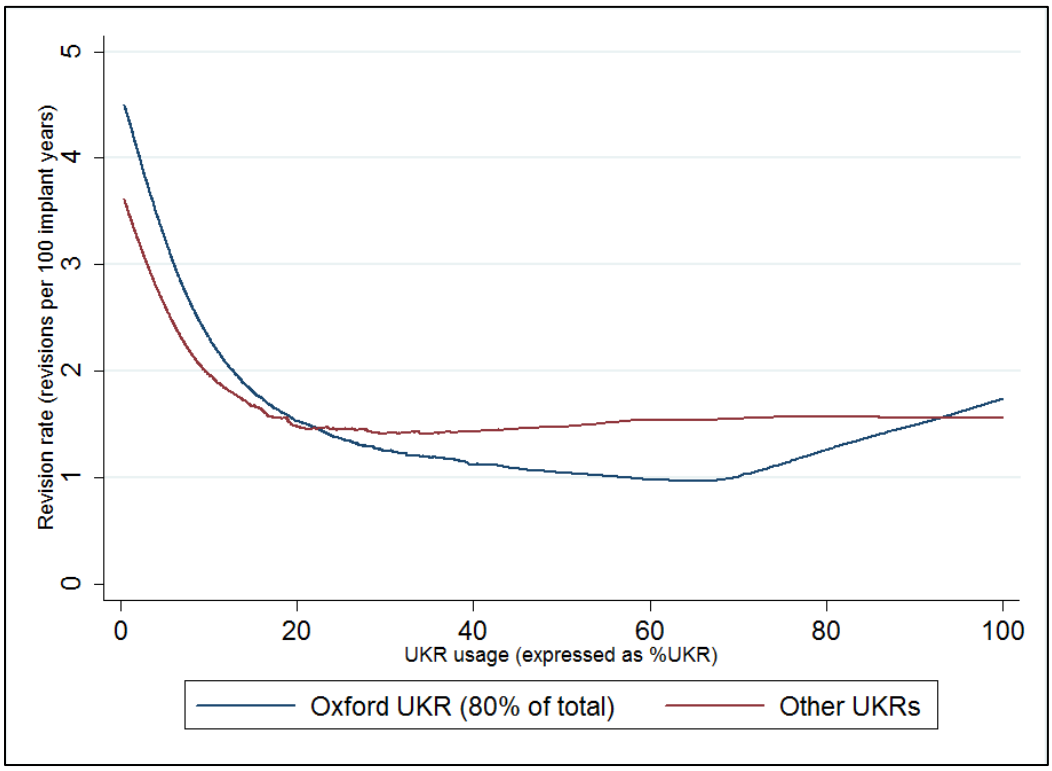


Figure 5-6: Effect of usage on revision rate

A sub-group analysis of the 29,182 cases who received the OUKR was performed. The functional form of the usage effect was similar to that of the other devices and of UKR overall. However, this device appeared more sensitive to the effect of usage: the revision rate was lower when performed by higher-usage surgeons, but slightly higher with very low usage of UKR. The position of the knots appeared to remain applicable. Hazard ratios for the OUKR analysis are presented in Table 5-6.

		HR (95% CI)	P	HR (95% CI)	P	HR (95%CI)	P
		Univariable		Multivariable (whole group)		Multivariable (OUKR only)	
Usage group	Spline 1: 0-20% (per 10%)	0.76 (0.69-0.82)	<0.001	0.79 (0.73-0.87)	<0.001	0.74 (0.66-0.82)	<0.001
	Spline 2: 20-65% (per 10%)	0.95 (0.91-0.99)	0.02	0.96 (0.92-1.00)	0.082	0.94 (0.89-0.99)	0.027
	Spline 3: 65-100% (per 10%)	1.15 (0.98-1.34)	0.09	1.13 (0.97-1.32)	0.112	1.04 (0.83-1.25)	0.769
Age (per year)		0.96 (0.96-0.97)	<0.001	0.97 (0.96-0.97)	<0.001	0.97 (0.96-0.98)	<0.001
Gender (male)		0.89 (0.82-0.97)	0.008	0.91 (0.83-0.99)	0.027	0.87 (0.78-0.96)	0.008
Fixation (cemented)		1.09 (0.92-1.29)	0.282	1.08 (0.92-1.27)	0.348	1.31 (0.95-1.67)	0.115
ASA score		0.95 (0.88-1.03)	0.204	1.09 (1.01-1.18)	0.031	1.17 (1.06-1.28)	0.001
BMI		1.02 (1.01-1.04)	0.001	(excluded from multivariable models)			
Consultant performed		0.89 (0.78-1.02)	0.093	0.80 (0.70-0.92)	0.001	0.90 (0.76-1.04)	0.202
Unit type	NHS Hospital	(reference group)		(reference group)		(reference group)	
	Independent hospital	0.92 (0.84-1.02)	0.104	1.00 (0.90-1.10)	0.974	0.92 (0.81-1.03)	0.186
	ISTC	1.16 (0.92-1.46)	0.206	1.29 (1.02-1.63)	0.031	1.44 (1.29-1.75)	0.005
Surgical caseload (per 10 cases)		0.97 (0.96-0.9)	<0.001	0.97 (0.96-0.98)	<0.001	0.97 (0.96-0.98)	<0.001

Table 5-6: Univariable and multivariable usage models (whole group and single implant analyses are given)

In patients undergoing UKR under surgeons with low usage (≤5%), the overall five year survival was 90% (95% confidence intervals 88.4%-91.6%). If usage was above 20%, this increased to 94% (95% CI 93.7-94.3). Usage in the optimal range (40%-60%) produced a five-year survival of 95% (99% CI 93.9-96.1), which increased to 96% (99% CI 94.9-96.0) if OUKR (which is designed for broad indications) was used (Figure 5-7).

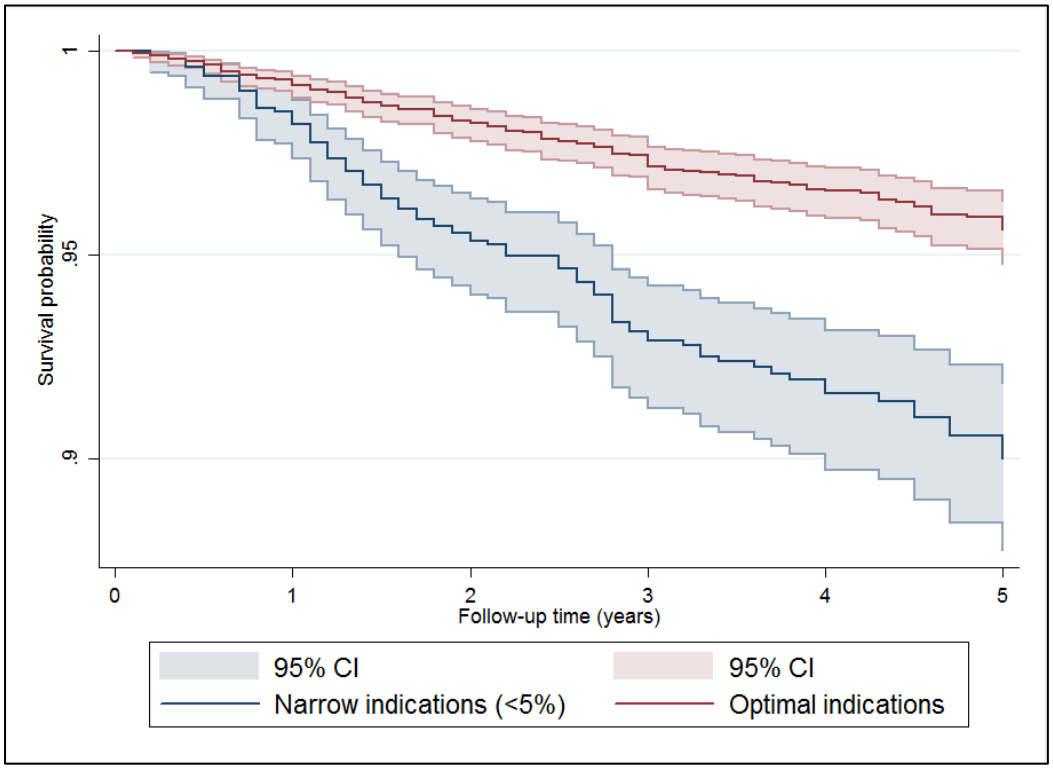


Figure 5-7: Survival in optimal and narrow usage groups (figures taken from single prosthesis analysis)

The matched analysis described in Section 5.3.3 was repeated to compare the 'optimal' usage group (restricted to the OUKR) to the population of TKRs. Matching was performed using the same HES and NJR variables (given in Table 5-2). Whilst the 'optimal' group was restricted to those with usage of between 40-60%, both high- and low-volume surgeons were included (Figure 5-8).

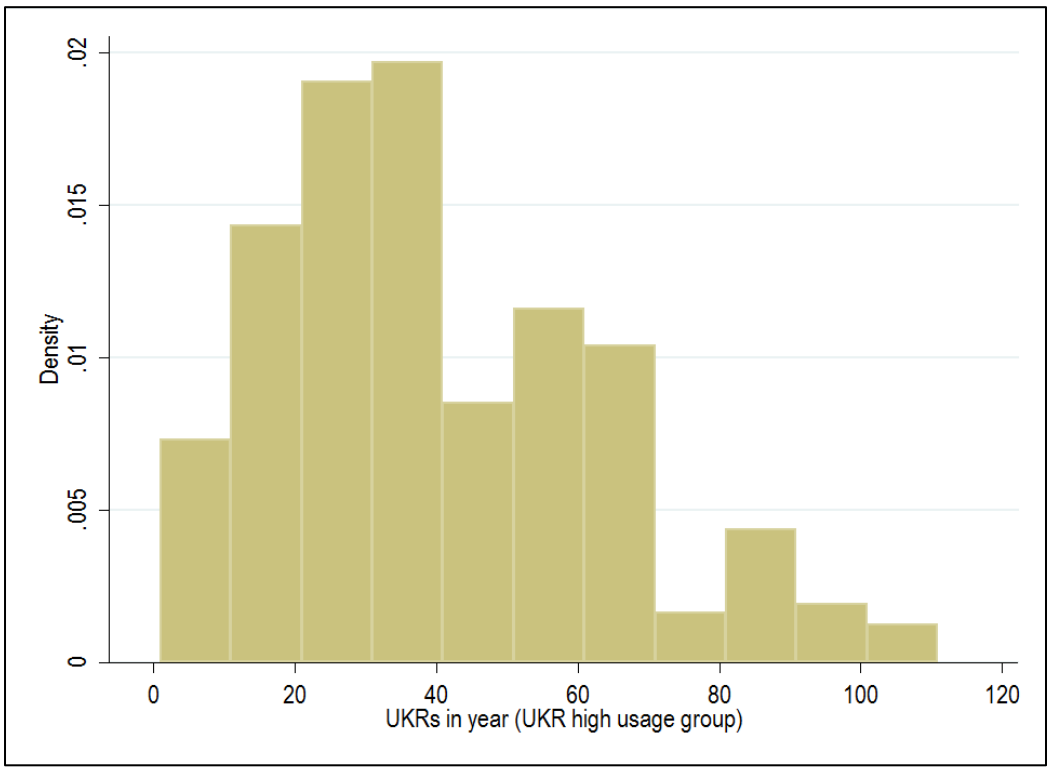


Figure 5-8: UKR caseload in the high usage group

Results of the matched analysis were similar to those achieved in the high-volume group in Section 5.3.3. Using NJR-recorded survival as the end-point, survival was similar for the two procedures up to five years, with the survival hazards moving further apart as the overall number of patients reduced beyond five years (Figure 5-9). The final Cox Hazard Ratio was 1.99 (95% CI 1.54-2.58, p<0.001) favouring TKR. If reoperations are included, a similar relationship is observed between TKR and UKR, but the overall survival is similar by eight years (HR 1.11, 95% CI 0.95-1.30, p=0.186).

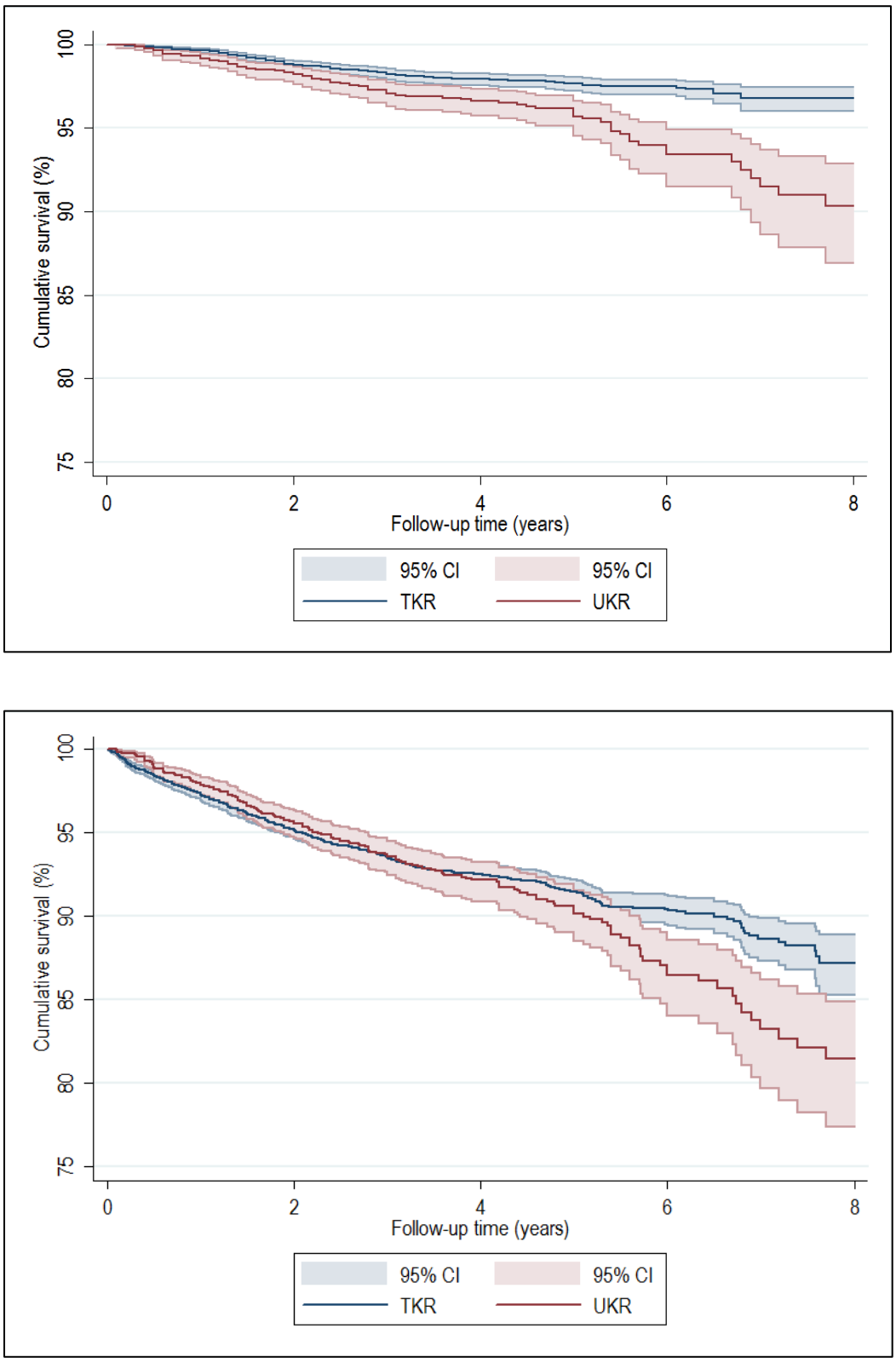


Figure 5-9: Matched survival analysis: usage comparison
Top: Revision rate (as defined by the NJR)
Bottom: Revision/reoperation rate (taken from HES dataset)

5.4. Discussion

5.4.1. Summary of results

This study has demonstrated an important effect of caseload on the outcomes of UKR, both in terms of revision rate and patient-reported outcome. Whilst there is a caseload effect with TKR, it is not as marked as that seen in UKR. The effect of caseload is partly explained by patient selection, with low-volume surgeons electing to operate on younger, healthier patients who may be earlier in the disease process. Patients who undergo UKR under the care of a high-volume surgeon (who performs 30 or more cases per year), can achieve similar medium-term survival compared to matched patients who undergo TKR, with a superior OKS. Increasing UKR usage has been shown to be a viable way to achieve a higher caseload; indeed, increasing usage up to around 50% results in improved survival. This suggests that whatever the negative effect of operating on patients who are deemed to be non-'ideal', this is outweighed by the survival and functional benefit conferred by increasing annual caseload. This finding was more marked when the analysis was restricted to the OUKR; this is not surprising as this implant was designed with broader indications in mind. OUKR performed within the 'optimal' usage criteria resulted in revision/reoperation rates similar to that achievable with TKR.

5.4.2. Determination of cut-points

In order to facilitate the comparison of patients in low, medium and high-volume groups, cut-points have been used, which were selected on the basis of the data. Other approaches would be to take the top 25-50% of surgeons as being 'high volume' (Robertsson *et al* used this approach when determining the effect of unit volume on outcome, taking the top quarter of units as the 'high volume' set[215]), or introducing

clinically plausible cut-points *a priori*. This latter approach is taken by the New Zealand Joint Registry (who subdivide surgeons into those performing more or fewer than one case a month), and by Baker *et al*, who defined thresholds at 25, 50, 100 and 200 cases over 7 years, taking ≥100 cases to represent high volume[8,91]. In fact, the thresholds are similar by each method: in this study, the threshold for low volume was ≤10 cases per year, compared with 12 cases per year[8] or 100 cases over seven years (roughly 14 cases per year, assuming participation in all years of the registry)[91].

However, the effect of surgical caseload on outcome is continuous; examination of the relationship between caseload and revision risk demonstrates that a plateau is not reached until over 30 cases per year are performed (which restricts the analysis to a small number of surgeons), and no discernible plateau is reached when PROMs are studied. Attempts to produce meaningful thresholds on the basis of continuous predictors are fraught with difficulty and are of questionable value[316]. As such, the thresholds used here should not be taken to be either minimum or optimum figures for UKR caseload.

5.4.3. Application to practice

Whilst all surgeons performing fewer than around 30 cases per year may derive an appreciable survival benefit by increasing their UKR caseload, the greatest concern would appear to be the very low-volume users (i.e., those performing fewer than five cases per year), who attain the very worst results. This group, which comprises nearly half of all users of UKR, are those who may be best advised to modify their practice, either by abandoning the use of UKR, referring suitable patients elsewhere, or by increasing their usage.

5.4.4. Limitations and further work

Whilst the observed difference between the results of high- and low-volume surgeons are in part explained by the surgical and patient factors explored in this study, there remains a residual difference in survival and PROMs between the caseload groups despite matching for these factors. Other factors are likely to include more subtle patient factors (such as the stage of disease of patients selected for UKR), and surgical technique. Future studies of outcomes in UKR should include the study of pre- and post-operative radiographs and analysis of surgical technique.

Likewise, the validity of UKR usage as a surrogate for indications relies upon surgeons drawing their patients from a similar population. Whilst this is reasonable in most cases, it does not take tertiary referral practice into account. This is only likely to become a problem in surgeons with the highest proportion of UKRs. Future studies of the indications for UKR would benefit from the examination of pre-operative radiographs.

5.5. Conclusions

This study has confirmed the importance of surgical caseload in determining the survival of UKR, and, for the first time, demonstrated a significant effect of surgical caseload on patient-reported outcome. The reasons for this difference are complex and not fully explained by variables recorded in the NJR; however, patient selection by lower-volume surgeons appears to be an important factor. The examination of matched patients has demonstrated that high volume surgeons can achieve revision/reoperation rates similar to those observed following TKR, with superior patient-reported outcomes. The examination of the usage effect has suggested that an increase in UKR caseload may be achieved by broadening surgical indications and hence by increasing UKR usage. If

surgeons increase their surgical caseload (by increasing their UKR usage); patients would benefit from the advantages of UKR without the unacceptably high revision rate.

Results, Part Two: Optimising fixation in Unicompartmental Knee Replacement

Chapter 6 Quality of fixation in cemented and cementless UKR

6.1. Introduction

As has been outlined in previous chapters of this thesis, UKR survival data from NJR annual reports has failed to match the excellent long-term survival of published studies of UKR. The work presented in Chapters 3-5 of this thesis have demonstrated important factors associated with an increased revision rate, as well as outlining the advantages of UKR over TKR, including a significantly improved rate of morbidity, mortality, readmission and reoperation, and a significantly reduced inpatient stay.

As demonstrated in Chapter 3 (Table 3-6 on page 91), the most common reason for revision of UKR in the NJR is aseptic loosening. Similar findings are reported by the AOANJRR, which reports that 48.3% of revisions are for loosening or lysis of any component[317].

Published series from high volume units generally demonstrate very low rates of failure by aseptic loosening, both in mobile and fixed-bearing designs[11-13,89,90,98,175,318]. Pandit *et al* report a single case of aseptic tibial loosening in a series of 1000 Phase 3 OUKRs with an overall failure rate of 4% at ten years[13], Price and Svard report nine cases of femoral or tibial loosening in a series of 682 OUKRs (phases 1-3) with an overall failure rate of 9% at 16 years[12], whilst Foran *et al* report no cases of loosening in a series of 62 patients with the Miller-Galante prosthesis with an overall failure rate of 6% at a minimum follow-up of 16 years[175].

* A version of this chapter ("Improved fixation in cementless unicompartmental knee replacement: five-year results of a randomized controlled trial") was published in the *Journal of Bone and Joint Surgery (American volume)* in August 2013.

These findings suggest that the diagnosis of aseptic loosening may be related to surgeon experience. Currently, most designs of UKR are cemented and many are performed using a minimally invasive technique. Cementation is challenging in minimally invasive UKR, and cementation errors (which are particularly prevalent in inexperienced hands) may lead to loosening, pain and excess wear[213,247]. Loose fragments of cement can cause pain and mechanical symptoms within the knee and may need to be removed arthroscopically[319]; excess cement that is not removed may prevent normal bearing movement and lead to excess wear and failure[247], and components that are not fully seated due to excess cement may tighten the soft tissues causing pain[47].

In loose joint replacements, the bone-implant (or bone-cement) interface becomes replaced by a layer of soft tissue, manifesting radiographically as a thick, poorly-defined radiolucent area, known as a pathological radiolucency[320]. Often, a fine, well-defined radiolucent line is present at the bone-cement interface of well-functioning cemented UKR and TKR[321-323]. These 'physiological' radiolucencies have not been demonstrated to be associated with pain or loosening, but indicate sub-optimal fixation as they demonstrate a layer of fibro-cartilage at the interface[324]. It is believed that if this layer of fibrocartilage is not present, the fixation will be of higher quality. If a patient complains of persistent pain following a UKR and is found to have a physiological radiolucency, surgeons less familiar with these radiolucencies may attribute this pain to the presence of a radiolucent line, and convert the UKR to a TKR. These revisions are often unnecessary as anteromedial tibial pain can frequently be present in the early post-operative period and usually resolves spontaneously[47]. This may be a result of changes in bone stresses following surgery[325].

Cementless fixation has the potential to address many of these problems. As described in Section 1.12, whilst the OUKR has been implanted using cement since its inception in the 1970s, it has characteristics which make it particularly suitable for cementless fixation.

In order to test the effectiveness of cementless fixation in the OUKR, a randomised, controlled study was undertaken with the primary aim of comparing the quality of fixation of the cemented and cementless designs of the OUKR as evidenced by the incidence of radiolucent lines. The secondary aim of the study was to compare patient-reported outcomes of the two prostheses. Preliminary results have been published at one year[106]. This chapter reports the results of the same study at five years.

6.2. Patients and Methods

6.2.1. Patient recruitment and randomisation

A randomised, controlled trial was designed to compare cemented with cementless OUKR. The trial protocol was registered with the Oxfordshire Research Ethics Committee and ethical approval was granted (C02.101). On the basis of a power calculation (outlined in Section 6.2.4, Statistical analysis), 62 patients (with 63 knees) were recruited from the pre-operative assessment clinics of three senior surgeons at the Nuffield Orthopaedic Centre (Prof. David Murray, Mr Christopher Dodd and Prof. Andrew Price).

Inclusion criteria were patients with anteromedial osteoarthritis fulfilling the standard indications for OUKR (given in Section 1.6.2)[47]. In common with previous studies, neither anterior knee pain, full-thickness cartilage loss in the patellofemoral joint, obesity, age, nor activity level were considered contra-indications to UKR[64,67,83,86].

Patients who had previously undergone osteotomy or Anterior Cruciate Ligament (ACL) reconstruction were excluded.

The treatment allocation sequence was determined using a computerised random number generator. Allocations were placed in a series of opaque, sealed envelopes which were kept in the operating theatre. Once the surgical approach to the knee had been performed and the suitability for UKR established (after examination of the ACL and lateral joint surfaces), the next envelope in the sequence was opened and cemented or cementless OUKR performed accordingly.

6.2.2. Implant design and surgical technique

Patients in the cemented group received the Oxford Phase 3 UKR which is described in detail in Section 1.6.3. The cementless implant is similar but modified to allow cementless implantation (Figure 6-1).

Figure 6-1: Cementless Oxford Unicompartmental Knee Replacement

The tibial component is identical to the cemented version except that the cement pocket is filled with a layer of porous titanium and the surfaces in contact with bone are coated with calcium hydroxyapatite (HA). The femoral component is similarly filled with porous titanium and coated with HA on the inner surface. In order to improve primary fixation, its central peg is cylindrical rather than conical (as it is in the cemented version) and there is another, smaller, peg anteriorly to confer rotational stability. The anterior

part of the femoral component extends a further 17° to allow implantation in a more flexed position and to support the anterior peg. Neither the femoral pegs nor the vertical lateral tibial wall are covered with porous titanium but both are HA-coated. Aside from these modifications, the cementless femoral component is identical to the cemented version. Identical mobile meniscal bearings, manufactured from direct compression-moulded UHMWPE, were used in both groups.

The standard operative technique was performed using phase 3 instrumentation[47]. To secure good primary fixation in cementless implantation, a specially designed 'toothbrush' saw was used to create a narrower keel slot than used with cemented implantation, and both components were firmly impacted after implantation. The femoral component was implanted between 5° and 10° flexed relative to the position required for the cemented prosthesis to minimise the risk of shear forces at the interface in high flexion. The operative technique is otherwise identical to that used for the cemented implant. Surgery was performed by one of six surgeons. Most cases (49/63, 78%) were performed by one of the three senior surgeons named in Section 6.2.1. The remainder were performed by one of three senior trainees under direct or indirect supervision of one of the three senior surgeons. The post-operative regime was identical for the two groups, with early weight bearing encouraged in all patients.

6.2.3. Post-operative follow-up and data collection

6.2.3.1. Clinical assessments

All patients were assessed prospectively at the pre-operative visit and then at six months, one, two and five years post-surgery by a research physiotherapist. Both assessor and patient were blinded to the method of fixation used. Clinical assessment

included the OKS[285], KSS-Fcn, KSS-Obj[138] and Tegner Activity Score (TAS)[326] . These are described in detail in Section 1.8.2.

At surgery, operative findings, implant sizes and operative time data were recorded using a standardised form (Appendix 3). Patients were seen by the same blinded physiotherapist for functional assessment, using the same scores as collected pre-operatively, at six months, one, two and five years following surgery. Complications which occurred between visits were reported back to the research physiotherapist who recorded them contemporaneously.

6.2.3.2. Radiological assessments

Post-operatively and at six months, one and five years, anteroposterior and lateral radiographs were taken using a technique designed to produce an accurate image of the bone-implant interface. The radiographs were performed under fluoroscopic guidance, by adjusting the x-ray beam until it is parallel to the bone-implant interface (either the underside of the tibial component on the anteroposterior view, or the flat, posterior surface of the femoral component on the lateral), before the definitive image is recorded digitally[322]. Radiographs were assessed by two assessors blinded to the clinical outcome.

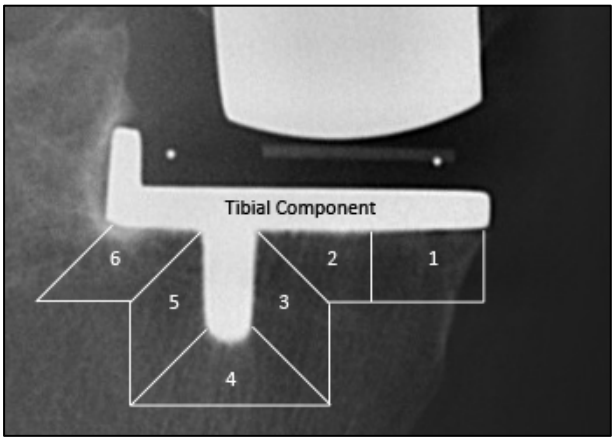


Figure 6-2: Zones of radiolucency beneath the tibial component

Radiolucencies were defined as being physiological (less than 2 mm in depth, with a sclerotic margin, appearing within the first post-operative year before remaining unchanged on subsequent radiographs) or pathological (which are thick, progressive and not associated with a sclerotic margin). The area under the tibial component was divided into six zones (Figure 6-2); if all six zones were involved, the radiolucency was considered 'complete', if fewer than six zones were involved, the radiolucency was considered 'partial' (Figure 6-3). In common with previous studies of the cemented OUKR, the vertical, lateral wall was considered to be non-weight bearing; no significance was attached to radiolucencies present in this zone[322].

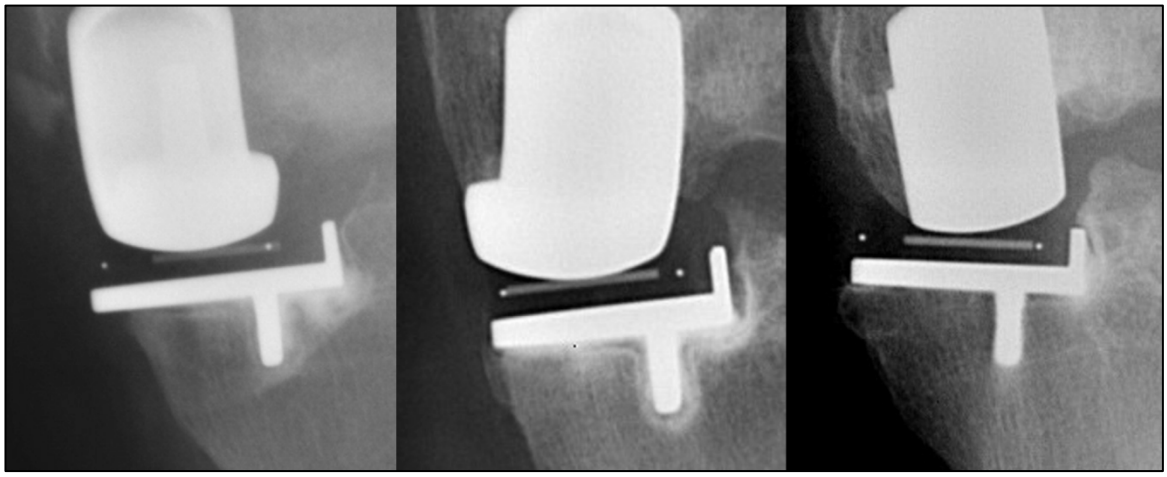


Figure 6-3: Radiolucencies beneath the tibial tray of the OUKR
From left to right: cemented, partial (zones 1-5); cementled complete; cementless, partial (zone 6)

6.2.4. Statistical analysis

A power calculation was performed with the expectation that the frequency of radiolucencies in cemented OUKR would be 70%, with a halving of this figure in the cementless group being considered clinically significant. For 80% power, with a significance level set at 0.05, 30 patients were required per group. Using values for PROM outcomes recorded in a previous, large study of cemented OUKR[13], a difference of six points for the OKS, ten points for the KSS-Obj, twelve points for the KSS-Fcn and

one point for the TAS would attain significance at the same power with the same sample size.

Each outcome score was analysed both as an absolute score pre-operatively and at one, two and five years, and as change scores at the same follow-up intervals (one, two and five year ΔOKS, ΔKSS-Fcn, ΔKSS-Obj and ΔTAS). Descriptive statistics revealed normal distribution of surgical duration, pre-operative and change scores, but negative skewness of one and five year data. Negative logarithmic transformations were performed to transform the data distribution to normality and parametric tests (independent samples t-tests) were used for duration of surgery and all PROMs. Results tables contain non-transformed data. Fisher's exact test was used to compare the proportion of radiolucencies in the two groups.

For this Section, analyses were performed using SPSS version 20 for Windows (IBM Inc., Armonk, NY).

6.3. Results

The study groups were well-matched for age (cemented 63.8 yrs, range 46-78, cementless 64.7 yrs, 45-82), gender (cemented 20:12, 63% male, cementless 16:14, 53% male) and body mass index (cemented 28.9, 20.1-37.7, cementless 27.9, 21.3-39.9). There was no statistically significant difference between the pre-operative scores of the two groups on any measure.

There were no revisions. One patient (from the cemented group) died within six months of surgery, and three further patients died between the second and fifth years, all from causes unrelated to the UKR (two cementless group and one cemented). One patient

(cementless) left the study through ill-health at the same time-point. Final clinical analysis was performed on 58 patients, 31 cemented and 27 cementless. One patient (cemented group) had moved out of the study catchment area after the first year and was unable to attend for his final radiographic follow-up, completing his OKS and KSS-Fcn assessments by post; final radiographic analysis was therefore performed on 57 patients.

One patient (cemented) developed Complex Regional Pain Syndrome (CRPS) and continues to experience symptoms despite medical treatment (five year OKS 8 (ΔOKS -13), KSS-Fcn 40, KSS-Obj 9, TAS 2). One patient (cementless) developed a post-operative haematoma and underwent exploration, lavage and bearing exchange on day ten. This patient has recovered fully and has undergone no further surgery. There were no other complications. Mean surgical time (expressed as the time that the patient was in the operating theatre) was 95.7 minutes (range 65-135 minutes) in the cemented group and 86.5 minutes (range 50-110 minutes) in the cementless group, a significant difference ($p=0.049$).

6.3.1. Radiological outcome

At five years, there was no evidence of femoral or tibial loosening in either group, indicated either by implant subsidence or a 'pathological' radiolucency. No radiolucency of any type was observed adjacent to the femoral component in any patient in either group at any stage. At five years, one patient (cementless) had radiological evidence of progression of osteoarthritis with narrowing of the joint space in the retained, lateral compartment. This was asymptomatic and PROM scores remained excellent (OKS 45, AKSS-F 100, AKSS-O 85, TAS 3). None of the remaining five-year radiographs demonstrate any adverse features. Radiological results are summarised in Table 6-1.

	Cemented				Cementless			
Radiolucency	Post-op	1yr	2yr	5yr	Post-op	1yr	2yr	5yr
Complete	0	8	11	9	2	2	0	0
Partial	0	8	12	11	9	7	2	2
None	32	16	9	11	19	21	28	25

Table 6-1: Radiological outcomes

20/30 patients in the cemented group had a physiological radiolucency at five years, compared with 2/27 in the cementless group (a significant difference, $p<0.001$). All radiolucencies were <1 mm thick. Both radiolucencies in the cementless group were partial; 9/20 radiolucencies in the cemented group were complete. Therefore the number of complete radiolucencies in the cemented group was 9/30, compared with 0/27 in the cementless group ($p=0.01$). There was no progression of radiolucencies in the cementless group from one to five years and radiolucencies which were present immediately and at six months post-operatively (representing incomplete seating of the tibial component) resolved by one year (Figure 6-4). In the cemented group, radiolucencies developed over the first year and remained stable thereafter. There was complete agreement on radiographic findings between the two assessors.

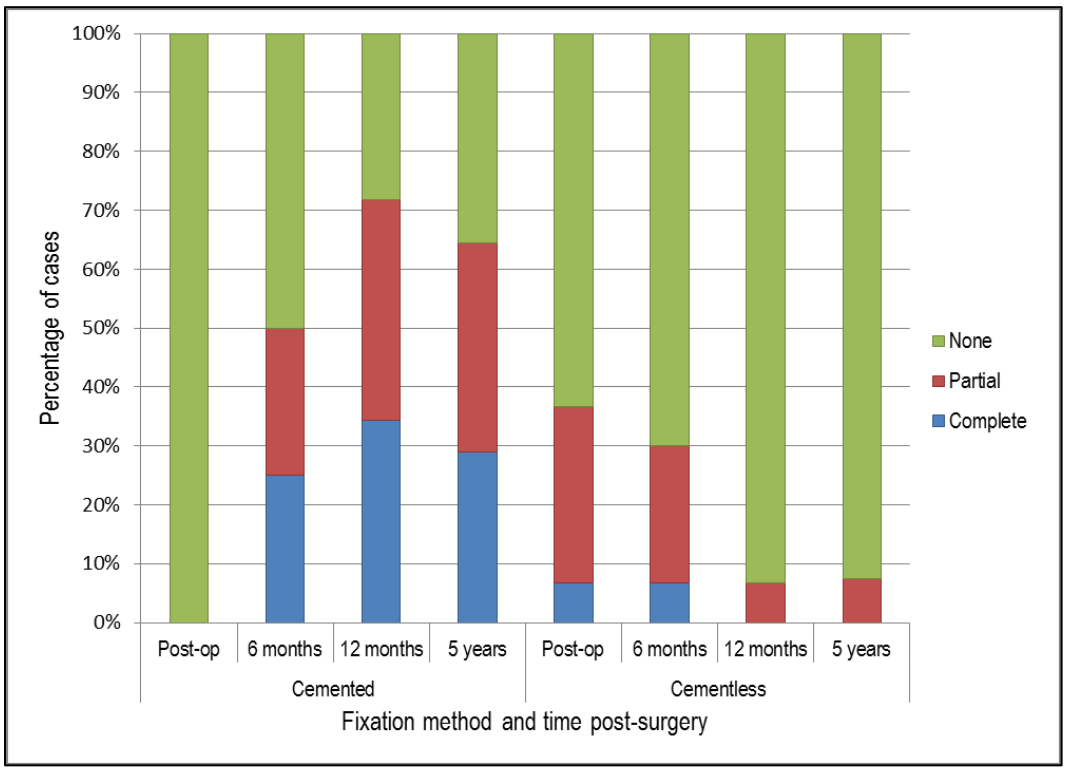


Figure 6-4: Progression of radiolucencies

6.3.2. Patient-Reported Outcome Measures

Overall, all PROMs were significantly improved at one and five years compared with pre-operative scores. Scores remained stable from the first to the fifth post-operative year (Table 6-2).

		Pre	1yr	2yr	5yr
OKS	Cemented	21.7 (6.4)	39.0 (9.2)	38.8 (9.0)	39.0 (10.4)
	Cementless	21.1 (6.1)	41.7 (5.3)	41.5 (6.5)	39.4 (9.9)
KSS-Obj	Cemented	44.2 (17.7)	87.7 (10.8)	80.6 (18.1)	80.1 (19.3)
	Cementless	41.6 (11.1)	88.1 (8.4)	84.5 (13.5)	78.8 (14.0)
KSS- Fcn	Cemented	60.6 (12.6)	87.5 (16.0)	86.6 (14.5)	78.8 (18.4)*
	Cementless	60.3 (13.8)	90.5 (11.7)	91.5 (12.9)	92.0 (12.7)*
Tegner	Cemented	1.9 (0.8)	2.9 (0.9)	2.5 (0.8)*	2.6 (0.8)
	Cementless	1.9 (0.7)	3.1 (1.1)	3.1 (1.1)*	2.9 (0.6)

Table 6-2: Clinical outcomes
A statistically significant difference is indicated by an asterisk (*)

At two and five years, neither the absolute or change OKS displayed any significant difference between the groups (Figure 6-5). At five years, mean OKS was 39.0 (SD 10.4) in the cemented group and 39.4 (9.9) in the cementless group (p=0.88); ΔOKS was 17.9 (9.7) in the cemented group and 18.4 (9.5) in the cementless group (p=0.84). At five years KSS-Fcn demonstrated a significantly superior outcome in the cementless group both for absolute (92.0 (SD 12.7) vs 78.8 (18.4), p=0.003) and change scores (30.8 (17.1) vs 16.4 (17.8), p=0.003), although there was no significant difference by either score at two years (Figure 6-6). The Minimum Clinically Important Difference (MCID) in the KSS-Fcn has been estimated at between 11.5 and 20.5 points[327], which suggests a clinically important difference. The five year difference remains statistically significant if the patient with CRPS is excluded (the mean cemented score rises to 80.17 (SD17.2), p=0.005 for absolute KSS-Fcn, 16.43 (17.8), p=0.004 for ΔKSS-Fcn). The TAS was significantly better in the cementless group at two years (mean 3.1 (SD 1.1) vs 2.5 (0.8), p=0.04), but the difference did not persist to five years. Neither the KSS-Obj nor ΔKSS-Obj demonstrated any significant difference between groups at any time-point. There was no significant change in clinical outcome in each group or overall following the first year.

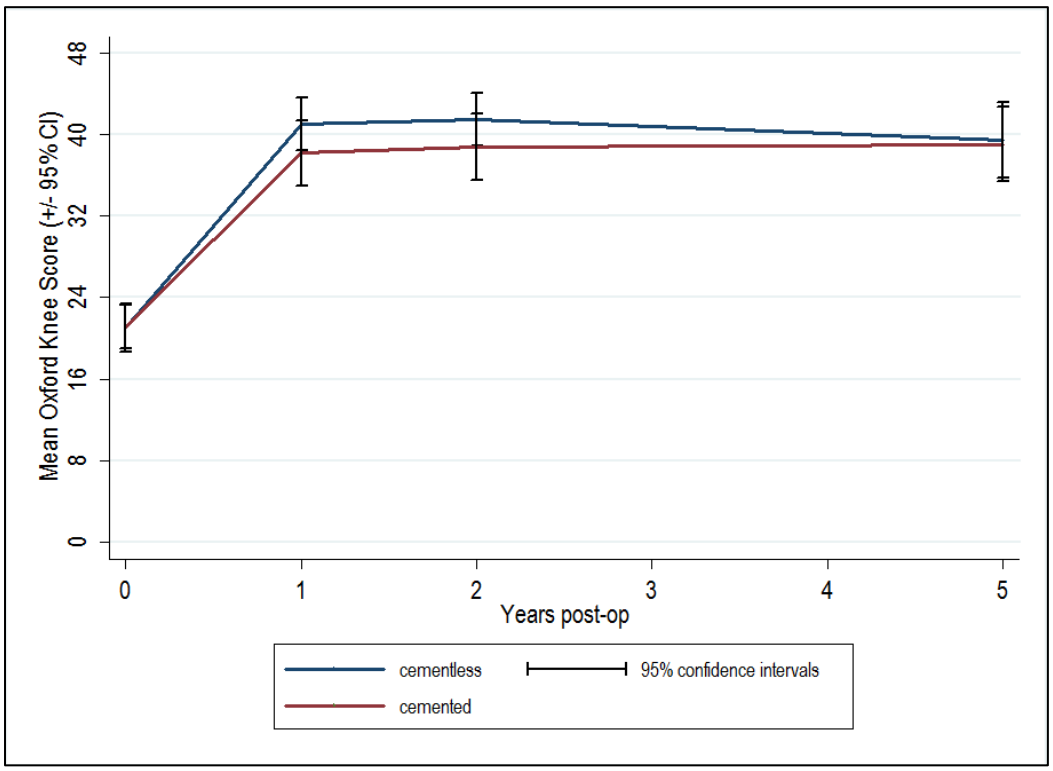


Figure 6-5: Clinical outcomes: OKS

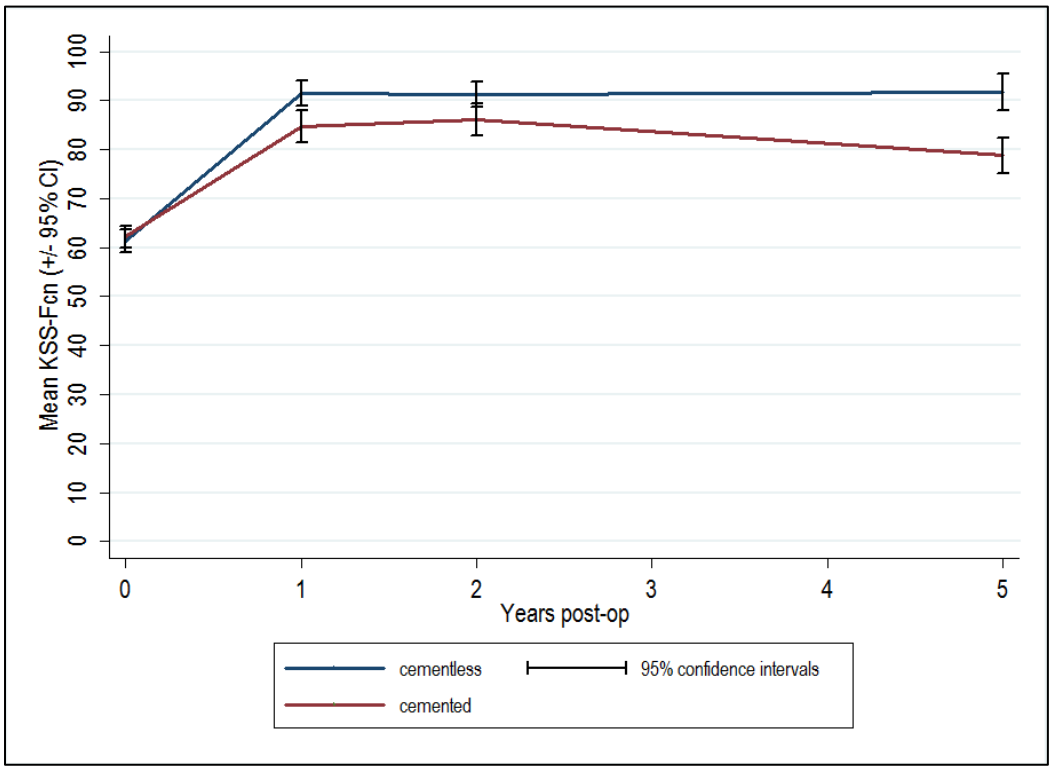


Figure 6-6: Clinical outcomes: KSS-Fcn

6.4. Discussion

This study demonstrates that cementless fixation in OUKR is associated with a significantly reduced incidence of radiolucencies compared to cemented fixation at five years, with equivalent or superior patient-reported outcomes. There were no complete radiolucencies in the cementless group, indicating secure fixation in all knees. Radiolucencies did not progress between one and five years, suggesting that once the cementless component is securely fixed, it will remain so for subsequent years. The elimination of cementation conferred the additional advantage of reducing the operative time by a mean of over 11 minutes. Although it was not formally assessed, the surgeons involved in the study found the cementless procedure to be simpler than the cemented. As well as being quicker, the cementless technique appears to be forgiving of sub-optimal technique of implantation, as evidenced by the radiolucencies associated with inadequate seating of the tibial tray disappearing within the first year.

This study was powered to detect a significant difference in radiological outcomes and a larger number of patients would be required to achieve sufficient power to determine a difference in patient-reported outcome. Whilst the apparent superior functional performance of the cementless implant (by a single outcome measure) is encouraging, this finding should be treated with a degree of caution until it is replicated in studies with larger numbers. PROMs will be compared using registry data in Chapter 9.

The method of assessing radiographs was a limitation of the current study. In this study, radiographs were assessed visually and findings recorded according to a standardised method. This method is not sensitive to the true density of bone below the tibial tray, and it was not able to detect whether these radiolucencies are associated with subsidence of the implant. Further studies using more quantitative tools are necessary to explore

these findings further. Since this study has been completed, a new method of quantitative assessment of radiolucency has been devised, and studies have been initiated using bone densitometry and RSA to examine the cementless OUKR[328-331].

The size of the study population limits the conclusions we can draw about complications or contra-indications. Following the satisfactory one-year results in this study, and in order to assess the complications and contra-indications to cementless fixation, a large, multi-centre study was recruited. The results of this, second, study are presented in the following chapter.

Chapter 7 Safety and effectiveness of cementless UKR

7.1. Introduction

The RCT reported in Chapter 6 has demonstrated radiological evidence of excellent fixation, with a very low incidence of radiolucent lines associated with the cementless OUKR. The secondary outcomes, PROMs, suggest that the patient-reported outcomes are at least as good as in the cemented device. These results suggest that the cementless device may improve fixation and, it is hoped, improve the revision rate of UKR overall.

However, the RCT provides inadequate evidence to confirm the new implant's safety, or to quantify the incidence complete radiolucencies and less common complications. It is also important to identify patients who may be at greater risk of complications with the cementless device. For this purpose, a multi-centre cohort of 1,000 patients has been recruited from three centres; in this chapter, the results of this study are presented.

The aims of this study are fourfold:

1. To assess the incidence of complete radiolucencies in a larger cohort with a more diverse group of units and surgeons,
2. To quantify the incidence of complications with the new implant,
3. To identify contraindications to the use of the cementless implant, and
4. To compare the outcomes of the cementless implant to an existing cohort of cemented OUKRs.

[*] A version of this chapter ("Cementless fixation in Oxford unicompartmental knee replacement: a multicentre study of 1000 patients") was published in the *Bone & Joint Journal* in February 2013.

7.2. Patients and methods

7.2.1. Patient recruitment

Cementless OUKR was performed in 1,000 consecutive knees (906 patients) in three institutions by 14 surgeons. In addition to Oxford, patients were recruited from Christchurch in New Zealand and from Musgrave Park Hospital in Belfast, Northern Ireland. None of the surgeons had used the cementless OUKR before, but experience of the cemented device varied between centres, with one (Belfast), never having used the OUKR before.

All participating surgeons used the cementless OUKR for all patients fitting the indications for medial UKR during the study period. The only exceptions were rare occasions when cementless components were unavailable, or visiting surgeons were being taught the cemented procedure. The majority of the cases (892/1,000) were performed by one of seven senior consultants, with the remainder of the cases being divided between consultants and senior trainees.

7.2.2. Indications, prosthesis and surgical technique

The cementless prosthesis has been described in detail in Chapter 6; again, procedures were performed using an MIS approach without eversion or dislocation of the patella.

All patients had anteromedial osteoarthritis (OA) or avascular necrosis (six cases). All cases conformed to the standard indications as described by Goodfellow *et al*[94] and described in Section 1.6.2, having full-thickness cartilage loss with bone-on-bone contact in the medial compartment, preservation of full-thickness cartilage on the unaffected, lateral compartment, and functionally intact Anterior Cruciate (ACL) and Medial Collateral Ligaments. The indications and the postoperative rehabilitation regime were the same as those used in Chapter 6. Patients with 'extended indications', including

those who had undergone ACL reconstruction or high tibial osteotomy were excluded. Osteoporosis was not considered a contra-indication to cementless fixation. Postoperative rehabilitation was standardised between centres and was the same as that used for cemented implantation. Early active knee motion, early weight-bearing and discharge were encouraged.

7.2.3. Data collection and follow-up

Pre-operatively, the OKS was collected together with data on patient demographics and co-morbidities.

Intra-operatively, findings were recorded on a standardised form (Appendix 3). Severity of osteoarthritis in the operated and non-operated compartments, degree of damage to the ACL, bone cuts and implant sizes were recorded.

7.2.3.1. Clinical assessment

Postoperatively, patients were seen at one year by independent assessors. Clinical follow-up intervals beyond one year varied according to local practice. Assessment included anteroposterior and lateral radiographs with fluoroscopic alignment to ensure true anteroposterior and lateral radiographs of the implants; see Section 6.2.3.2. In a small number of cases where this was not available, digital radiographs were used with the x-ray source aligned to the components using low-dose images without fluoroscopic guidance. Only radiographs which were considered to be perfectly aligned were accepted and used in the analysis.

7.2.3.2. Radiological assessment

Tibial and femoral radiolucencies were assessed using the same techniques used in Chapter 6. Femoral radiolucencies were assessed using the lateral radiograph by examination of the flat area at the posterior femoral condyle and the area around the

femoral pegs. The extent of tibial radiolucencies was assessed using the AP radiograph by dividing the area under the tibial tray into six zones (as in Figure 6-2), and radiolucencies were described as partial or complete depending on whether all six zones were involved[322]. In common with earlier studies of the cemented prosthesis, the area lateral to the vertical wall of the prosthesis did not form part of this analysis as it is not considered weight-bearing[13].

All radiographs were analysed twice (by the author), at a one-month interval to assess intra-observer reliability. A subset of 100 radiographs (10%) were reviewed by two further raters (Prof. Murray and Mr Pandit, two of the supervisors of this thesis) to assess inter-observer reliability. Complications, further surgery and Oxford Knee Score were recorded at each follow-up appointment. The minimum follow-up was 18 months. The radiographic and clinical outcomes of a subset of these patients (231 knees at two years with radiographic data available on 196) have been published separately by their originating unit[59].

7.2.4. Comparison to previous study

Implant survival, radiological outcome, complications and outcome were compared to a previously-published study of 1,000 cemented OUKRs[13].

7.3. Results

Results are presented at a mean of 38.2 months post-surgery, all patients are at least 18 months post-operative (range 19-88 months, SD 15.5) and have had at least their one-year clinical follow-up appointment. At the time of analysis, 272/1,000 (27.2%) patients had undergone formal clinical review beyond one year postoperatively (between two and seven years). Thirty one patients (3.1%) were lost to follow-up and 19 patients (1.9%)

had died of causes unrelated to their surgery (four patients died in the first postoperative year). The mean age of the cohort was 66.0 years (range: 39-89 years). 567 of the patients (56.7%) were male.

7.3.1. Loss to follow-up, complications and revision

A total of 19 patients (1.9%) underwent further surgery of whom five patients were revised to a Total Knee Replacement (0.5%). Revision prostheses with stems and/or wedges were used in two cases (0.2%). Four patients had an additional implant (domed lateral UKR in two knees, patellofemoral replacement in one, patellofemoral and lateral arthroplasties in one), and eight patients had a bearing exchange for infection (two patients, with the bearing being exchanged at the time of debridement and lavage of the joint) or bearing dislocation. In two cases, the bearing dislocation was secondary to a traumatic ACL rupture and ACL reconstruction was performed when the bearing was exchanged. Reasons for revision are displayed in Table 7-1.

Three patients sustained periprosthetic fractures during surgery which were addressed at the same time (with two being revised to TKR and one undergoing a simultaneous ORIF with the UKR still in situ). One further patient sustained a periprosthetic fracture intraoperatively which went un-noticed intraoperatively; the implant subsided and became well-fixed, and the fracture united without further surgery. One patient sustained a transverse proximal tibial fracture one year postoperatively following trauma (UKR was well-fixed and the patient was treated with a circular frame). Re-operations took place a mean of 15.5 (range 0-40) months following primary surgery.

Study ID	Centre	Time to reoperation (m)	Reason for reoperation	Surgery performed	Implant retained
16	3	40	Lateral progression	Domed lateral OUKR	Yes
17	3	40	Lateral progression	Domed lateral OUKR	Yes
46	3	53	Traumatic ACL rupture and bearing dislocation	ACL reconstruction and bearing relocation	Yes
61	3	15	Bearing dislocation	Bearing relocation	Yes
192	1	24	Patellofemoral progression	Patellofemoral replacement	Yes
211	1	9	Avascular necrosis of lateral femoral condyle	TKR	No
335	3	17	Traumatic ACL rupture and bearing dislocation	ACL reconstruction and bearing relocation	Yes
432	1	10	Deep infection	Two stage revision to TKR	No
448	3	18	Lateral progression	TKR	No
488	3	0	Intra-operative periprosthetic fracture	TKR	No
576	3	11	Bearing dislocation	Bearing relocation	Yes
602	3	15	Bearing dislocation	Bearing relocation	Yes
651	3	20	Traumatic ACL rupture and disease progression	ACL reconstruction, lateral and patellofemoral replacements	Yes
663	3	0	Intra-operative periprosthetic fracture	TKR	No
749	1	2	Superficial infection	Wound washout and bearing exchange	Yes
791	2	0	Superficial infection	Wound washout and bearing exchange	Yes
860	2	0	Intra-operative periprosthetic fracture	Open reduction and internal fixation	Yes
878	3	9	Bearing dislocation	Bearing relocation	Yes
932	2	12	Traumatic peri-prosthetic fracture with well-fixed prosthesis	Circular external fixator	Yes

Table 7-1: Failure mechanisms and re-operations

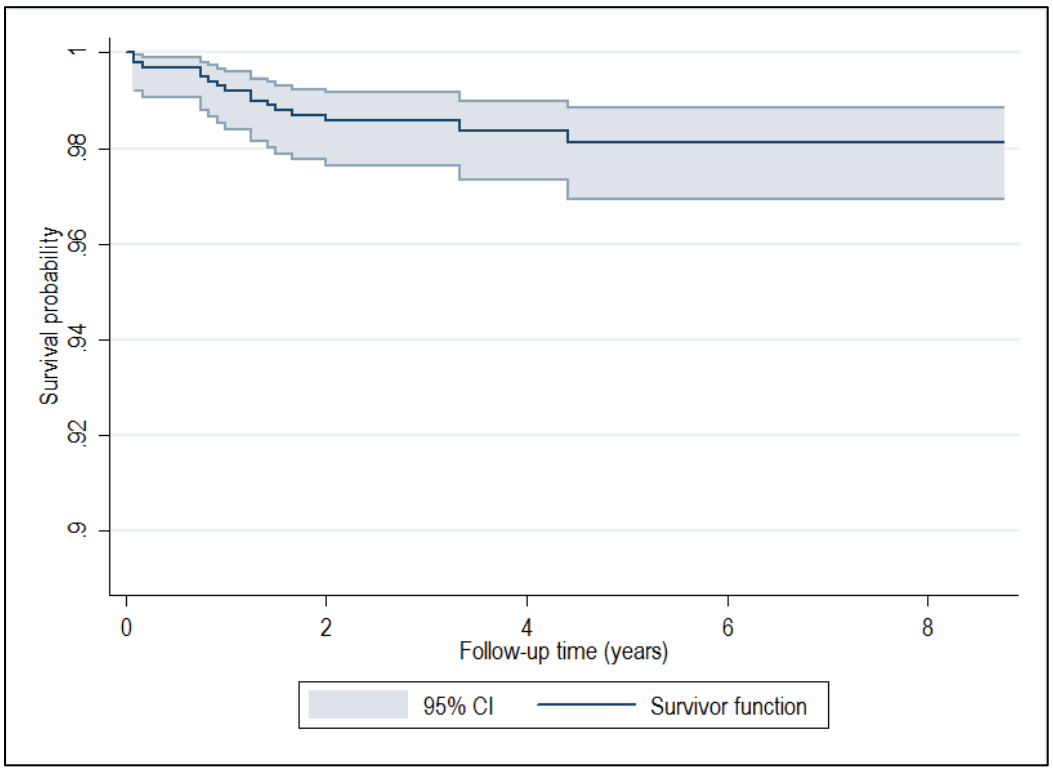


Figure 7-1: Kaplan-Meier plot of overall survival

Using all-cause reoperation as the definition of failure, the cumulative survival rate at five years is 97.2% (95%CI 95.6-98.8). A Kaplan-Meier curve is presented in Figure 7-1 and a yearly life table in Table 7-2. Restriction of the implant survival analysis to implant-related re-operation (excluding the traumatic fracture and debridements for early infection), produces a cumulative survival rate at five years of 97.4% (95%CI 96.7-99.0). The last failure was at 54 months, and therefore the survival rate remains constant from years 4-6 (number at risk at five years, 139; number at risk at six years, 58).

As stated earlier, 31 patients were lost to follow-up. In most cases, these patients were from the New Zealand cohort; in many cases, patients were referred from rural hospitals and would not submit to the travelling required for longer-term follow-up. None of these patients is known to have been revised. In the worst case scenario, where each of these patients is considered to have been revised, five year survival would fall to 94.9% (95% CI 92.8-96.4).

Year	Number entering	Withdrawals	Number at Risk	Re-operations	Cumulative survival
1	1,000	3	998.5	9	99.1%
2	988	264	856.0	6	98.4%
3	718	357	539.5	3	97.9%
4	358	170	273.0	0	97.9%
5	188	98	139.0	1	97.2%
6	89	62	58.0	0	97.2%
7	27	27	13.5	0	97.2%

Table 7-2: Life table for multicentre study

7.3.2. Patient-reported outcome

Mean OKS was 20.9 (SD 7.8) pre-operatively and 40.1 (7.8) at one year (Figure 7-2). Mean change in OKS (ΔOKS) was 19.3 points (SD 8.9). 272/1,000 patients (27.2%) have had scores recorded after more than a year of follow-up, with a mean follow-up of 2.67 years (2-7 years, SD 1.1). Mean OKS in this subgroup is 41.5 (SD 6.7) at final review.

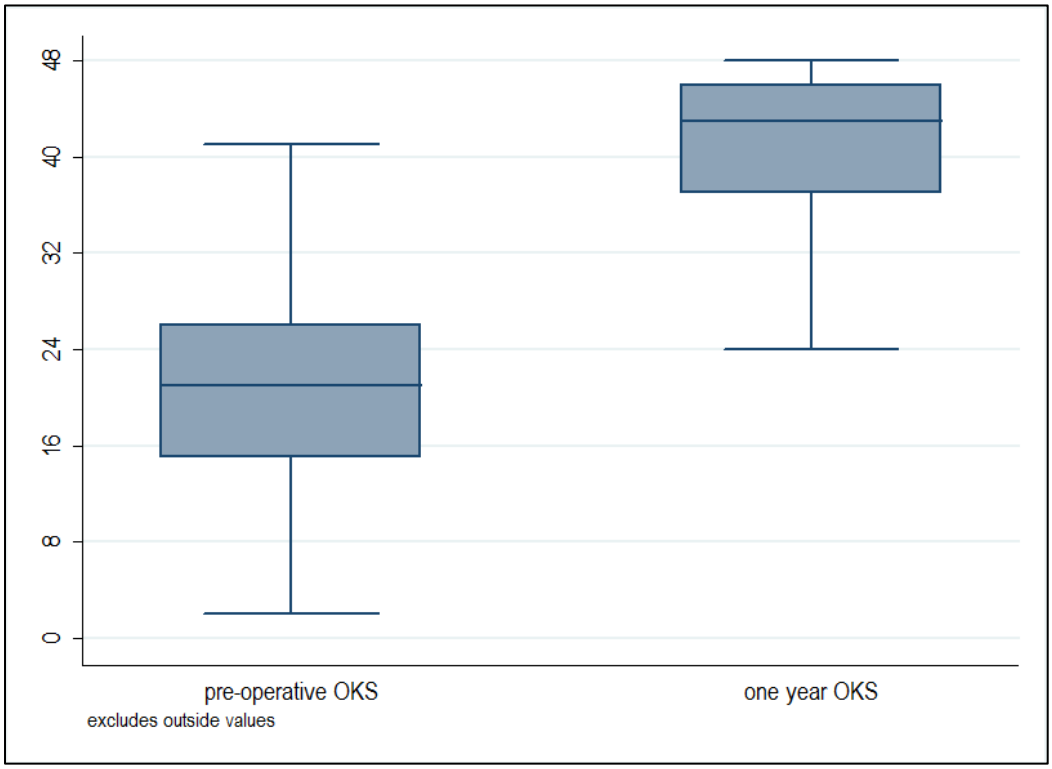


Figure 7-2: Pre-operative and one year OKS for entire group

PROMs varied significantly between centres (Table 7-3). Centre 2 has a significantly inferior OKS at one year compared with the other two centres ($p<0.001$ in both cases), but the pre-operative scores are significantly inferior in this group. As a result, the ΔOKS in centres 2 and 3 are equivalent, with centre 1 having a significantly poorer ΔOKS than both centre 2 ($p<0.001$) and centre 3 ($p=0.001$).

		Overall	Centre 1	Centre 2	Centre 3
Cases		1,000	189	240	571
Mean (SD) OKS	Pre-operatively	20.9 (7.8)	24.4 (7.4)	15.1 (5.3)*	22.4 (7.5)
	One-year	40.1 (7.8)	40.9 (6.8)	35.9 (8.7)*	41.1 (6.9)
	Change	19.3 (8.9)	16.6 (8.4)*	20.8 (9.1)	19.4 (8.8)

Table 7-3: Mean OKS by centre.
Asterisks indicate statistically significant differences

7.3.3. Radiographic outcomes

No femoral radiolucencies were observed in any radiograph. 809 of the 1,000 patients had accurately-aligned tibial radiographs available. All 809 radiographs were analysed in the manner described above. Intra-observer (kappa=0.71, $p<0.001$) and Inter-observer error (kappa=0.73 $p<0.001$) were within acceptable limits[332]. There were 72 partial radiolucencies, all of which were less than 1 mm thick, and 0 complete radiolucencies. This equated to 8.9% of interpretable radiographs. The commonest site for a partial radiolucency was zone 6 (53 cases), followed by zone 1 (22 cases); the full details are given in Table 7-4.

Zone	Radiolucencies	Percentage of total
1	22	20%
2	13	12%
3	6	5%
4	10	9%
5	7	6%
6	53	48%

Table 7-4: Location of radiolucencies

The frequency of radiolucencies varied between centres, with centre 2 having a significantly higher proportion of radiolucencies (34/232 interpretable radiographs, 14.7%) compared with centres 1 and 3 (12/183 and 26/394 respectively, both 6.6%, p=0.001, Table 7-5). There was no significant difference between patients with and without a radiolucency in terms of patient-reported outcome (ΔOKS 17.97 with, and 19.18 without a radiolucency, p=0.284) or implant survival (reoperation in 2/70 with and 11/726 without a radiolucency, p=0.324).

	Overall	Centre 1	Centre 2	Centre 3
Cases	809	183	232	394
Radiolucency	72	12	34	26
% radiolucencies	8.9	6.6	14.7	6.6

Table 7-5: Radiolucencies by centre

There was no progression of arthritis in any radiograph. In three cases (0.03%), the tibial implants appear to have settled into a position of slight valgus mal-alignment with the lateral side of the component subsiding in the immediate postoperative period before becoming well fixed with good bone ingrowth by one year (Figure 7-3). Outcome is similar to the group as a whole at one year (mean OKS 39.3, p=0.86; ΔOKS 24.7, p=0.39).

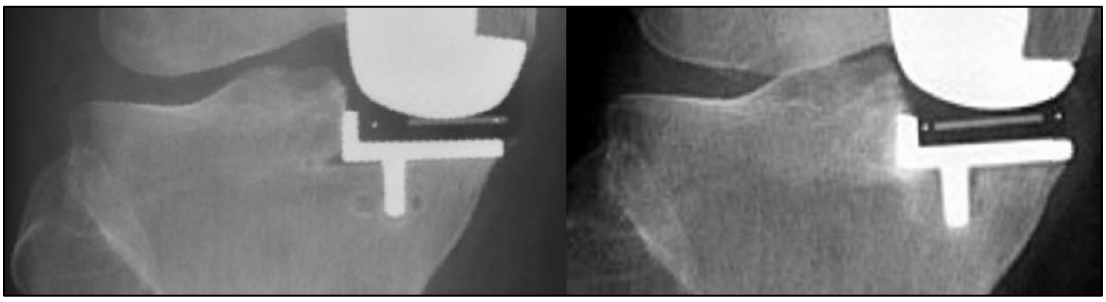


Figure 7-3: subsidence of tibial tray into valgus
Postoperative (left) and one year (right) radiographs

In one case (0.01%), the tibial component has settled into varus with a partial radiolucency. Reviewing the postoperative radiographs, the prosthesis was not seated

properly which may have been due to incomplete clearance of the keel prior to prosthetic implantation (Figure 7-4). The keel appears well-fixed at one year and the prosthesis remains in situ, but patient-reported outcome was suboptimal with an OKS of 30 (ΔOKS 10). No adverse radiographic features were noted in any other radiograph.

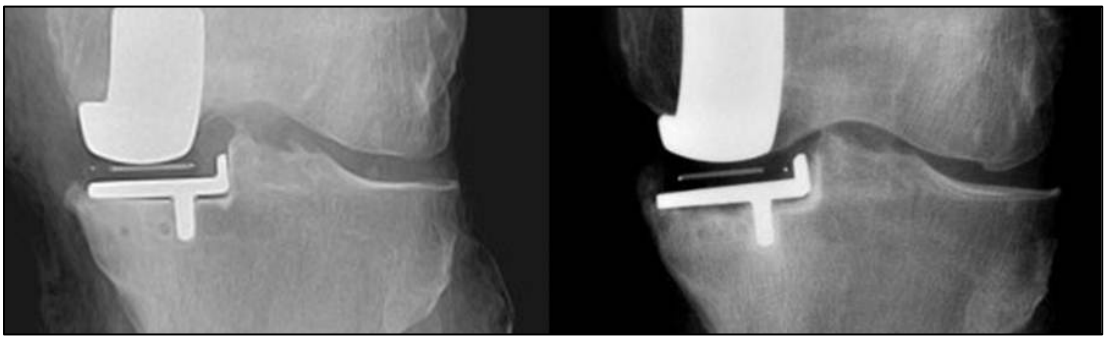


Figure 7-4: incompletely seated implant
Postoperative (left) and one year (right) radiographs

7.3.4. Comparison to previous series

Comparison was made to a previous single-centre study of 1,000 cemented phase 3 OUKR[13]. In this series, 29 re-operations were reported at a follow-up of one to eleven years (mean 5.6 years). The current series is of much shorter follow-up but comparison can be made by examining the results of the cemented cohort at 53 months (the time of the last reoperation in the current cohort) or 38.2 months (the mean follow-up of the current cohort).

	Cementless cohort	Cemented cohort
N	1,000	1,000
Age	66.1 (39-89)	66.0 (32-88)
Gender (%M)	566 (57%)	520 (52%)
Pre-operative OKS	20.9 (7.9)	24.7 (8.7)
Follow-up	38.2 (19-88)	67.2 (12-110)

Table 7-6: Baseline values of cemented and cementless cohorts

In the cementless cohort, there were a total of 19 re-operations, between 0 and 53 months. By an equivalent point in the cemented cohort, there had been 21 re-operations. The two cohorts are not significantly different at this stage (Fisher's exact test, p=0.87). At 38.2 months, the mean follow-up of the cementless cohort, the cementless cohort had 16 re-operations and the cemented cohort had 17, which is also not significantly different (p=1.00).

Periprosthetic tibial fracture, a complication not encountered in the cemented cohort, occurred four times in this cohort of cementless implants, although this difference did not reach significance (Fisher's exact test, p=0.12). The patients with this complication (two men and two women) ranged from 62 to 82 years of age, with a mean age of 71.5 (SD 8.2); the age difference between the groups does not reach statistical significance (independent samples t-test, p=0.23).

In terms of PROMs, the cemented cohort had a pre-operative score of 24.7 (SD 8.7), a one year score of 41 (6.9) and a ΔOKS of 16.3 (8.4). Both pre- and post-operative scores for the cementless cohort were lower than that of the cemented cohort, but the ΔOKS score was significantly better. This may be explained by the difference between centres, and isolation of the analysis to patients treated in centre 1 (which produced the previous, cemented, series) produced no significant difference in any of the three measurements.

7.4. Discussion

In this multicentre series of 1,000 cementless OUKRs, there were no complete radiolucencies, indicating secure fixation in all knees, and partial radiolucencies in 8.9%. The incidence of radiolucencies in this series is substantially lower than observed in all previously published series of cemented OUKR examined with fluoroscopically-aligned

radiographs (where the incidence of radiolucencies ranges from 62%[322] to 96%)[333]. The absence of complete radiolucencies compares with a rate of 30% in previous series[322].

These findings concur with the findings of the RCT in Chapter 6. At a mean of 38.2 months post-op (range 19-88 months), the rate of complications and revision is not significantly different from the previously published series of cementless OUKR and PROMs are equivalent.

The technique for implantation of the cementless prosthesis is similar to that of the cemented OUKR. However, in order to seat the prosthesis to allow good primary fixation in cementless replacement, more impaction is required. This raises the potential for an increased rate of periprosthetic fractures, which are a rare complication of cemented OUKR normally associated with errors in technique[334-336]. In cadaveric studies, a lower load is required to generate a periprosthetic fracture in tibiae implanted with a cementless implant than those implanted using cement (when associated with previously-defined technical risk factors)[337]. Whilst there is an equivalent rate of reoperation and revision in this series compared with previous series of the cemented implant, there are four periprosthetic fractures in this cohort. This complication was not encountered in the previous cohort of 1,000 cemented OUKRs and, whilst this difference does not reach statistical significance, the possibility of periprosthetic fracture must be borne in mind when implanting the cementless device. It appears that implantation with an extended sagittal saw cut and breech of the posterior tibial cortex during tibial preparation increase the risk of periprosthetic fracture[336,337]; care must be taken to avoid these risk factors. The RCT has demonstrated that the implant is relatively tolerant of incomplete seating, tending to settle within the first year (Chapter 6). However, this tolerance can be exceeded and it appears to be particularly important to clear the keel slot completely prior to impaction to allow the tibial tray to settle (Figure 7-4).

Three patients in this series demonstrated findings of valgus-posterior subsidence. In no case was the subsidence substantial (with subsidence of around 1 mm below the cut tibial plateau at the lowest point, Figure 7-3) and in no case was patient-reported outcome affected. At the time of the conduct of the study, a similar, but more severe case was observed (this case was not included in this series as the patient was ACL-deficient and did not conform to the standard indications). This appears to be uncommon (with a prevalence in this series of 0.3%). However, the aim of this study was to identify rare complications, and these appearances are investigated further in Chapter 8.

Prior to the study it was believed that there may be groups of patients, such as those with softer bone, for whom cementless fixation would be contra-indicated. To identify potential contra-indications, in all centres all patients appropriate for UKR were treated with cementless components. As no subgroup was found to have poor outcomes there appear to be no specific contra-indications to cementless fixation. Similarly, the postoperative rehabilitation regime employed was the same as that used for the cemented implant, and it has been found to be adequate.

7.4.1. Strengths and limitations

This is a multi-centre study and benefits from diversity of operating surgeons and centre-specific practice. In all centres, these cases represent the first use of the cementless implant and in one centre, the first use of the OUKR; the figures therefore cover the learning curve phase. The majority of the data presented here was taken from outside the designing centre. Although there were small but significant differences between the centres (which are a manifestation of centre-specific practice), overall, the results of the three centres were similar. The results from the designing centre were not appreciably better than the other centres (in fact, the ΔOKS was inferior in this centre). This demonstrates that good results can be achieved with the cementless OUKR in units other

than the designing centre. However, even with a multi-centre study, it can not be demonstrated incontrovertibly that these findings can be generalised to the wider population of UKR surgeons. To further explore this, an NJR-based study of the cementless OUKR has been undertaken and the results are presented in Chapter 9.

All cases in this series are at least 18 months post-operative and have had at least their one year clinical and radiological follow-up appointment. This follow-up is short in the context of the lifetime of a prosthesis, but previous series have demonstrated that PROMs plateau in the first year following knee or hip replacement[338,339], that the majority of complications associated with the OUKR occur within the first year[12], and that radiolucencies, if they occur after cemented OUKR, also occur within 12 months of implantation[322]. This is unlikely to be substantially different with the cementless device, as evidenced by the results of the RCT.

7.5. Conclusions

At a minimum of 12 months follow-up, results of cementless OUKR are equivalent to outcomes expected from the cemented implant with a similar rate of complications and a lower incidence of radiolucencies at one year. No contra-indications to the cementless device have been demonstrated, but care must be taken to avoid errors in implantation which increase the risk of peri-prosthetic fracture. Valgus subsidence is an unexplained phenomenon but not one which appears to contribute to clinical outcome on the basis of this study. This is explored further in Chapter 8.

The study presented in this chapter supports the findings of the RCT in Chapter 6; on the basis of this study the cementless OUKR appears to be as safe and effective as the cemented implant, with no additional contra-indications to its use.

Chapter 8 A study of the bone-implant interface in cementless Oxford UKR

8.1. Background and aims

In the previous two chapters, the cementless OUKR has been demonstrated to produce significantly better fixation on radiological measures, with similar or improved patient-reported outcome measures. The multicentre study (Chapter 7) has demonstrated equivalent implant survival to the cemented version, in the hands of both experienced and inexperienced surgeons. However, three of the 1,000 UKRs in this series were observed to settle into a valgus position within the early postoperative period, an appearance only very infrequently seen with the cemented prosthesis. Whilst these patients were well-functioning and radiologically stable at one year, these appearances warrant further investigation to determine the frequency of this finding in the population of users of the device, the natural history of these findings and their optimal management. This also gives an opportunity to investigate the forces across the bone-implant interface in the cementless OUKR in more detail.

As such, users of the cementless device were contacted to determine if they had observed similar findings to those reported in the multicentre series, and whether any patients had undergone revision, either for valgus subsidence or any other reason. A series of six cases exhibiting these appearances was assembled and is described in Section 8.2. The appearances of these cases were studied and a hypothesis developed as to why they arose. To test this hypothesis, mechanical tests were conducted using a

[*] Part of this chapter ("Valgus subsidence of cementless Oxford Unicompartmental Knee Replacement", corresponding to Section 8.2) will be published in the *Bone & Joint Journal* in 2014.

simplified *in vitro* model of the tibial bone-implant interface. This is discussed in Section 8.3.

8.2. Case series

8.2.1. Case identification and data collection

Six cases exhibiting appearances of valgus subsidence were identified. All of the patients had undergone cementless OUKR for anteromedial osteoarthritis and, unless otherwise stated, conformed to the classical indications of Goodfellow *et al*, described in Chapter 6.

The patients originated from three units, Oxford, Hillingdon Hospital in West London, and SportsClinic Germany, in Hamburg. Surgery was performed by both experienced and inexperienced surgeons, and in all cases, an MIS technique was used without eversion or dislocation of the patella. All surgeons provided surgical notes, clinical and radiological details both immediately post-operatively, demonstrating the appearances described, and at the latest follow-up. Findings are summarised in Table 8-1.

8.2.2. Findings

8.2.2.1. Case one

A 79 year old man underwent a cementless OUKR for anteromedial osteoarthritis eighteen months following a successful cemented, contralateral OUKR. At operation, he was found to be Anterior Cruciate Ligament (ACL) deficient, but the decision was made to persevere with UKR as the other conditions were met, and in light of the success of the OUKR performed on the contralateral knee which was also ACL deficient. At six weeks, the patient had an effusion with 5-10^{o} of flexion deformity; radiographs demonstrated no adverse features (Figure 8-1, left-hand image). Given the reassuring

radiographic appearances, and as the patient was mobile and comfortable, physiotherapy was arranged.

At four months, having flexed the knee fully, the patient complained of pain deep within the knee, and radiographs taken at the time demonstrated that the tibial tray had subsided from a position 4° varus relative to the mechanical axis of the tibia to 8° of valgus. Tibial tilt had increased from around 4° to 9°, with the component appearing loose (Figure 8-1, centre image), and revision of the tibial component was arranged. By the time of the pre-operative visit, the pain had improved and the position of the implant had stabilised, and surgery was cancelled in favour of conservative management. By the end of the third post-operative year, the implant had stabilised and the Oxford Knee Score was 39/48. His latest radiograph, at five years, demonstrates excellent fixation with no radiolucency (figure Figure 8-1, right hand image); however, the patient has developed degenerative spinal disease and his OKS has declined (bilaterally) to 29/48.

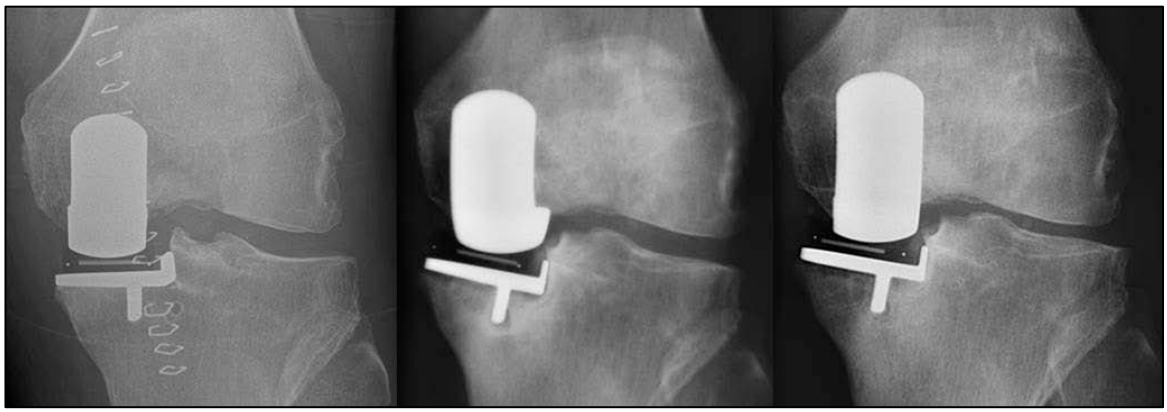


Figure 8-1: AP radiographs of patient 1
Left: postoperative image. Centre: five-months postoperative. Right: five years postoperative

8.2.2.2. Case two

A 66 year old man underwent an uncomplicated cementless OUKR for anteromedial osteoarthritis. The operation itself was uncomplicated and the immediate postoperative radiograph demonstrated the implant to be in a satisfactory position. In the fourth

postoperative week, the patient developed increasing pain over the anteromedial tibia, and radiographs at that point demonstrated subsidence of the implant into valgus, with lucency below the keel of the prosthesis (Figure 8-2). The patient was instructed to partial weight-bear with crutches and was reviewed at eight weeks. At this point, the pain had subsided and the implant had stabilised. He has reported no further problems.

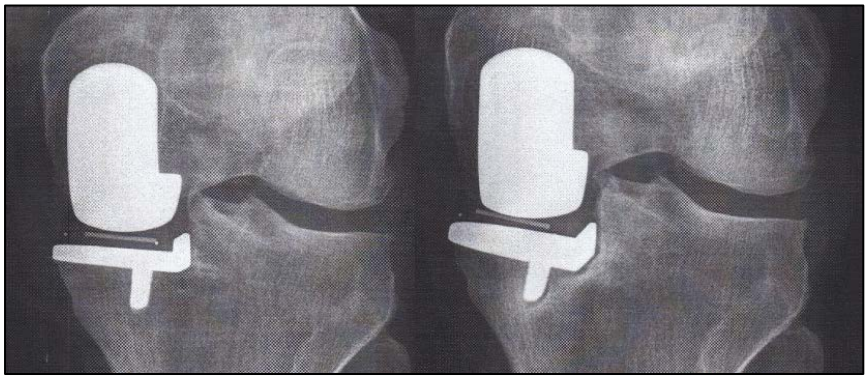


Figure 8-2: AP radiographs of patient 2

8.2.2.3. Case three

A 66 year old man underwent an apparently successful OUKR with an uneventful first six postoperative weeks. Over the subsequent weeks (and without a clear precipitant), the medial postoperative pain, which had been receding, progressed and a radiograph demonstrated subsidence of the implant into valgus. Pain did not improve with partial weight-bearing and the decision was made to revise to a cemented tibial component. At revision, the implant was found to be loose, with bone ingrowth restricted to the keel (Figure 8-3). Revision to a cemented tibial component rendered the patient pain-free.

Figure 8-3: Explanted component from patient 3

8.2.2.4. Case four

This patient underwent a cementless OUKR at the age of 65 years. He had made a good postoperative recovery but found the knee stiff, with difficulty achieving full extension. Over the following six months, the stiffness did not improve and the knee became progressively more painful. Postoperative radiographs demonstrate an undersized tibial component in a good position (Figure 8-4). Subsequent radiographs demonstrated progressive subsidence into a valgus position with clear subsidence of the posterior part of the tibial component on the lateral radiograph (Figure 8-4). As the pain was not improving, the patient underwent revision surgery. At revision, the tibial component was found to be well-fixed, with an un-displaced fracture of the posterior tibial cortex. The patient has been revised to a total knee replacement, and has made an uneventful recovery.

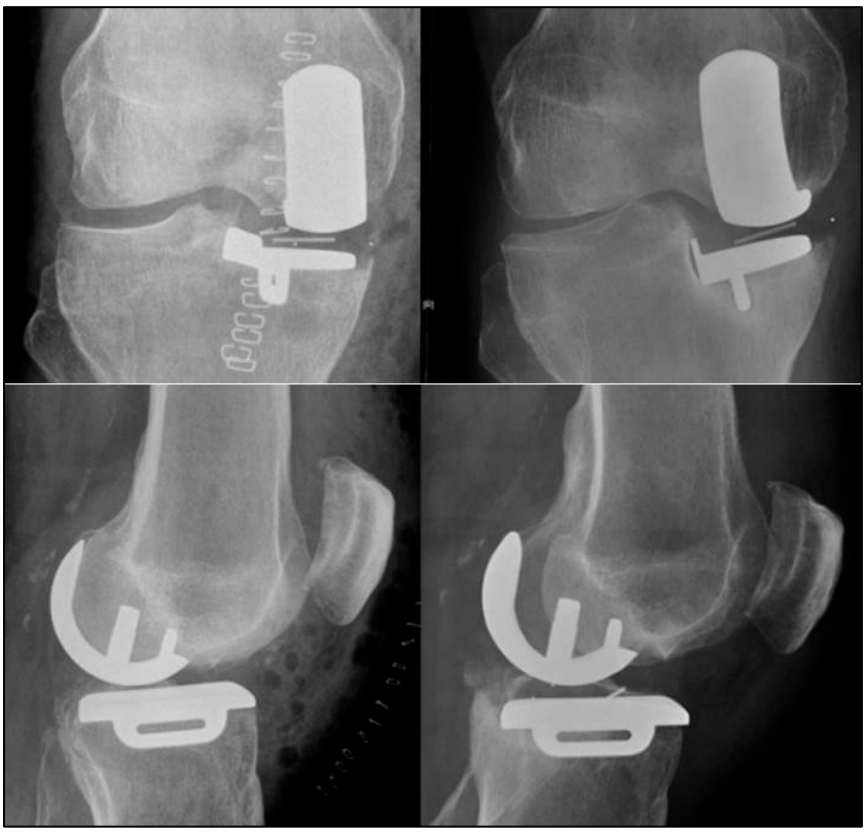


Figure 8-4: Radiographs of patient 4
Clockwise from top left: AP post-op, AP pre-revision, lateral pre-revision, lateral post-op

8.2.2.5. Case five

A 62 year old female underwent cementless OUKR for anteromedial osteoarthritis. The first six postoperative weeks were uneventful and pain was not a major feature. The patient re-presented at six months with increasing anteromedial tibial and femoral pain and reduction in mobility. The radiograph demonstrated subsidence into valgus with minimal increase in tibial slope. Pain persisted beyond one year, but became localised to the femur predominantly. The persistent pain precipitated a surgical exploration, where the tibial and femoral components were both found to be well-fixed, but there was evidence of anterior femoral impingement. A debridement of the impingement lesion was performed with insertion of a 2 mm thicker bearing. At latest follow-up, two years and one month following primary surgery, the patient is improved with an OKS of 35 (a 21 point improvement on her pre-operative score).

8.2.2.6. Case six

A 76 year old male underwent cementless OUKR (having previously undergone a successful contralateral cementless OUKR). Radiographs demonstrated satisfactory implant alignment (Figure 8-5, left-hand image). After two pain-free postoperative weeks, the patient developed exquisite anteromedial knee pain on weight-bearing. Radiographs taken at three months demonstrated the characteristic valgus-posterior subsidence (Figure 8-5, right hand image). The decision was made at this point to plan revision surgery, but by the pre-operative outpatients appointment (three months following primary surgery), the radiographs demonstrated no further subsidence, and there was improvement in symptoms. This continued, and at two years following surgery, radiographs show a well-fixed prosthesis and the OKS is 36/48.

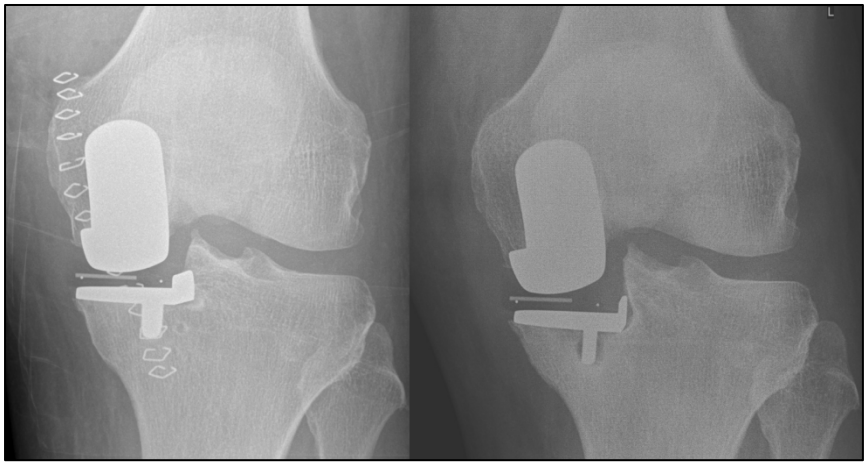


Figure 8-5: Radiographs of case six
Left: postoperative radiograph; right: three months.

Patient	Age	Gender	Latest follow-up (m)	Clinical status / further surgery
1	79	M	58	Knee asymptomatic, OKS 39 at two years. Now degenerative spinal disease, OKS 29 bilaterally with pain-free knees.
2	66	M	38	Asymptomatic and discharged. OKS not recorded prior to discharge.
3	66	M	Revised at <6 months	Tibial component revised to cemented UKR
4	65	M	Revised at <6 months	Revised to TKR
5	62	F	25	Debridement of impingement lesion and bearing exchange. OKS 35 at two years.
6	76	M	24	Asymptomatic. OKS 36

Table 8-1: Summary of patients in series

8.2.3. Discussion of findings

Whilst the six patients described above arise from three separate institutions, their clinical and radiological findings are similar. All patients had a good early result from their OUKR before experiencing a deterioration in their symptoms. All were demonstrated to tip into a valgus position in the early postoperative period, with subsidence of the posterior part of the tibial tray, which appeared loose on radiographs taken at that time. In four of the six patients, there was clinical improvement and radiographic evidence of good fixation within the first postoperative year. The remaining two were revised in the early postoperative period; one was found to be well-fixed and the other to have partial bony ingrowth around the keel. It is not clear what would have happened had these cases not been revised; the experience from the other cases presented suggests that the symptoms are likely to have settled.

When deciding on the optimal management for such patients, the risks of watchful waiting (the potential for further bone loss which may complicate revision surgery), should be weighed against the risk of performing revision surgery which proves to be unnecessary. None of the cases presented here demonstrate any progression of bone

loss; in fact, all show radiographic evidence of secondary osseointegration with clinical improvement.

The explanation for these cases remains unclear. There was no radiographic evidence of osteopenia in any of the patients and the demographic profile of these patients is not dissimilar to those documented in Chapter 7, and previous studies of cemented and cementless OUKR[13,59]. Postoperative radiographs appear to show implant positioning within acceptable limits and, aside from the undersizing of the tibial component in case four, there were no obvious errors in implantation. The majority of operations were performed by high-volume surgeons familiar with the procedure. All cases displayed some symptoms immediately following surgery, but this is a relatively common and temporary finding, even in well-fixed cemented components, and is thought to be a result of an increase in patients' level of activity following surgery[47]. In unrevised patients, symptoms appear to settle spontaneously.

8.2.4. Suggested mechanisms

Consideration of the pattern of subsidence and the natural history of this group of patients suggests that the appearances may result from impingement of the mobile bearing against the lateral wall of the tibial tray during flexion in the early post-operative period. The bearing tends to move away from the lateral wall in extension and therefore such impingement would not be detectable on an AP, standing radiograph. In normal circumstances without impingement, the centre of load lies within the central third of the tibial component in both the sagittal and coronal planes, and the load beneath the tibia is entirely compressive. In the case of femoral component malalignment where the femoral component is positioned slightly lateral relative to the tibia, impingement of the mobile bearing on the lateral wall may occur. This may result in

subluxation of the femur in the bearing and subsequent tilting of the bearing relative to the tibial tray (Figure 8-6).

It is hypothesised that this alters the loading of the tibial component, leading to excessive compressive loads lateral to the tibial keel, with unloading of the medial part of the tibial component. These excessive loads, if applied prior to full integration of the tibial plateau, may cause the tibial component to subside into valgus. Once in this position, the bearing will no longer impinge on the wall and normal loading is restored. The porous titanium and hydroxyapatite coating of the cementless implant allows bone ingrowth and fixation in this new position.

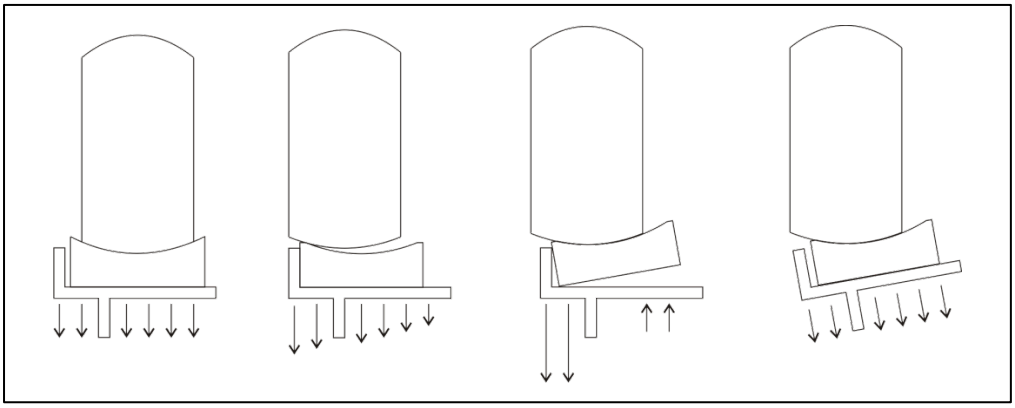


Figure 8-6: Possible mechanism for subsidence

If the same conditions were to be applied to cemented components, a different situation arises. Collapse into valgus can occur in the same way with cemented tibial components, but once this has occurred, the tibia is rendered loose and will not re-integrate. In this situation, revision surgery becomes necessary.

Another factor that may predispose to collapse of the tibial component into valgus is damage to the lateral part of the horizontally-cut surface of the tibial plateau. This may occur if the vertical saw cut is too deep. Extensive damage may occur if the saw cut is

initially too medial and another deep cut is performed more laterally, leading to an area of bone which is unsupported.

All of these cases demonstrate some subsidence of the posterior part of the implant. In one of the revised cases (case four), there was evidence of a fracture of the posterior cortex at the time of revision, which is likely to have occurred at the time of primary surgery. This case appeared to be slightly undersized and, as such, may be different from the other cases. However, subsidence into an increased posterior slope was a universal finding and it may be that a proportion of these cases represent occult posterior cortical fractures. Factors predisposing to periprosthetic fractures include deepening the posterior cortical sagittal saw cut during implantation[337], damage to the posterior cortex during curettage of the keel cut[336]; failure to fully clear the keel cut and excessive force of impaction may also be risk factors.

8.2.5. Conclusions

These appearances are rare: in the series reported in Chapter 7, similar appearances were present in only three cases, although none was to the same extent as those reported here. In the cases presented here, these appearances appear to follow a benign course with conservative management; however, they warrant investigation. If the hypothesis put forward in Section 8.2.4 is correct, and these cases are self-limiting, a further understanding of this phenomenon will allow unnecessary revisions to be avoided. If these hypotheses are not true, then this represents a worrying implant-related complication and modifications to the implant or implantation technique may be required.

In the following Section, the proposed mechanism will be further investigated using a mechanical study of the pressures beneath the tibial tray during normal loading conditions and conditions akin to those postulated in Section 8.2.4.

8.3. Mechanical study of the bone-implant interface

The mechanism proposed in Section 8.2.4 suggests that the cases described may have arisen as a result of impingement of the bearing against the lateral wall in deep flexion. To test this theory, a mechanical study was conceived. The aim was to use a simplified model of the tibial bone-implant interface to examine the effect of tibial wall impingement on pressure distribution below the tibial component, and to determine whether recreation of the proposed mechanism results in implant subsidence.

8.3.1. Materials and methods

8.3.1.1. Experimental rig

A simplified *in vitro* model of cancellous bone was constructed using commercially-available cellular polyurethane foam blocks (Sawbones, inc., Malmö, Sweden), which have previously been validated as an alternative to cadaveric bone for mechanical testing of orthopaedic implants[340]. For the purposes of this test, a cellular polyurethane foam block with a density of 0.32 g/cm was selected; this has mechanical properties which are similar to healthy, non-osteoporotic adult human cancellous bone[341].

Cementless OUKR tibial components were implanted into the blocks using the recommended surgical technique. Firstly, a saw guide was secured to the surface of the block using a bone pin, and a tibial keel cut was made using a 'toothbrush' saw and then cleared with a pick; both of these instruments are specific to the OUKR and designed for this purpose. The pin and guide were then removed before the tibial component was

inserted using an introducer and firmly impacted using a hammer. Following implantation, and prior to testing, the implant was cyclically loaded up to 2.2 kN ten times using a servo-hydraulic materials testing machine (Dartec H10, Dartec ltd, Stourbridge, UK) to ensure full seating of the implant.

The forces at the bone-implant interface were measured using K-Scan pressure sensors (Teksan inc., South Boston, MA). These are digital, thin-film (0.2 mm thick) sensors which relay real-time pressure data to a computer[342]. The sensors represent matrices of rows and columns and pressure is recorded at each row/column intersection, or sensel (Figure 8-7). Dimensions of the sensor are given in Table 8-2.

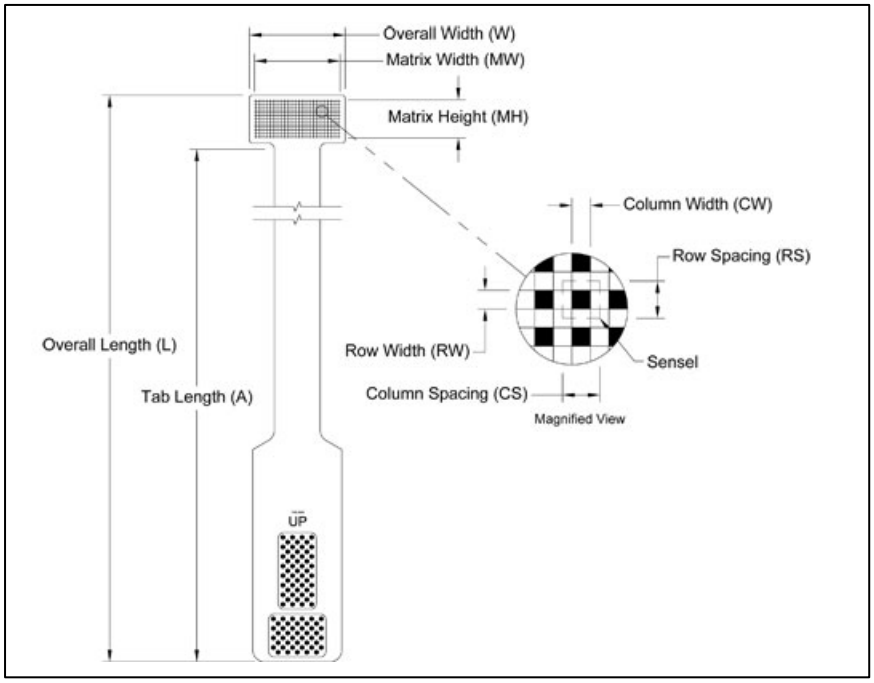


Figure 8-7: Tekscan K-Scan 4201 sensor
Image reproduced from Tekscan product manual

Length (L)	Width (W)	Tab length (A)	Matrix		Columns			Rows			Sensels	
			Width (MW)	Height (MH)	No.	Width (CW)	Pitch (CS)	No.	Width (RW)	Pitch (RS)	No.	Per cm^2
430.8	50.8	402.3	45.7	21.1	24	1.1	1.9	11	1.1	1.9	264	27.6

Table 8-2: Dimensions of Tekscan sensor
Letters in parentheses refer to the corresponding measurement in Figure 8-7.

At each sensel, the change in electrical resistance is measured; using these data, and the known area of the sensel, the computer software calculates the pressure. Using the data from all 264 sensels, the pressure distribution over the entire area can be calculated. For this study, two K-Scan 4201 sensors were used, positioned medial and lateral to the keel slot prior to implantation of the tibial component (Figure 8-8). The dimensions of this sensor allow testing of sizes AA-B of the Oxford tibial tray. The superior border of each sensor was trimmed to allow the sensor to record pressures all the way up to the keel.

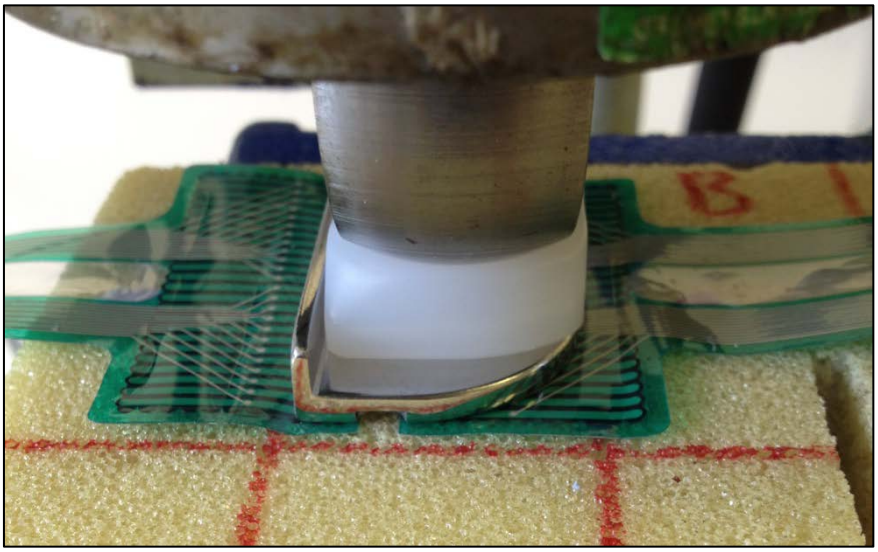


Figure 8-8: Tekscan sensors below implanted tibial tray
Note trimmed edges of sensor adjacent to keel

Once the component was implanted, the polyurethane block was mounted onto a bidirectional vice which was secured to the baseplate of the materials testing machine. The materials testing machine consists of a test-frame with an adjustable cross-head, on which is mounted a hydraulic piston head fitted with a 10 kN load cell. Loads were delivered through a custom-made attachment with the same geometry as the OUKR medium femoral component. A 2 megapixel digital camera (Logitech Webcam Pro 9000, Logitech International S.A., Romanel-sur-Morges, Switzerland) was mounted onto the

test frame, aligned to produce a lateral view of the tibial tray at the level of the surface of the block (Figure 8-9).

Following the test, the component was explanted and the polyurethane 'bed' was examined visually. The visual inspection was corroborated by examination of the blocks using a laser profilometer to provide an accurate description of the pattern of subsidence displayed by the tibial component.

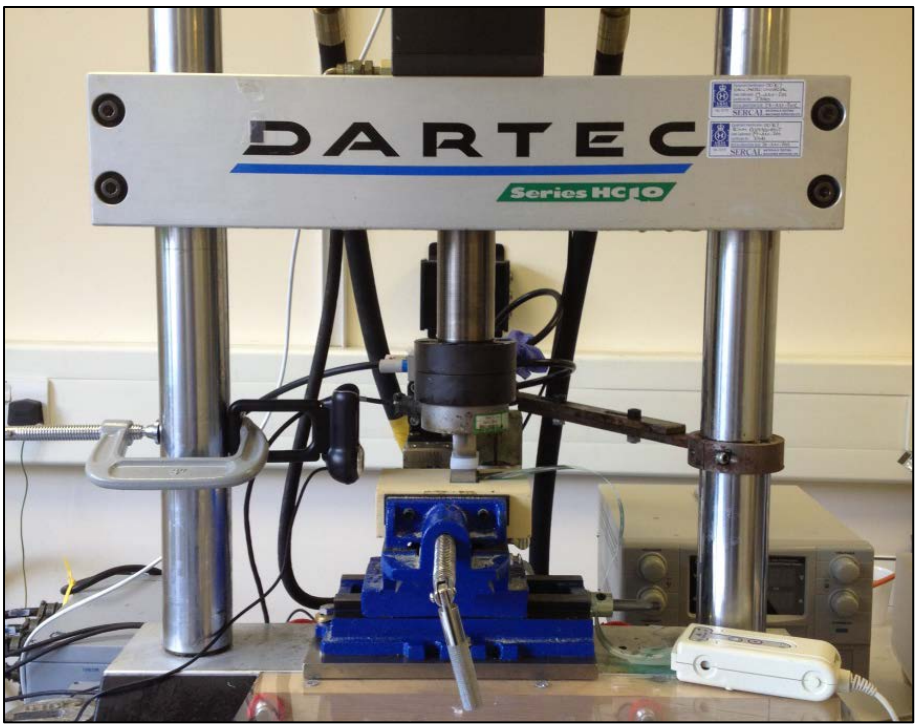


Figure 8-9: Testing rig during conditioning

8.3.1.2. Conditioning, Equilibration and Calibration

To ensure consistency and accuracy of measurements taken using the Tekscan sensors, each sensor underwent a pre-test protocol of conditioning, equilibration and calibration prior to use.

The pre-test protocol was undertaken using the same basic rig as described in Section 8.3.1.1. A testing interface was constructed to mimic the conditions expected in the main

tests, whilst applying loads evenly across each sensor[343]. Therefore, a solid polyurethane block of similar density was substituted for the cellular block (the solid block has a smooth surface to facilitate the even application of load). The load was applied using the material test machine actuator, through an UHMWPE bearing mounted on a stainless steel block which had been machined to fit the dimensions of the sensor exactly.

For each sensor, conditioning was performed by evenly applying loads through the testing interface. Conditioning is the pre-loading of new sensors to reduce the effect of drift (the change in sensor output when a constant load is applied) and hysteresis (differences in sensor output with repeated applications of the same force). As recommended by the manufacturers, the load applied for conditioning was 20% greater than the maximum anticipated loading during the tests (2.22 kN). Load was increased in a linear fashion over 10 seconds, held constant for 5 seconds, and decreased over the following 10 seconds. Loads were applied four times per sensor with 120 seconds between each cycle.

Equilibration is the digital compensation for subtle differences in the sensitivity of each sensel. Equilibration was performed by applying a load of 1kN to all sensels simultaneously for 20 seconds; the Tekscan software adjusts for differences in output detected when all sensels are loaded simultaneously.

Calibration was performed using the power calibration function within the Tekscan software. During this process, two loads are applied sequentially, at 20% and 80% of the anticipated maximum load (0.36 and 1.5 kN). The Tekscan software plots a curve through 0 and the two measured points (Figure 8-10). Power calibration was chosen as it has been demonstrated to be the more accurate of the two calibration processes when loading in the mid-range of the Tekscan sensor[344].

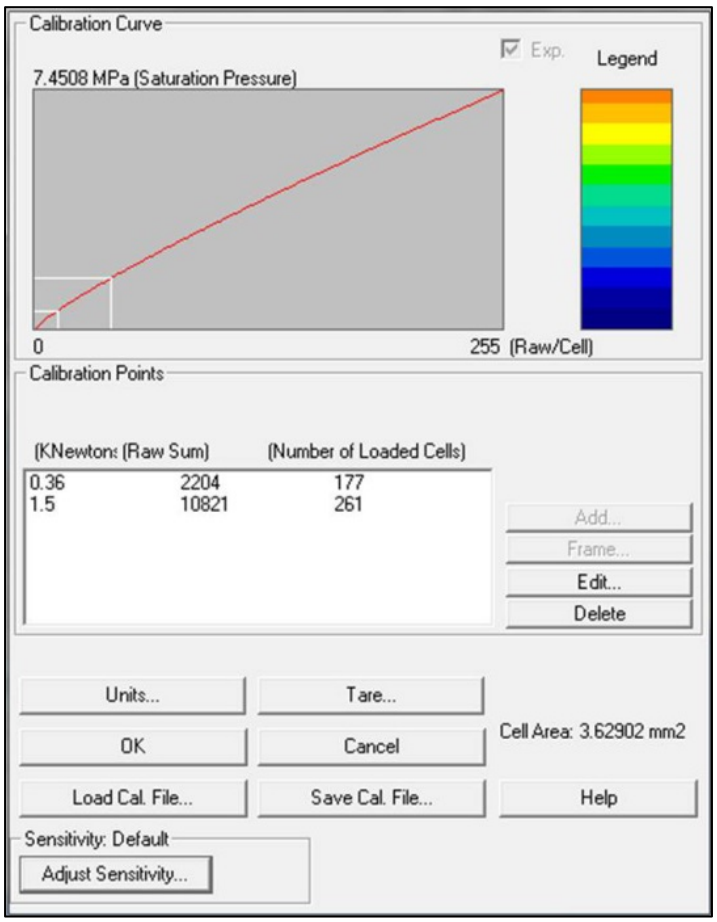


Figure 8-10: Calibration of the Tekscan sensor
The red curve is plotted through 0 and the two points of calibration (white squares). The raw output of the sensor is calibrated to the known pressure applied.

8.3.2. Testing protocols

Two separate static testing protocols were conducted. The first protocol was intended to simulate normal loading of the tibial tray during a step-climb activity. The second was intended to replicate the impingement of the mobile bearing against the lateral tibial wall.

8.3.2.1. Protocol one – normal loading

Protocol one was designed to mimic the normal loads expected through the tibial tray during a normal daily activity. Loading data were obtained from two previous studies using instrumented total knee replacement implants[345,346]. In one case, these data were available in the public domain, and in the other, they were received by presonal

communication with the senior author (Dr D'Lima, Scripps clinic, La Jolla, CA). Loading data used represented the expected maximum load on the medial compartment of the knee in the process of stepping up a single 10 cm step. The step-up activity was selected as this involved the highest loads expected through a flexed knee in normal conditions, and as this best matched the history given by the patients described in Section 8.2. Loads were calculated for the entire movement from 0-90°, in 10° increments. The position of the mobile bearing at each of these increments was derived from a previous fluoroscopic study of the OUKR[347]. The bearing tends to move from posterior to anterior as the knee flexes, reaching the anteroposterior mid-point of the tibial tray by 70° of flexion, before reversing its course and moving posteriorly between 70° and 90°. For the purposes of this study, the highest loading figures for each bearing position were selected. As the anteroposterior path of the bearing reverses at high flexion, only 8 bearing positions were used for the 10 increments of flexion. Bearing position and loading data are given in Table 8-3.

Knee flexion angle (°)	Bearing position (mm)	Load (N)
0	-7	1100
10	-6	1100
20	-5	1200
30	-4	1100
40	-3	1400
50	-2	1600*
60	-1	1700*
70	0	1700
80	-1	1700
90	-2	1850

Table 8-3: Loading protocol for normal loading study
Bearing position is relative to the anteroposterior midpoint of the tibial tray.
When a bearing position is duplicated during knee flexion, the higher load is uesd.
Loads not applied are indicated with an asterisk

The mediolateral position of the bearing was set at 1 mm from the lateral wall; this is the recommended position for the bearing to track in the OUKR. The position of the bearing was controlled during set-up using a 1 mm shim, which was removed prior to testing.

Within each test, loading data were collected for each bearing position three successive times. Whilst the Tekscan sensors remained *in situ* throughout, it was only possible to read data from one at a time; hence medial and lateral loads were recorded sequentially for each bearing position. A total of 5 tests were performed; three with one size A tibial component; and two further tests with different tibial components of the same size to allow for manufacturing tolerances. As such, a total of fifteen measurements were made for each bearing position. Following the main tests, two further tests were carried out with smaller (size AA) and larger (size B) tibial components, to assess whether the findings with the size A tray were generalizable to other sizes. For each test, a new keel slot was made and the tibial tray was implanted using the standard technique.

8.3.2.2. Protocol two: Bearing-wall impingement

Protocol two was designed to replicate the abnormal loading hypothesis presented in Section 8.2.3. Rather than taking serial measurements through the anteroposterior path of the bearing as in protocol one, in protocol two, serial measurements were taken with the bearing moving from medial to lateral, and impinging on the lateral tibial wall.

Loads were applied with the bearing in the position corresponding to 90^{o} of knee flexion. This position was chosen as it corresponds to the history given by the patients in Section 8.2.2, and because it is the point at which the largest load is transferred through the tibial tray. The rig was set up in the same way as in Section 8.3.1.1. However, the tibial tray was implanted in a position perpendicular to that used in Section 8.3.2.1., allowing the

mediolateral position of the bearing relative to the tibial tray to be recorded with the digital camera.

The testing protocol is outlined in Table 8-4. The bearing was initially positioned far medially with the bearing overlapping the medial edge of the tibial tray. It was then incrementally moved laterally until it impinged against the tibial wall. As with protocol one, each position was repeated 5 times with different A bearings, before being repeated with AA and B tibial components, as per the previous set of tests.

Position number	Position (relative to lateral wall)
1	5 mm medial
2	3 mm medial
3	1 mm medial (normal)
4	3 mm lateral
5	5 mm lateral

Table 8-4: Protocol 2

8.3.2.3. Analysis of bone block following explantation

Following each test, the polyurethane blocks were retained and labelled according to the test performed. The blocks were inspected visually before being analysed using a laser surface profilometer (Tiab Ltd., Banbury, Oxfordshire). The laser profilometer is mounted on a test frame (Figure 8-11) with a motorised base which allows samples to be moved in five degrees of freedom (*x, y, z,* yaw and pitch). The block was mounted onto the base of the test frame, with the laser centred on the centre of the keel slot. The block was scanned using the laser in a raster pattern, with each row being 100 microns from the previous row; in total, a 60 mm x 60 mm area was scanned.

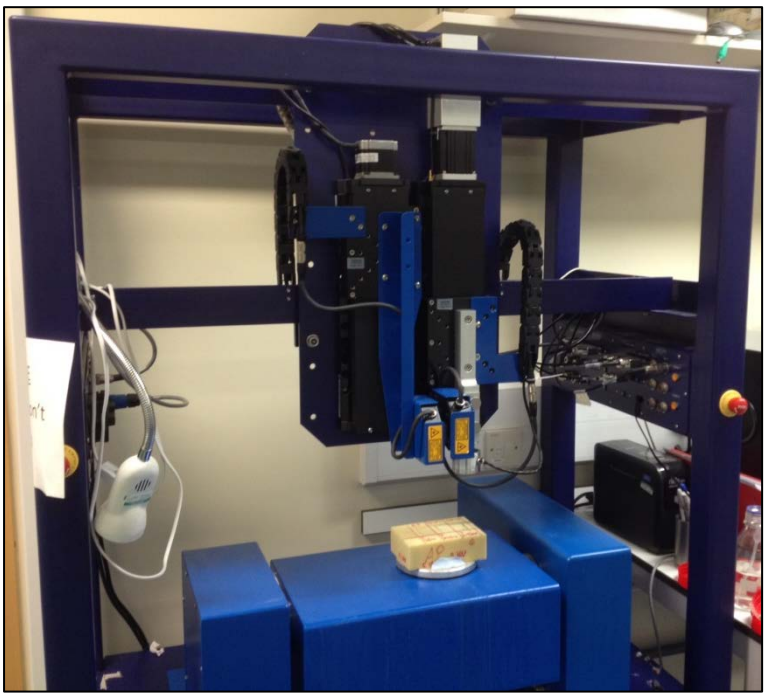


Figure 8-11: Laser profilometer mounted on test-frame
Polyurethane block is mounted on the mobile base

8.3.2.4. Data processing and analysis

Pressure data were collected and stored on a computer attached to the material test machine. The Tekscan software outputs data in two formats and both were stored. The calibrated and equilibrated pressure data are outputted into an ASCII file containing matrices of sensel values for each frame of data collection. The second format, the Tekscan proprietary movie format, contains the raw, uncalibrated and unequilibrated data from the sensors together with tags indicating the calibration and equilibration values. New ASCII files can be produced from this movie data and errors of calibration and equilibration can be corrected *post-hoc* using the raw data contained in the movie file. The material test machine also outputs data on actuator position and load; this was also stored.

At each position, a 2 megapixel digital photograph was taken together with a calibration grid (Figure 8-12). These images were stored to keep a record of the precise bearing position during each set of tests.

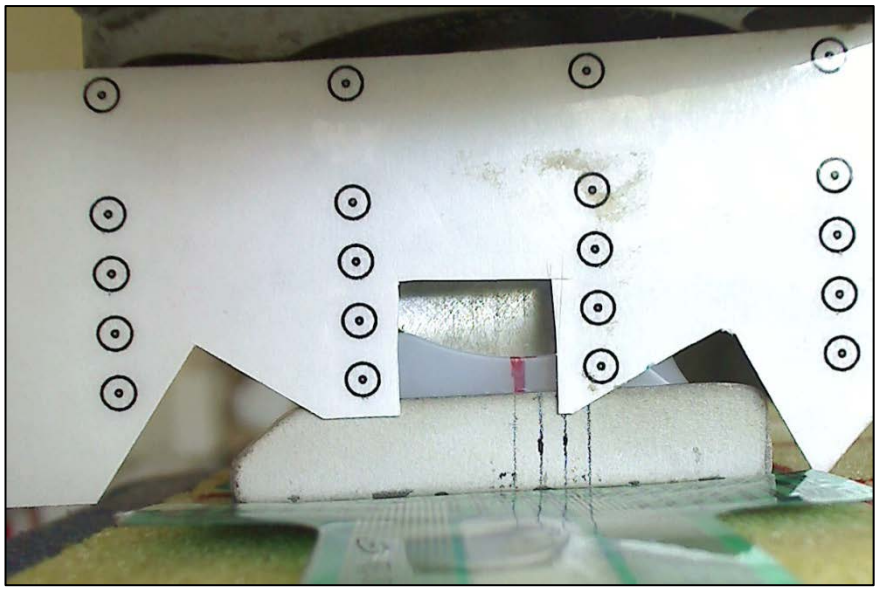


Figure 8-12: Tibial assembly with calibration grid

ASCII files for each test were processed using a separate Matlab programme. The programme was written for this purpose by Dr Elise Pegg, post-doctoral engineer at NDORMS. The file-names of each file were coded so that each medial output could be linked to the corresponding lateral output. The software first identifies the frame with the maximum overall pressure. It automatically crops this frame to the size of the tibial tray, and defines the area loaded medially and laterally. Using the known dimensions of each sensel and the corresponding pressure output, the total load is calculated and divided by the loaded area to give the overall pressure medial and lateral to the keel. The same process is performed to define the pressure at the raised rim and in the central portion of the implant. Therefore, the following data are outputted: medial pressure, lateral pressure, co-ordinates of pressure centroid, pressure around the rim of the tibial

tray and pressure in the interior of the tibial tray. Data were outputted into a spreadsheet which was imported into Stata for the graph production and analysis.

Pressure distribution and pressure centroid position were described graphically: the location of the pressure centroid was mapped against the known geometry of the tibial tray and the mean pressures medially and laterally were plotted using line plots. Medial and lateral loads were compared using non-parametric tests given the small number of observations. As data were paired (medial and lateral; rim and interior), they were compared using Wilcoxon's Signed Ranks test.

Laser profilometer data were again outputted as ASCII files and imported into a Matlab programme (which had been previously written and used by Dr Cameron Brown, post-doctoral engineer at NDORMS). Using this programme, an image was produced representing the profile of the block, presented as a colour map. This allowed an accurate description of the pattern of subsidence beneath the tibial tray.

8.3.3. Results

8.3.3.1. First test: normal bearing movement

Throughout the simulated 'normal' movement, the pressure centroid moved anteroposteriorly as the position of load application varied. The mediolateral pressure centroid remained medial to the keel, under the central portion of the bearing (Figure 8-13).

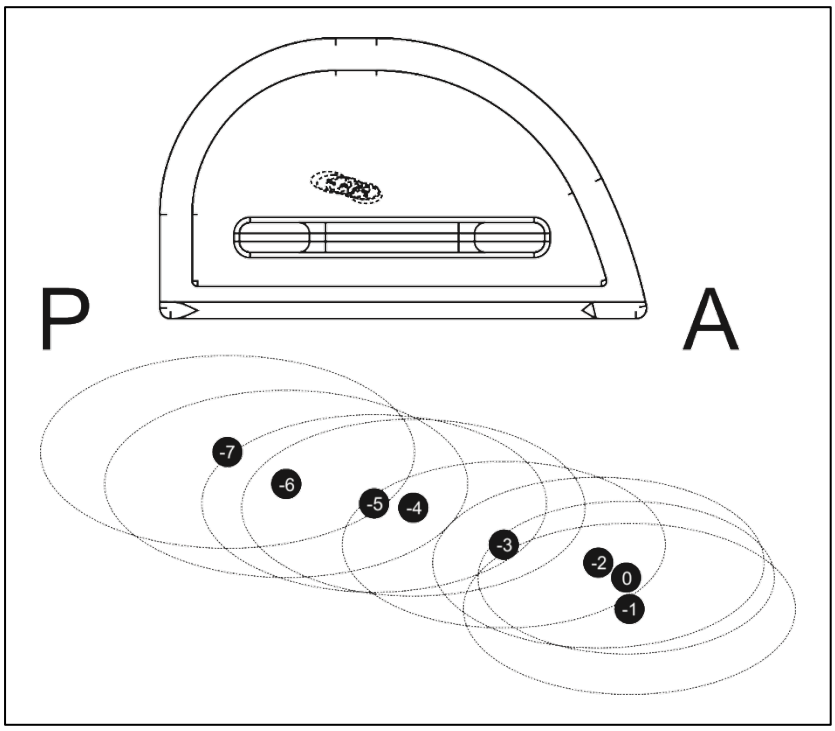


Figure 8-13: Pressure centroids during normal loading
Pressure centroids are given in the context of the tibial tray (above), and enlarged to indicate their relationship to the bearing position (numbers within each circle).
The central, solid, circle represents the median centroid; the dotted 'halo' represents 95% confidence intervals. Anterior and posterior are labelled 'A' and 'P'.

Pressure remained evenly distributed between medial and lateral parts of the tibial tray throughout normal loading (Table 8-5 and Figure 8-14). At no position was a statistically significant difference recorded between the pressure medial and lateral to the keel.

AP bearing position	Load applied	Medial pressure (median and IQR)	Lateral pressure (median and IQR)	Significance (Wilcoxon)
0	1700	0.93 (0.88-0.95)	0.98 (0.88-1.00)	0.689
-1	1700	0.89 (0.65-0.95)	0.85 (0.74-0.93)	0.733
-2	1850	0.91 (0.68-0.98	0.85 (0.75-0.94)	0.732
-3	1400	0.62 (0.53-0.85)	0.64 (0.61-0.65)	0.864
-4	1100	0.58 (0.48-0.78)	0.49 (0.47-0.56)	0.319
-5	1200	0.60 (0.50-0.79)	0.52 (0.47-0.58)	0.306
-6	1100	0.58 (0.48-0.75)	0.40 (0.38-0.53)	0.3
-7	1100	0.55 (0.47-0.74)	0.38 (0.35-0.53)	0.157

Table 8-5: mediolateral pressure distribution during normal loading

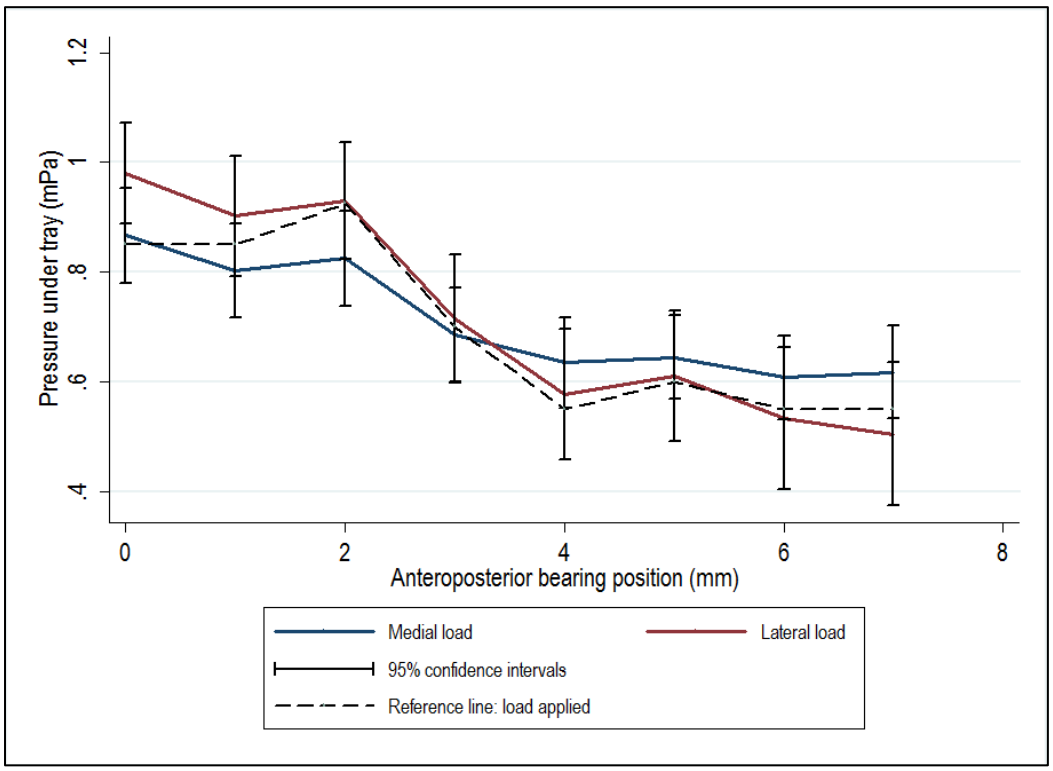


Figure 8-14: Medial and lateral pressures during normal movement

Distribution of the pressure between the rim and the central part of the tibial tray varied between implants due to variations in the thickness of the plasma-sprayed porous coating. Whilst in some implants, the porous coating was the same thickness as the rim of the tibial tray, this varied and in some prostheses the rim was proud. In those cases, the load was borne almost entirely by the rim of the tibial tray (Figure 8-15). For the three size 'A' tibial trays used during these tests, the pressures recorded in the rim and central part of the tibial tray are displayed in Figure 8-16. Following explanation of the tibial trays, there was no gross evidence of tibial subsidence.

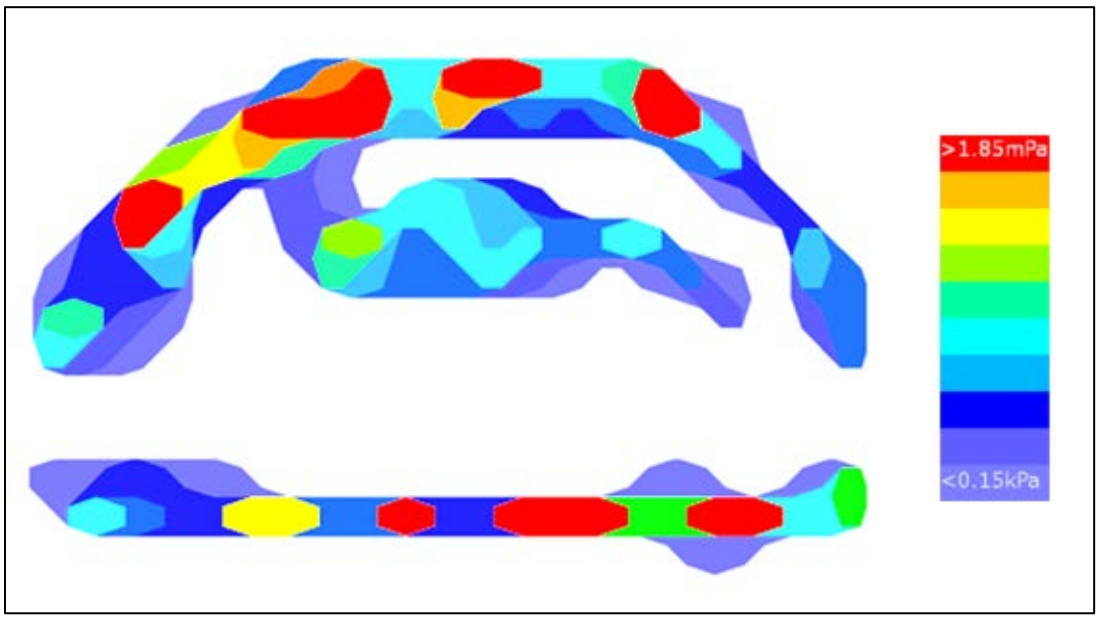


Figure 8-15: Pressure distribution below tibial tray
In this tray, the rim is proud of the porous-coated central portion and there are high pressures around the edge of the tray (key given to right of main picture)

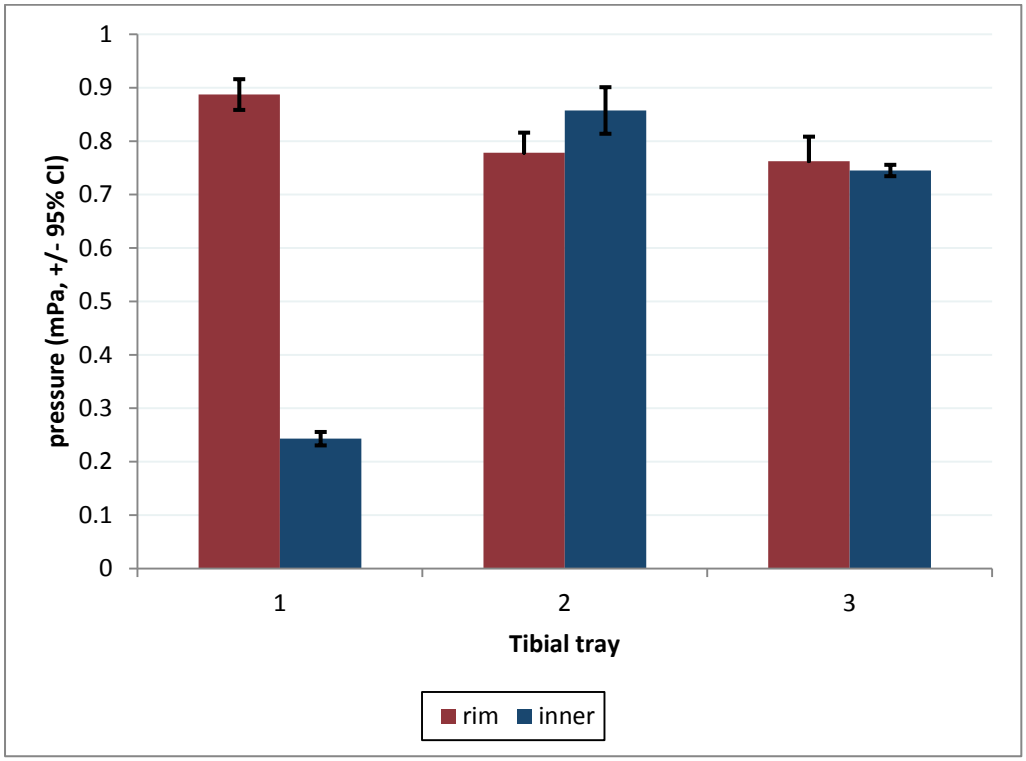


Figure 8-16: Pressures in the inner area and rim of the tibial tray.
Pressures are observed to vary according to differences in the thickness of porous coating.

8.3.3.2. Test two: Bearing-wall impingement

When the bearing was induced to impinge on the lateral wall of the tibial tray, the bearing tilted as anticipated (Figure 8-17; compare to Figure 8-6) and the pressure distribution under the tibial tray changed markedly (Table 8-6).

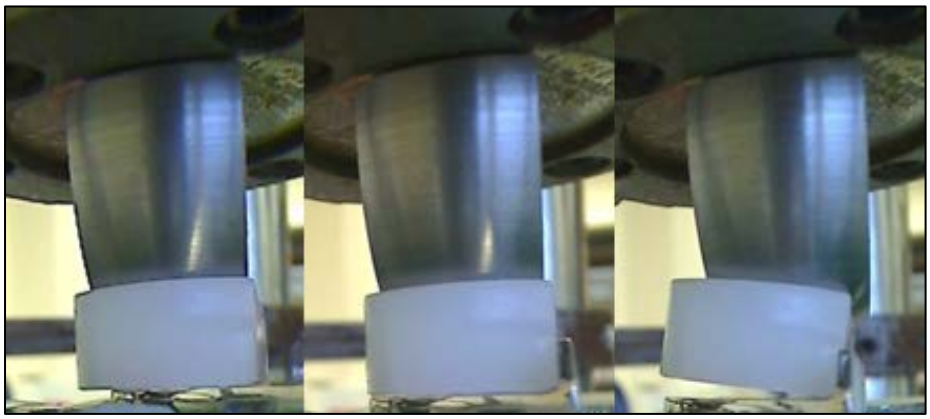


Figure 8-17: Bearing tips as it impinges on the lateral wall

The pressure centroid remained just medial to the keel until the point at which the bearing impinged onto the lateral wall (position 4), at which point the centroid moved lateral to the keel (Figure 8-18). This was reflected in changes in the pressure distribution medial and lateral to the keel. Pressure was higher medial to the keel when the bearing tracked medially (positions 1 and 2). There was no difference between pressures medially and laterally when the bearing returned to its normal tracking position (position 3). As the bearing impinged onto the wall, pressures immediately rose lateral to the keel (Figure 8-15).

ML bearing position	Load applied	Medial pressure (median and IQR)	Lateral pressure (median and IQR)	Significance (Wilcoxon)
1	1850	1 (0.61-1.08)	0.33 (0.15-0.48)	<0.01
2	1850	0.95 (0.74-0.97)	0.68 (0.36-0.76)	<0.01
3	1850	0.69 (0.53-0.71)	0.77 (0.53-0.86)	0.33
4	1850	0.44 (0.39-0.58)	0.98 (0.90-1.08)	<0.01
5	1850	0.37 (0.30-0.60)	0.97 (0.85-1.08)	<0.01

Table 8-6: Medial and lateral pressures during abnormal loading

When loads were applied with bearing-wall impingement, the posterolateral corner of the tibial tray was observed to subside, compressing the underlying cellular polyurethane foam. Along with the blocks from the previous test, each of the blocks was examined using the laser profilometer.

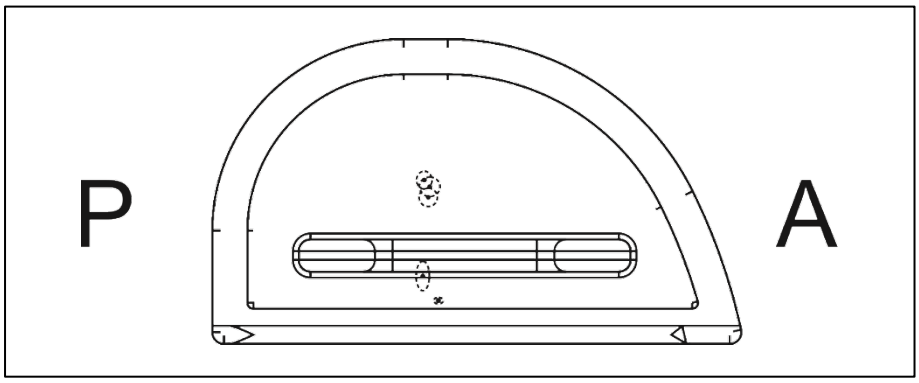


Figure 8-18: Mediolateral pressure centroids (superimposed on tibial tray)

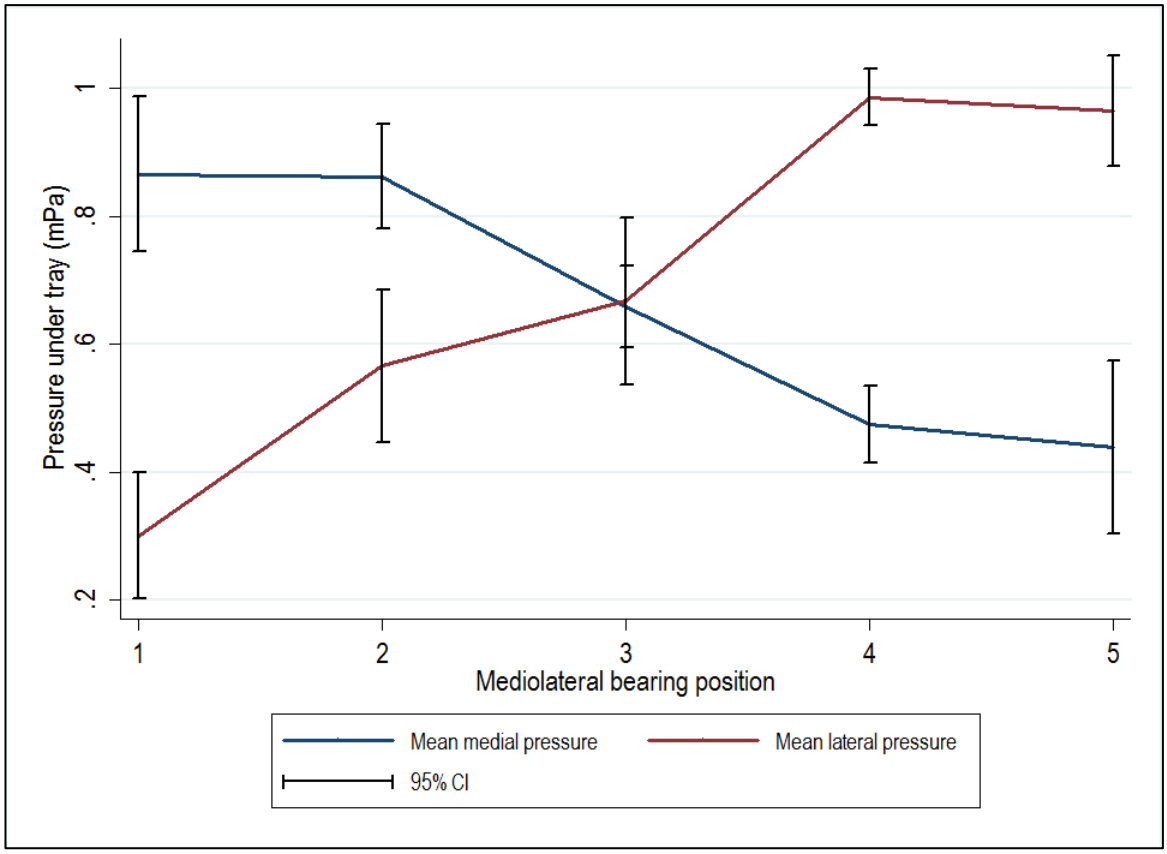


Figure 8-19: Pressures medial and lateral to keel (mediolateral loading)

8.3.3.3. Analyses of other sizes

Further tests were performed with size AA and size B tibial components. In each case, a single test with three repetitions was performed throughout the range of bearing positions examined in the anteroposterior and mediolateral tests in Sections 8.3.2.1 and 8.3.2.2. As centroid positions were calculated as an absolute distance from the posteriolateral corner of the implant, the values for centroid position varied between the implants examined. However, the patterns of loading were very similar in each of the sizes. In all cases, the centre of pressure remained medial to the keel in normal loading; in all cases, bearing-wall impingement led to the pressure centroid moving lateral to the keel and resulting in high pressures over the lateral corner of the implant.

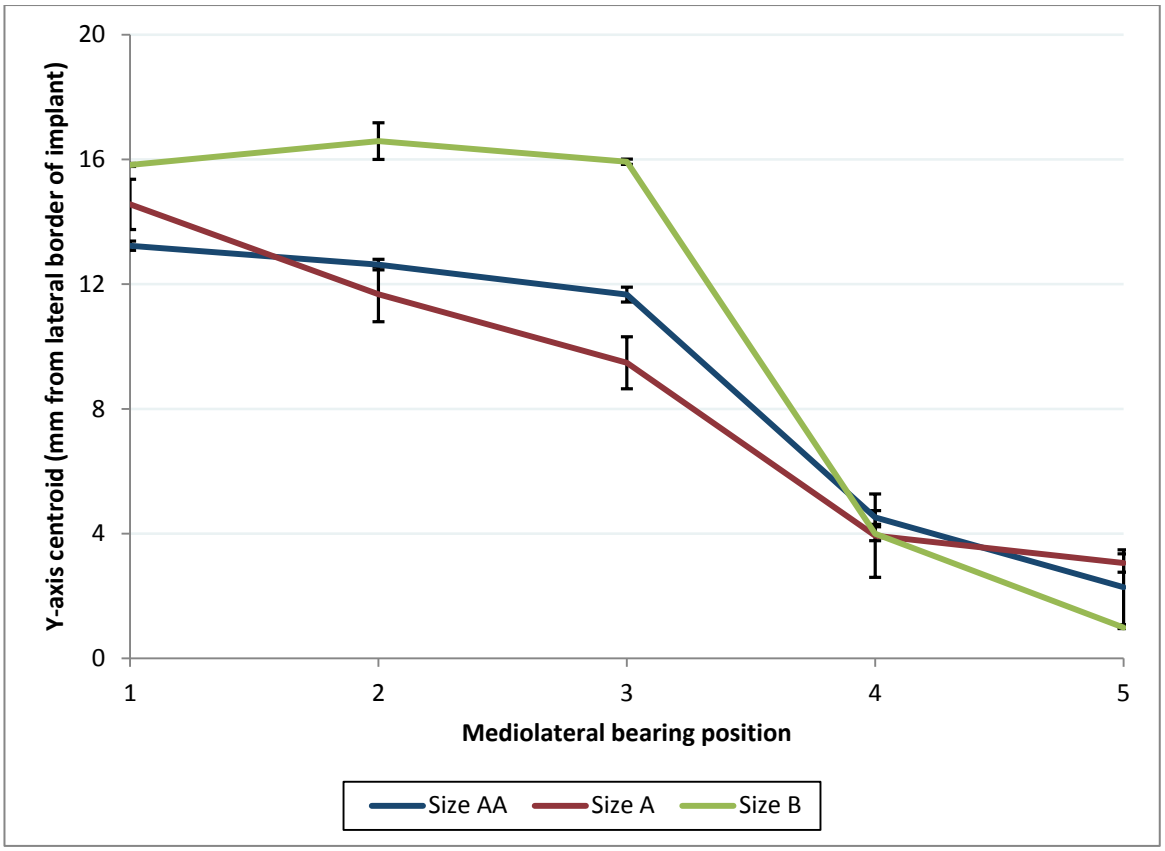


Figure 8-20: Pressure centroids with different tibial sizes (mediolateral loading)

8.3.3.4. Analysis of bone block following explantation.

All blocks from the normal and abnormal loading tests using size 'A' tibial trays were examined using laser profilometry. The colour maps for the normal loading blocks are given in Figure 8-21, and for abnormal loading blocks, Figure 8-22.

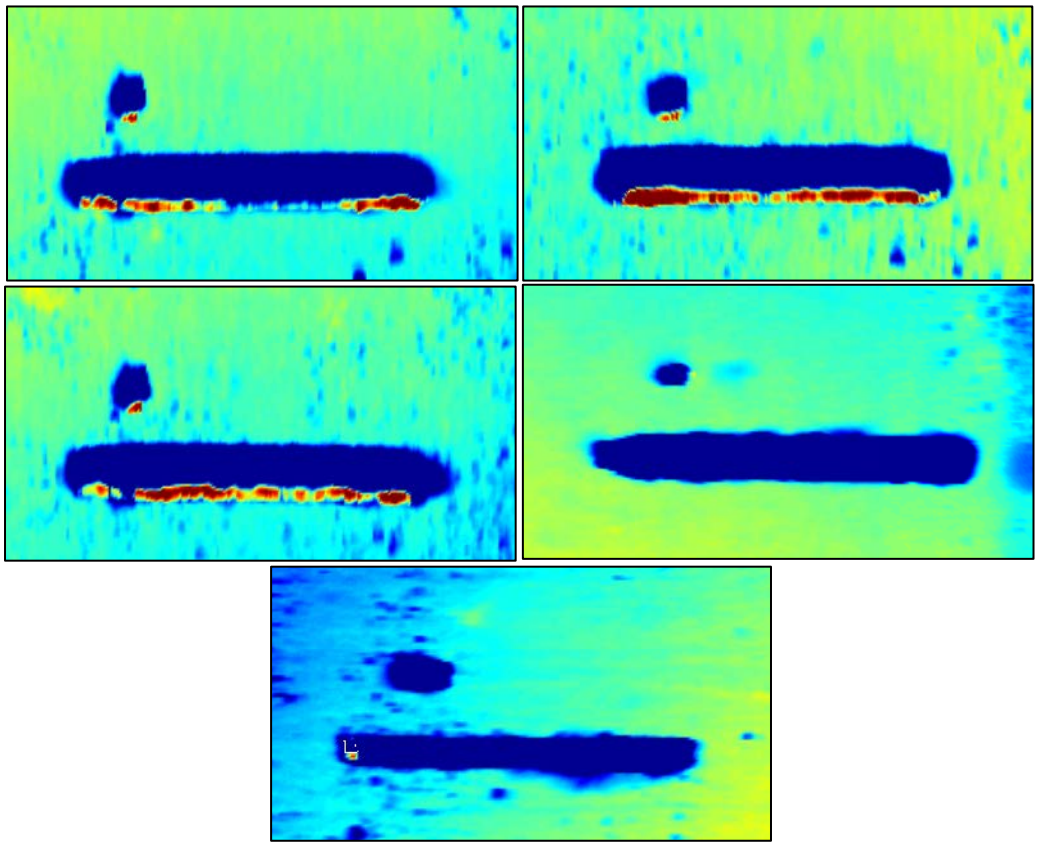


Figure 8-21: Colour maps from polyurethane following normal loading

Following the normal loading test, there is no evidence of subsidence in any of the blocks tested. However, in abnormal loading, the tibial tray has been observed to make an impression in the posteromedial corner of the footprint of the tibial tray, to a depth of between 0.5 and 0.9 mm, depending on the block examined.

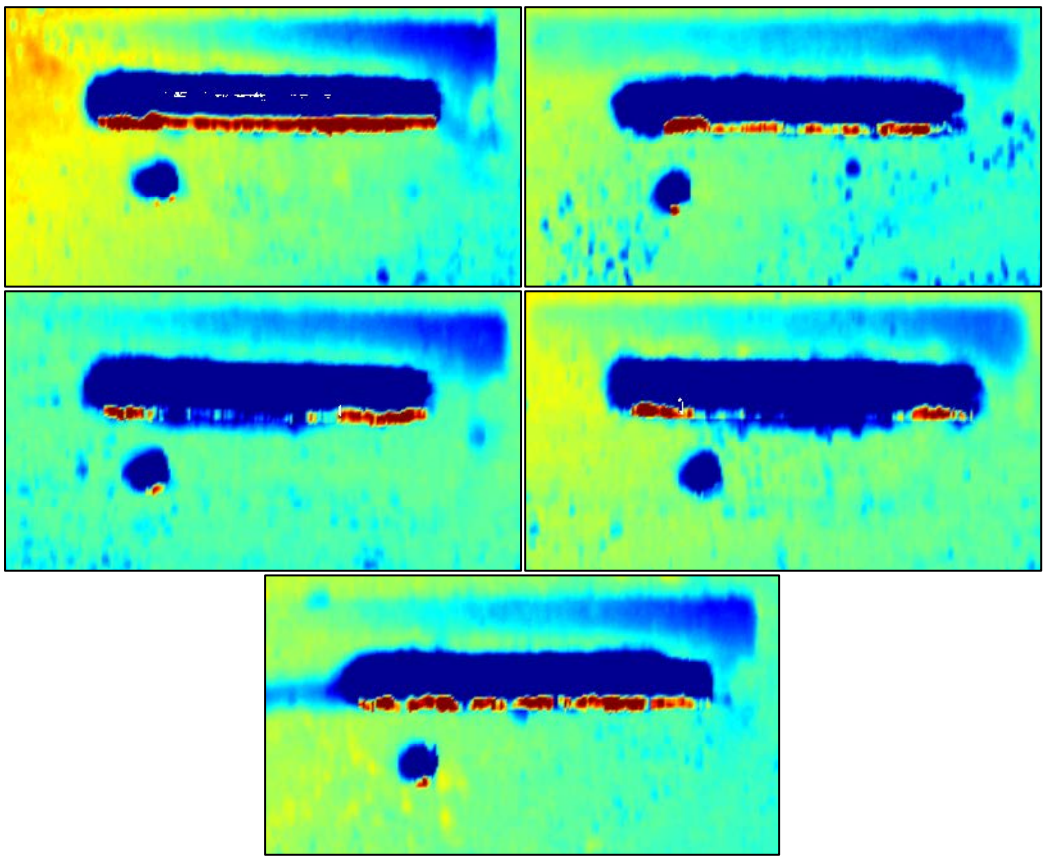


Figure 8-22: Colour maps from polyurethane blocks during abnormal loading

8.3.4. Discussion

8.3.4.1. Summary of results

The tests detailed above demonstrate that the pressures below the tibial tray remain fairly constant during simple activities when the bearing tracks normally. However, when the conditions hypothesized in Section 8.2.4 are recreated, the pressure distribution beneath the tibial tray changes markedly, with very high pressures lateral to the keel and particularly in the posterolateral corner. This causes subsidence of the tibial tray, in a manner similar to that observed in Section 8.2. Whilst high pressures were observed under the medial tibial tray when the bearing tracked very far medially (Figure 8-19, position 1), there was no corresponding tibial subsidence. These high observed medial pressures may be due to loading on the raised edge of the tibial tray and could be

avoided by reducing the height of this edge (or by making the depth porous coating more consistent). In fact, the bearing is unlikely to track this far medially given the presence of the medial capsular and ligamentous structures, and this (together with the medial support provided by the tibial cortex), suggests that this sort of abnormal loading is unlikely to be a problem *in vitro*.

Overall, the findings of this study support the hypothesis put forward, and suggest that avoidance of bearing-wall impingement is important in avoiding the appearance of such cases. Minor alterations to the implant itself may also be useful in rendering the implant less sensitive to such errors of implantation. If porous coating was applied to the lateral wall of the tibial component, the lateral corner may be better-supported and the position of the tray may be more stable in the early postoperative period, even in the presence of bearing-wall impingement. Reducing the height of the rim of the prosthesis relative to the depth of the porous coating in the central area may also be helpful in distributing the loads applied to the tibial component more equally. The importance, or otherwise, of these changes should be investigated in future studies (Section 8.4).

8.3.4.2. Limitations

The study presented here has a number of limitations. The model used was greatly simplified, both in terms of replication of relevant anatomy and physiology. In the case of anatomy, the 'bone bed' was entirely representative of cancellous bone, without a cortex to provide additional support. There was no lateral wall of bone, which may provide an additional buttress against the lateral wall of the implant and mitigate against subsidence.

Another simplification was the use of bone substitute, rather than cadaveric bone. Bone substitute was chosen to maintain consistency of anatomy and bone density between

tests. It is impossible to replicate osseointegration with the use of such media, but given that the cases presented early in the post-operative period where full osseointegration was not likely to have occurred, this was considered sufficient. Likewise, the density of bone-substitute represented normal, healthy adult bone. Whilst there was no evidence of osteopenia radiographically in any of the patients studied, all were of an age group where some osteopenia might be expected, and a more detailed test would have included 'bone' of different density.

8.3.4.3. Future work

Future work will attempt to address some of these limitations. Having successfully interrogated a simplified model, the tests may be repeated with a more anatomically accurate bone-substitute. Composite tibiae are available, which replicate the normal tibial anatomy as well as providing both cortical and cancellous bone. If the findings of this study are replicated with a more anatomically accurate model, it will give additional credence to the proposed mechanism. The repetition of these tests in more osteopenic bone would also bring more insights in relation to the patients studied. The use of composite bones for the further study of this implant will allow the assessment of the importance of implantation errors in the development of subsidence and the related problem of peri-prosthetic fracture.

The tibial implants studied in this and earlier chapters are fully hydroxyapatite-coated, but only have porous coating in the 'cement pocket' and on the keel. Extending the porous coating to the edges of the implant and reducing the height discrepancy between the rim and the central portion may allow the loads applied to the component to be more evenly distributed in the underlying bone. Likewise, coating the lateral wall in porous titanium has the potential to improve early osseointegration, and may improve the

resistance to subsidence. More detailed simulations, *in vitro* and *in vivo* tests, the latter involving RSA, would test this hypothesis.

8.4. Conclusions

A series of cases of cementless subsidence have been presented. The four patients in whom the implant was retained have recovered with conservative management and have fared well in the two years following primary surgery. In both revised cases, a degree of secondary osseointegration was noted.

The proposed mechanism has been explored using a simplified *in vitro* model of the bone-implant interface. With the caveats given in Section 8.3.4.2, the proposed mechanism has been demonstrated to be viable. Cases such as these appear to be rare: in over 3,000 cementless OUKRs implanted worldwide, these are the only cases which have come to the attention of the manufacturer or the designing centre. However, further investigation is necessary, and small modifications to the implant itself may be useful in preventing this phenomenon (see Section 8.3.4.3). In the meantime, a publication based on this work should assist surgeons in avoiding this problem, and should serve to ensure that such cases remain rare. As with any new implant, however, continued vigilance and monitoring using data from joint registries will ensure that further problems of this sort will be noted and addressed in a timely fashion.

Chapter 9 Cementless OUKR in the National Joint Registry

9.1. Introduction

As has been covered extensively in earlier chapters, a discrepancy exists between the high levels of implant survival achieved by high-volume UKR surgeons (and which are reported in the published literature), and the poor survival achieved by the wider population of surgeons and reported in NJRs. This discrepancy suggests that many of the factors explaining this unacceptably high reported revision rate are modifiable. The primary concern of this thesis has been the identification of those modifiable factors with the aim that, if they are addressed, the UKRs performed by the wider population of surgeons can achieve survival and functional results close to those reported by specialist centres.

In the first part of this thesis, important factors regarding selection for UKR, and the practice of UKR surgery have been explored. The second part has focussed upon modifications made to the implant itself to make fixation more reliable, with the aim of reducing the revision rate. In Chapters 6 and 7, the cementless implant was demonstrated to be reliable and safe with superior radiographic evidence of fixation compared to the existing, cemented implant. In Chapter 8, the rare complication of tibial subsidence was described and the aetiology and risk factors for it were delineated. The positive results of these studies raise the hope that the cementless OUKR has the potential to improve the long term survival of UKR, by providing more secure fixation, and by reducing the incidence of radiolucent lines, the misinterpretation of which can lead to unnecessary revisions.

However, the clinical studies of the cementless OUKR have largely taken place in the type of high-volume units which might be expected to achieve excellent results from the OUKR, regardless of the fixation method used. Notably, the entirety of patients in the RCT, and a fifth of the patients in the multi-centre study underwent their surgery in Oxford, which, as the designing centre, has published very good long-term survival from the cemented OUKR[13,98]. Having demonstrated the safety and effectiveness of the cementless implant in these centres, it remains to be seen whether this will translate to superior results in the National Joint Registry.

The aim of this chapter is to examine the early results of the cementless OUKR in the NJR, both in terms of implant survival and patient-reported outcome. Propensity-score matching, similar to that used in Chapters 3 and 4, will be used to create matched cohorts for comparison.

9.2. Methods

9.2.1. Data sources

As in previous analyses, the master database used in this chapter derives from the extract of 552,012 knee replacements extracted from the NJR in August 2012. Primary exclusions were made, data cleaning and outlier analysis was performed (see Chapter 2), and all UKRs were extracted from the database for analysis. At the time of the NJR extract in August 2012, and with permission of the manufacturer of the Oxford UKR, a second NJR extract was produced with detailed implant-level data on the OUKRs implanted. This second dataset contained serial numbers for every OUKR contained in the register. By cross-referencing these serial numbers with the published surgical technique manuals for the OUKR, the design phase, size and mode of fixation of all

OUKRs in the NJR were identified. These implant-level data were linked with the cleaned master database using NJR case-level identity codes.

9.2.2. Linkage

9.2.2.1. Survival analysis comparison

As the cementless OUKR was introduced in 2006 and only became widely available in 2008, the number of cementless OUKRs in the NJR was relatively small at the time of data extraction. Restriction of the analysis to operations recorded in the HES database reduces these numbers further (Figure 9-1).

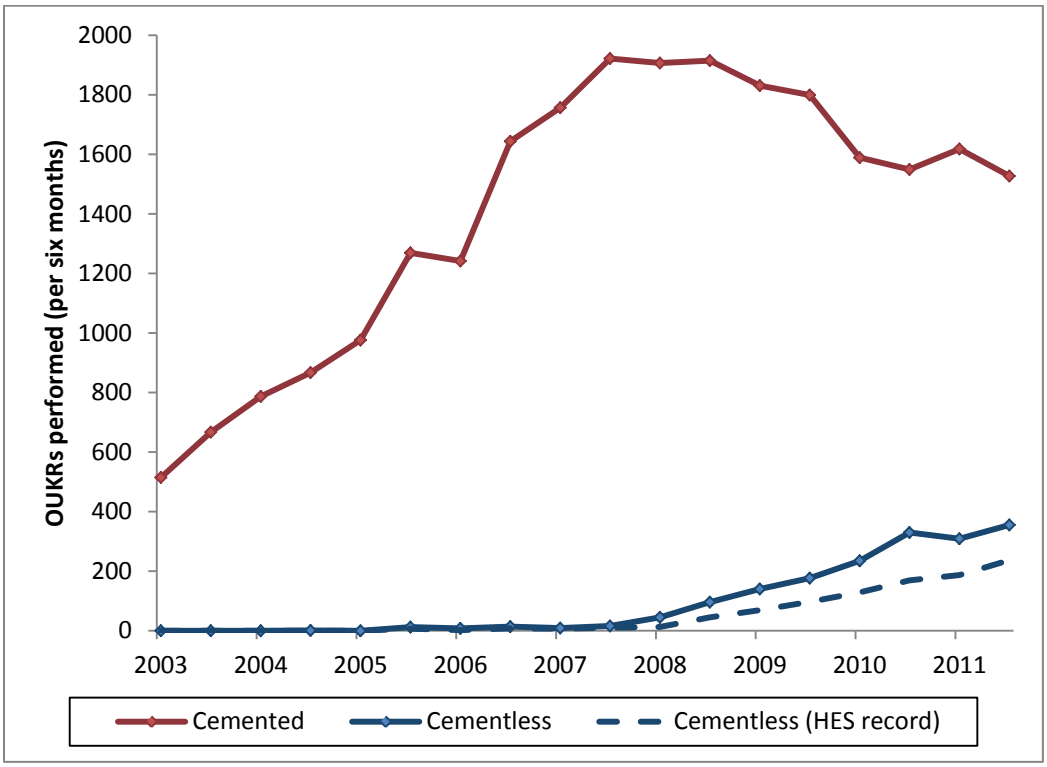


Figure 9-1: Numbers of cemented and cementless OUKRs recorded in the NJR

Restriction of the analysis to HES linked patients would reduce the potential for unmeasured confounding by including three extra variables, deprivation, ethnicity and Charlson co-morbidity index, but at the cost of sample size: of the 1,838 cementless OUKRs in the cohort, 1,041 (56%) had a linked HES record. The reduction in sample size

is particularly important given the relative rarity of revision in the short-term following knee replacement. To inform the decision of whether to restrict the analysis to HES records, the importance of each element was determined.

Firstly, a power calculation was undertaken using the method described by Schoenfeld for use with survival data[348]. Given the size of the sample, the minimum detectable effect size (expressed as a hazard ratio) was determined for an expected revision rate of 1% per year, given a power of 80% and a significance level of 0.05. The results are given in Table 9-1. Both datasets are relatively small and only large effect sizes would be detectable with either. However, the use of cementless fixation would have to more than halve the revision rate to be detectable using the smaller, NJR/HES linked dataset.

		NJR only	NJR/HES
Patient numbers	Knees	1,838	1,041
	Of which revised	29	16
Detectable difference (HR)		0.56	0.46

Table 9-1: Minimum detectable differences given sample sizes for cementless OUKR with and without HES linkage

Secondly, logistic regression was used to assess the extent to which differences in the three variables available in HES led to confounding by indication. All the available HES and NJR variables (as investigated in Chapter 4) were entered into the model. None of the three were determined to have a significant effect on treatment allocation (p values ranged from 0.56-0.73). On the basis of these two tests, the NJR dataset was used without the extra HES-linked fields.

Overall numbers were substantially smaller for the PROM comparison. Of the 1,838 cementless OUKRs in the NJR cohort, only 258 patients (14%) had complete PROM datasets. Again, a power calculation was performed, and on the basis of the means and standard deviations for six-month OKS in UKR as a whole (as determined in the crude

data given in Chapter 3), this sample size was sufficient to detect a difference of 2.4 points at six months with a power of 80% and a significance level set at 0.05.

9.2.3. Exposures

Using the implant-level NJR data described in Section 9.2.1, patients receiving OUKR were categorised on the basis of whether the implant was cemented or cementless. Hybrid OUKRs, where one component was cemented and the other cementless, were excluded from the analysis. Other exclusions were the same as those described in previous chapters, and included complex primary UKRs, and those performed for diagnoses other than osteoarthritis.

9.2.4. Outcomes

Both implant survival and patient-reported outcome were examined. Given the short amount of time that the cementless OUKR has been in use (shown in Figure 9-1), survival analysis for both cohorts was censored at three years. As in previous chapters, the reasons given for revision and the type of revision (simple or complex) were examined separately.

Patient-reported outcomes of interest included the OKS, the EQ5D (both overall and by domain) and patient-reported satisfaction level. These outcomes are explained in more detail in Chapter 3.

9.2.5. Confounders

The confounder information given in the NJR is reported in previous chapters. Given that more implant information was available than in the previous analyses, implant size (given as the size of the femoral component) and design of the tibial bearing (newer, 'anatomical' designs being less prone to dislocation) were included in the analysis. In addition, given that a large proportion of the cementless OUKRs were performed in

Oxford during the process of the implant's introduction, the Nuffield Orthopaedic Centre and the two allied private hospitals were identified using their unique NJR codes, and were entered into the model as a binary variable (i.e., performed in Oxford or elsewhere). BMI was excluded from the model due to the high level of missing data, and the fact that BMI has not been shown to be a significant predictor of revision or PROMs in any of the previous analyses of NJR datasets performed as part of this thesis.

9.2.6. Statistical analysis

Prior to matching, baseline values in each cohort were examined and compared (Table 9-2 and Table 9-3). Un-matched analyses were conducted to examine the survival and patient-reported outcome in the group as a whole. Separate propensity score matches were made for the survival comparison (using the entire population of patients) and the PROM comparison (using only those with PROM data); the techniques for propensity score matching are described in detail in Chapter 3. Following matching, univariable regression analyses (Cox and linear regression for the survival and prom outcomes respectively, and ordered logistic regression for the comparisons of satisfaction and individual EQ5D domains) were performed.

9.3. Results

9.3.1. Descriptive statistics

Following exclusions, 27,720 NJR records formed the study pool. Of these, 1,838 (6.6%) were cementless. Over a third of patients recorded as having had a cementless OUKR had their surgery in one of the Oxford hospitals (688/1,838, 37.4%), compared with only 5.9% of cemented OUKRs (1,534/25,882). Baseline values of the NJR dataset are given in

Table 9-2. 2,414/27,720 records could be linked to complete PROMs data; baseline values for this dataset are given in Table 9-3.

		Crude			Matched		
		Cemented	Cementless	Sig.	Cemented	Cementless	Sig.
Number of cases		25,882	1,838	-	3,666	1,222	-
Mean age at surgery (SD)		64.9 (9.4)	64.2 (9.9)	0.003	64.2 (9.6)	63.9 (9.8)	0.383
Gender (male)		13,568 (52.4%)	1,091 (59.4%)	<0.001	2,110 (57.6)	718 (58.7)	0.462
Unit type	Public Hospital	16,746 (64.7)	1,061 (57.7%)	<0.001	2,308 (63.0)	759 (62.1)	0.596
	Independent hospital	7,872 (30.4%)	775 (42.2%)	<0.001	1,349 (36.8)	461 (37.7)	0.561
	ISTC	1,264 (4.9%)	2 (0.1%)	<0.001	9 (0.25)	1 (0.16)	0.604
ASA score	1	6,152 (23.8%)	460 (25.0%)	0.222	826 (22.5)	286 (23.4)	0.528
	2	17,601 (68.0%)	1,218 (66.3%)	0.102	2,553 (69.6)	840 (68.7)	0.554
	3+	2,129 (8.2%)	160 (8.7%)	0.379	287 (7.8)	96 (7.9)	0.975
Cases performed by consultant		22,970 (88.8%)	1,652 (89.9%)	0.162	3,247 (88.6)	1,119 (91.6)	0.003
Mean cases / consultant per year (SD)		21.8 (21.4)	46.6 (40.4)	<0.001	30.5 (28.7)	31.7 (23.6)	0.187
Thromboprophylaxis – Chemical	Heparin / LMWH	14,771 (57.1%)	1,073 (58.4%)	0.134	2,151 (58.7)	671 (54.9)	0.021
	Aspirin	4,417 (17.1%)	453 (24.7%)	<0.001	692 (18.9)	278 (22.8)	0.003
	Warfarin	258 (1%)	14 (0.8%)	0.410	34 (0.9)	11 (0.9)	0.931
	Direct Thrombin Inhibitor	870 (3.4%)	98 (5.3%)	<0.001	269 (7.3)	89 (7.3)	0.949
	Other	1,569 (6.1%)	104 (5.7%)	0.836	283 (7.7)	100 (8.2)	0.601
	None/unspecified	3,997 (15.4%)	96 (5.2%)	<0.001	237 (6.5)	73 (6.0)	0.542
Thromboprophylaxis – Mechanical	TEDS	16,895 (65.3%)	1,649 (89.7%)	<0.001	3,077 (83.9)	1,040 (85.1)	0.330
	Foot/calf compression	6,218 (24.0%)	151 (8.2%)	<0.001	471 (12.9)	147 (12.0)	0.750
	Other	204 (0.8%)	17 (0.9%)	0.475	76 (2.1)	20 (1.6)	0.818
	None/unspecified	2,565 (9.9%)	21 (1.1%)	<0.001	42 (1.2)	15 (1.2)	0.342
Femoral Size	XS / S	5,563 (21.5%)	471 (25.6%)	<0.001	869 (23.7)	287 (23.5)	0.876
	M	14,107 (54.2%)	832 (45.3%)	<0.001	1,819 (49.6)	612 (50.1)	0.779
	L / XL	6,302 (24.4%)	535 (29.1%)	<0.001	978 (26.7)	323 (26.4)	0.866
Bearing design (number 'anatomical')		12,910 (50.7%)	1,594 (87.5%)	<0.001	3,003 (81.9)	998 (81.7)	0.847
Case performed in Oxford		1,534 (5.9%)	688 (37.4%)	<0.001	669 (18.3)	204 (16.7)	0.219

Table 9-2: Baseline variables in cemented and cementless OUKR (NJR dataset)

			Crude			Matched		
			Cemented	Cementles	Sig.	Cemented	Cementless	Sig.
Number of cases			2,156	258	-			-
Mean age at surgery (SD)			64.6 (8.9)	63.6 (9.3)	0.123	64.2 (9.3)	63.7 (8.8)	0.556
Gender (male)			1,138 (52.8)	154 (59.7)	0.019	230 (57.2%)	78 (58.2%)	0.488
Unit type		Public Hospital	1,620 (75.1)	208 (80.6)	0.076	312 (77.6)	89 (66.4)	0.080
		Independent hospital	432 (20.0)	50 (19.4)	0.911	59 (14.7)	45 (33.6)	<0.001
		ISTC	104 (4.8)	0 (0.0)	-	31 (7.7)	0 (0.0)	-
ASA score		1	470 (21.8)	64 (24.8)	0.377	97 (24.1)	30 (22.4)	0.988
		2	1,525 (70.7)	173 (67.1)	0.293	278 (69.2)	92 (68.7)	0.754
		3+	161 (7.5)	21 (8.1)	0.630	27 (6.7)	12 (9.0)	0.586
Cases performed by consultant			1,896 (87.9)	214 (83.0)	0.023	353 (87.8)	114 (85.1)	0.425
Mean cases per consultant per year (SD)			23.4 (21.7)	41.9 (29.1)	<0.001	26.4 (22.1)	28.3 (15.9)	0.005
Thromboprophylaxis	Chemical	Unfractionated/LMW heparin	1,373 (63.7)	168 (65.1)	0.607	257 (63.9)	84 (62.7)	0.849
		Aspirin	196 (9.1)	48 (18.6)	<0.001	42 (10.5)	15 (11.2)	0.419
		Warfarin	21 (1.0)	2 (0.8)	0.755	2 (0.5)	2 (1.5)	0.738
		Direct Thrombin Inhibitor	160 (7.4)	25 (9.7)	0.181	25 (6.2)	21 (15.7)	0.001
		Other	9 (3.5)	247 (11.5)	<0.001	54 (13.4)	6 (4.5)	0.003
		None/unspecified	159 (7.4)	6 (2.3)	0.005	22 (5.5)	6 (4.5)	0.455
	Mechanical	TEDS	1,404 (65.1)	232 (89.9)	<0.001	343 (85.3)	109 (81.3)	0.079
		Intermittent calf compression	623 (28.9)	20 (7.8)	<0.001	56 (13.9)	19 (14.2)	0.449
		Other	7 (0.3)	5 (1.9)	0.002	1 (0.2)	5 (3.7)	0.013
		None/unspecified	122 (5.7)	1 (0.4)	0.006	2 (0.5)	1 (0.8)	0.738
Femur size		XS / S	460 (21.3)	70 (27.1)	0.099	92 (22.9)	36 (26.9)	0.737
		M	1,221 (56.6)	109 (42.3)	<0.001	226 (56.2)	63 (47.0)	0.241
		L / XL	475 (22.0)	79 (30.6)	0.001	84 (20.9)	35 (26.1)	0.289
Bearing design (number 'anatomical')			1,715 (79.6)	229 (88.8)	<0.001	327 (81.3)	105 (78.4)	0.934
Pre-op EQ5D (SD)			0.495 (0.286)	0.464 (0.283)	0.100	0.493 (0.286)	0.486 (0.280)	0.747
EQ5D anxiety score		1	1,495 (69.3)	197 (76.4)	0.021	275 (68.4)	98 (73.1)	0.613
		2	602 (27.9)	56 (21.7)	0.038	122 (30.4)	32 (23.9)	0.352
		3	59 (2.7)	5 (1.9)	0.544	5 (1.2)	4 (3.0)	0.186
EQ5D VAS			71.6 (18.8)	73.4 (16.9)	0.142	73.0 (18.0)	74.1 (15.8)	0.643
Pre-op OKS			22.0 (7.5)	21.7 (7.8)	0.546	21.9 (7.5)	22.3 (8.1)	0.583
Admitted from own home			2,151 (99.8)	257 (99.6)	0.493	401 (99.8)	133 (99.3)	0.412
Patient-reported disability			872 (40.5)	110 (42.6)	0.503	175 (43.5)	51 (38.1)	0.677

Table 9-3: Baseline variables: linked NJR-PROM records

9.3.2. Survival comparison

In un-matched patients at three years, overall implant survival was 95.9% (95% CI 95.7%-96.2%). Survival was 97.3% (95% CI 95.8-98.2) in the cementless group and 95.9%

(95% CI 95.6-96.2%) in the cemented group, giving a hazard ratio of 1.33 for revision in cemented fixation compared to cementless (95% CI 0.91-1.93, p=0.14). The cementless OUKR appears to have a slightly higher revision rate in the very short term when compared to the cemented OUKR, but the survival hazard appears to plateau for the cementless device whilst the hazard ratio for the cemented device appears to continue declining. This may simply reflect the small numbers of patients at longer follow-up times in the cementless group.

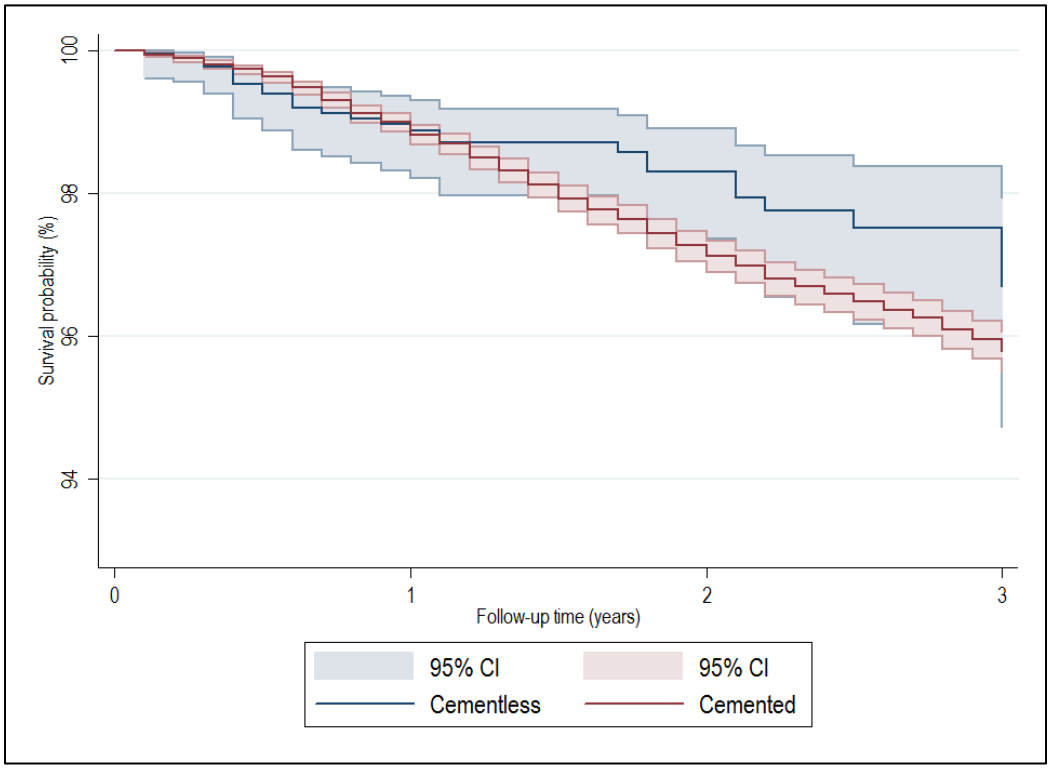


Figure 9-2: Unadjusted survival comparison for cemented and cementless OUKR

1,222 of the 1,838 cementless OUKRs were successfully matched to cemented UKRs using propensity scores. At three years, overall implant survival was 96.2% (95% CI 96.1-97.6). Survival was 96.7% (95.0-97.9) in the cementless group compared to 97.0% (96.1-97.7) in the cemented group. Again, there appeared to be a slight preponderance to early failure in the cementless group, but the difference had disappeared by the end of the

second year (Figure 9-3). The overall hazard ratio for revision was 0.80 (0.50-1.27, p=0.343), exhibiting a slight trend towards cemented fixation.

Revision reasons were compared in the matched groups (Table 9-4). As the number of revised patients was small, no statistically-significant differences could be discerned between the groups. However, whilst there did not appear to be a difference between the groups in terms of incidence of periprosthetic fracture or loosening, there was a trend to higher rates of failure due to pain and osteoarthritis progression in the cemented group.

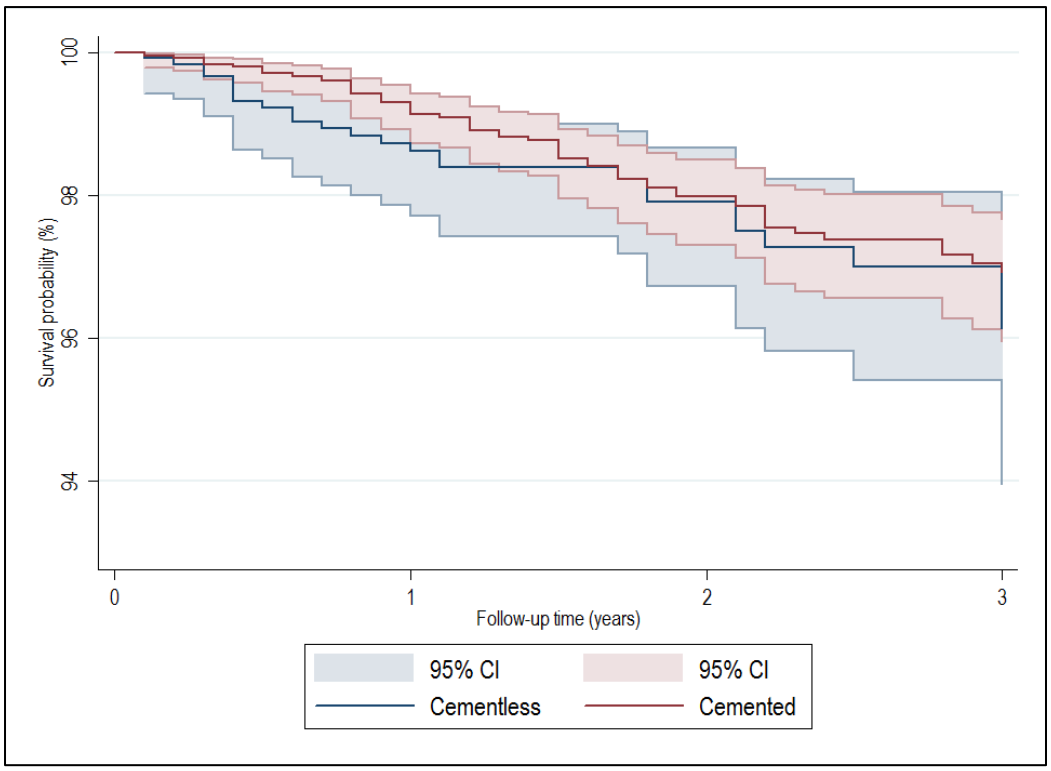


Figure 9-3: Kaplan-Meier plot: matched analysis of cemented and cementless OUKR

Reason	Cemented	Cementless	OR	Sig.
Loosening/lysis	15 (25%)	6 (22.2%)	1.17 (0.40-3.43)	0.78
Progression of disease	9 (15.0%)	2 (7.4%)	2.21 (0.44-10.98)	0.33
Pain	10 (16.7%)	2 (7.4%)	2.5 (0.51-12.29)	0.32
Other	9 (15.0%)	2 (7.4%)	1.01 (0.28-3.64)	0.98
Dislocation	8 (13.3%)	5 (18.5%)	0.68 (0.20-2.30)	0.53
Infection	3 (5.0%)	2 (7.4%)	0.67 (0.10-4.18)	0.66
Malalignment	2 (3.3%)	3 (11.1%)	0.27 (0.04-1.76)	0.17
Instability	1 (1.7%)	1 (3.7%)	0.44 (0.03-7.32)	0.87
Peri-prosthetic fracture	2 (3.3%)	1 (3.7%)	0.90 (0.08-10.33)	0.93
Stiffness	1 (1.7%)	0 (0.0%)	-	
Wear	0 (0.0%)	1 (3.7%)	-	

Table 9-4: Reasons for revision by fixation in OUKR (matched patients)
Odds ratios above 1 indicate trend to higher revision for the given reason in cemented fixation

Four periprosthetic fractures occurred during the initial cementless series reported in Chapter 7. The reasons for revision (Table 9-4) show no difference in the rate of fracture in cemented and cementless OUKR. Most fractures occur during surgery and may be recorded as adverse intra-operative events, rather than revisions; however, there is no difference in the rate of adverse events between the two implants either (Table 9-5).

Adverse event	Cemented	Cementless
Fracture	4 (0.1%)	1 (0.1%)
Patellar Tendon Avulsion	0 (0.0%)	1 (0.1%)
Ligament injury	3 (0.1%)	0 (0.0%)
Other	5 (0.1%)	1 (0.1%)

Table 9-5: Adverse events in cemented and cementless OUKR

9.3.3. Patient-reported outcome measure comparison

Overall, the mean OKS increased from 22.0 (SD 7.6) to 37.9 (9.4). In the crude analysis, the pre-operative OKS was lower, and the six month OKS was higher, in the cementless group compared to the cemented group. In the cementless group, the OKS increased from 21.7 (7.8) to 39.7 (8.7), whilst in the cemented group, it increased from 22.0 (7.5) to 37.7 (9.4).

134 of the 258 patients with cementless OUKRs and complete PROM records were matchable to corresponding cemented patients. In matched patients, the mean OKS was 40.2 (95% CI 38.8-41.5) in the cementless group, compared to 37.9 (95% CI 37.0-38.8) in the cemented group, a statistically significant difference (p=0.012). Similarly, a statistically significant difference was determined in the overall EQ5D index; whilst there was a trend towards superior EQ5D VAS scores, this was of borderline significance (Table 9-6).

		Mean pre-op score (±95% CI)	Mean post-op score (±95% CI)	Significance
OKS	Cemented	21.9 (21.2-22.7)	37.9 (37.0-38.8)	0.012
	Cementless	22.3 (20.9-23.7)	40.2 (38.8-41.5)	
EQ5D	Cemented	0.493 (0.465-0.521)	0.777 (0.753-0.801)	0.029
	Cementless	0.486 (0.438-0.554)	0.827 (0.797-0.857)	
EQ5D VAS	Cemented	73.0 (71.2-74.8)	76.3 (74.6-78.1)	0.061
	Cementless	74.1 (71.4-76.8)	79.6 (77.0-82.1)	

Table 9-6: Overall matched results by fixation method

As in previous analyses, the individual subscales of the EQ5D were examined individually in addition to the overall index. These are presented in Table 9-7. Significance values are estimated using ordered logistic regression. Whilst there was a trend to improved scores in all domains towards cementless fixation, the strongest effect (that of pain/discomfort) reached only borderline significance at p=0.058.

Domain	Difficulty level	Cemented	Cementess	Significance
Mobility	None	243 (60.4)	93 (69.4)	0.064
	Moderate	159 (39.5)	41 (30.6)	
	Severe	0 (0.0)	0 (0.0)	
Self-care	None	361 (89.8)	125 (93.3)	0.231
	Moderate	40 (10.0)	9 (6.7)	
	Severe	1 (0.25)	0 (0.0)	
Ability to undertake usual activities	None	233 (58.0)	89 (66.4)	0.074
	Moderate	157 (39.1)	43 (32.1)	
	Severe	12 (3.0)	2 (1.5)	
Pain / discomfort	None	178 (44.3)	70 (52.2)	0.058
	Moderate	206 (51.2)	63 (47.0)	
	Severe	18 (4.5)	1 (0.8)	
Anxiety / depression	None	318 (79.1)	113 (84.3)	0.183
	Moderate	78 (19.4)	20 (14.9)	
	Severe	6 (1.5)	1 (0.8)	

Table 9-7: Individual EQ5D domains by fixation

9.4. Discussion

9.4.1. Summary of results

This study has provided further evidence of superior performance of the cementless OUKR over the cemented OUKR in terms of patient-reported outcome, in addition to the significant difference (in a single metric) demonstrated in Chapter 6. No significant difference has been detected between the two prostheses in terms of implant survival; however, the number of patients analysed in this study was small, and the follow-up was short; further studies are necessary to detect whether there is a difference in survival between the two implants.

The matched analysis supports the findings of the multicentre study in Chapter 7, that the cementless OUKR is a safe and effective alternative to the cemented implant. Un-matched survival comparisons from Australia and New Zealand (Appendix 4) also suggest that survival of the two prostheses is at least equivalent. Unlike the data from

the AOANJRR, there is no evidence of a high rate of peri-prosthetic fracture in the cementless OUKR in England and Wales. Both this study and the data from Australia show a slightly higher revision rate in the very short term for the cementless prosthesis. In both cases, this disappears by the end of the first year. This may reflect revisions of cases such as those described in Chapter 8; improved understanding of those cases, with or without small modifications to implant design, may improve those short term figures.

A striking feature of this analysis is the good survival overall compared to that given in NJR annual reports. Part of the reason for this is the restriction of the analysis to a single device – whilst the NJR annual report gives a three-year survival figure of 95.4% for UKR overall, it gives a figure of 95.8% for the OUKR, which is close to the unadjusted figure reported here of 95.9%. However, following matching, three-year survival is 96.2%. The reason for this is apparent in Table 9-2: whilst the mean baseline number of cases per year for the cemented OUKR is 21.8, the mean number of cases per year for the cementless OUKR is 46.6, supporting the assertion that the early adopters of the cementless device were likely to be higher-volume surgeons (including those from the designing centre). During the matching process, these differences are attenuated by dropping the higher-volume cementless surgeons, as well as the lower-volume cemented surgeons. The result of this is that the number of cases per year, whilst similar in each group following matching, is substantially higher than observed in the general population; indeed, the mean number of cases per year is over the 30 case threshold for high use suggested in Chapter 5. Similarly, around a sixth of all cases in each group were performed in Oxford. As a result, it is not surprising that the overall survival is higher than expected for both implants, and neither is it surprising that little difference is detectable between the two implants, as excellent results can be expected from either fixation method in experienced hands (see Section 1.9.2 and Chapter 5).

These factors make the differences observed in patient-reported outcome more surprising. Even amongst surgeons expected to achieve very good results from UKR, a difference of over two points on the OKS is observed, with a commensurate difference in general quality of life as measured using the EQ5D. Whilst the numbers are small and only borderline significance is attained, the 'discomfort' domain of the EQ5D is lower in the cementless implant than the cemented implant; there is a similar difference in the number of patients revised for unexplained pain in the survival comparison. Along with the higher KSS functional scores reported in the RCT in Chapter 6, this study provides additional evidence that the use of the cementless UKR produces superior patient-reported outcomes, particularly in terms of pain.

9.4.2. Limitations and future work

In the context of registry studies, the number of patients in this study is relatively small. Whilst the numbers are much smaller in the PROM comparison than the survival comparison, survival analysis is particularly sensitive to small numbers given the relative rarity of revision. With the numbers included in this study, only a very large difference in survival (a hazard ratio of around 0.5) would be detectable. Likewise, the survival analysis in this study is only in the short term.

These limitations can be addressed by performing larger studies with longer follow-up. A study using patient-level data from Australia and New Zealand (unadjusted data from each have been summarised in the Appendix 4) would give a much more sensitive comparison of survival in the short (3-5 year) term. The number of cementless OUKRs being implanted each year is increasing in all three countries; therefore, it will not be very long before longer-term follow-up is available on a sizeable cohort of patients.

The second main limitation of this study relates to the surgeons performing the cementless procedure. As discussed in Section 9.4.1, the early adopters of the cementless prosthesis have tended to be higher-volume surgeons, and a large proportion of cementless OUKRs have been implanted in the designing centre in Oxford. This limits the external validity of the findings of this study. As there is less variation amongst high-volume surgeons with respect to revision rate, it also reduces the likelihood of determining a difference in revision rate between the two implants. Again, examination of data from Australia and New Zealand will improve this in part, by diluting the effect of the designer centre on the overall results, but until the cementless implant is used by a larger cohort of surgeons it will be difficult to determine the relative revision rates of each.

Chapter 10 Discussion

10.1. Summary of findings

The work within this thesis has provided important insights into the patterns and determinants of failure in unicompartmental knee replacement. It is hoped that dissemination of the findings of this thesis can change the practice of those performing UKR. If more UKR surgeons adopt the practices demonstrated to improve outcome, this will lead to a greater overall survival for patients undergoing UKR, and will allow more patients to benefit from the advantages of UKR, in terms of function, morbidity and mortality.

10.1.1. Part one: mechanisms of failure in UKR and TKR

The study presented in Chapter 3 represents the largest matched study of patients undergoing TKR and UKR. Both UKR and TKR are demonstrated to be highly effective procedures in relieving the pain of osteoarthritis and restoring function. Whilst TKR was revised less frequently than UKR, UKR was demonstrated to have a significantly lower level of perioperative morbidity and mortality, a significantly shorter associated inpatient stay, and significantly superior patient-reported outcomes and satisfaction levels. The differences between the two were particularly marked at the very best outcomes: the odds ratio of attaining a six month OKS above 41 was 1.6 for UKR. From this study, it was concluded that, even after matching for differences in patient factors, UKR had significant advantages over TKR. However, the revision rate for UKR remains significantly higher than that of TKR; as a result, far fewer patients than are eligible receive UKR and benefit from the advantages demonstrated in Chapter 3. The remainder of this thesis is concerned with identifying the factors associated with poor outcomes

and revision, with a view to addressing these problems and reducing the revision rate to an acceptable level.

In Chapter 4, a number of surgical- and patient-factors associated with revision and poor functional outcome are identified. Of particular interest is the finding that older patients, who are least likely to be offered UKR, are those who stand to benefit the most from receiving it. Young patients with very poor pre-operative scores are particularly at risk of poor functional improvement after UKR and should be treated with caution. Cases performed by a consultant, and those performed in high-volume units, were observed to fare particularly well. Whilst men are significantly more likely to be revised following TKR, this is not the case in UKR; in fact, men are less likely to be revised than women, although the difference is small. No justification is provided for restricting access to UKR on the basis of ASA grade or body mass index; similarly, other predictors of poor outcome, including ethnicity, deprivation and pre-operative anxiety, exert a similar effect in TKR.

In Chapter 5, the effect of surgical caseload was examined further. Surgical caseload (the number of cases performed per surgeon, per year) was demonstrated to exert a strong effect on both revision rate and patient-reported outcome. The revision rate did not reach a plateau until more than thirty cases were performed each year. Such high-volume surgeons were demonstrated to have revision/reoperation rates similar to those achieved in comparable patients undergoing TKR.

As surgeons are unable to change the population of patients presenting to them for knee replacement, it was observed that the main mechanism that surgeons have for increasing their caseload is broadening their indications for UKR, offering UKR to a greater proportion of their patients. The viability of this approach was explored by examining

the effect of surgical usage of UKR (i.e., the proportion of all knee replacements performed that are UKRs). It was found that revision rates were lowest when around 50% of all knee replacements by each given surgeon are UKRs. Surgeons with usage in the optimal range (40-60%) were demonstrated to achieve similar revision/reoperation rates to those observed in matched patients undergoing TKR.

10.1.2. Part two: fixation in unicompartmental knee replacement

Throughout the first Part, and in common with other reports from joint registries, aseptic loosening was demonstrated to be the most common reason for revision in UKR. It was observed that series from high-volume units report very low numbers of patients failing by this mechanism and that fixation represents an important target for interventions to reduce the revision rate of UKR. Reasons for the high rate of revision for aseptic loosening may include inadequate cementation technique, impingement from retained cement fragments, and misinterpretation of radiolucent lines (which are commonly seen adjacent to cemented UKRs) as indicating loosening. Many of these problems may be attributable to cement and cementation technique, and elimination of the need for cement may largely address the problem of loosening. As such, a number of studies were undertaken to assess the viability of cementless fixation in UKR.

In Chapter 6, a randomised controlled trial was reported, comparing radiological and clinical outcomes of cemented and cementless Oxford UKR. The cementless OUKR was demonstrated to be associated with a lower incidence of radiolucencies, and equivalent or improved functional outcomes, at five years. In Chapter 7, a much larger, multi-centre study was conducted to assess the safety and effectiveness of the cementless implant, and to identify any contra-indications to cementless fixation. A cohort of 1,000 patients underwent cementless OUKR in three institutions, and were assessed at a minimum of one year of follow-up. In common with the RCT, the proportion of patients with a

radiolucency was very low compared to that expected following cemented OUKR (a partial radiolucency was observed in 8.9% of patients), and no implant was found to be loose or associated with a complete radiolucency. In patients suitable for UKR, no contra-indications to cementless OUKR were identified; the incidence of complications and revision surgery were similar to that reported in previous studies of cemented OUKR.

In the multi-centre study in Chapter 7, three cases were observed to subside into a position of slight valgus within the first postoperative year. Whilst all were asymptomatic, these appearances have only rarely been observed in the cemented OUKR; in Chapter 8, these cases were explored further. A series of six similar cases was described. Whilst two had been revised in the early postoperative period, the un-revised patients were observed to stabilise, becoming well-fixed and asymptomatic.

A mechanism was proposed which involved impingement of the tibial bearing onto the lateral wall of the tibial implant in deep flexion, before full osseointegration had occurred. This hypothesis was tested using a simplified *in vitro* model of tibial loading. During normal loading, pressures remained equal medial and lateral to the tibial keel and the centre of pressure remained within the central part of the implant. However, impingement against the lateral wall was observed to generate high pressures under the posterolateral corner of the implant, resulting in valgus subsidence in the same pattern as observed in the cases described.

Having demonstrated the safety and effectiveness of the cementless prosthesis in the two clinical studies, and explored a possible mechanism of early failure in Chapter 8, the final study compared cemented and cementless OUKR using national data. Matched cohorts were assembled using the same propensity-score techniques as used in Chapters

3 and 5, and the two implants were compared in terms of implant survival and patient-reported outcome. Whilst the sample size was small and the follow-up short, patients receiving the cementless implant demonstrated significantly superior patient-reported outcomes at six months, with equivalent survival up to three years following surgery.

10.2. Limitations and future work

The aim of this work was to understand the factors leading to failure after UKR and to investigate mechanisms by which these factors could be modified. This is a large subject and can only be covered in part by a doctoral thesis: much work remains to be done. The first part of this work has focussed on large, national-level datasets and as such, whilst it can provide an accurate overall picture of the factors affecting outcome in UKR, it cannot provide information on individual cases or surgeons. Future work should investigate the technical factors predisposing to failure by examining radiographs of failing and non-failing patients. It may be that experience and usage (as explored in Chapter 5) are simply surrogates for technical skill. A greater understanding of the technical errors predisposing to failure would allow improvement in training of new surgeons and may improve outcomes further.

An alternative tactic would be to examine and target the different mechanisms of failure. For example, whilst loosening appears to be very dependent on experience, progression of disease appears to occur as often in high-volume surgeons as it does in national registries. It may be that some reasons for revision may be improved as a result of the work contained in this thesis, but that others require further work to be understood. For instance, a study of the pre-operative histological and radiological appearances of patients undergoing UKR may identify patients more at risk of arthritis progression.

As covered in Section 1.13, this work was performed in a unit well-known for research into UKR. The principal supervisor was on the design team of the most widely-used UKR and both he and the unit where this work was performed receive funding from the manufacturer of this prosthesis, Biomet. Such issues are difficult to avoid in a sector where industrial funding is widespread and charitable or other funding sources are very limited; the author is confident that the work presented here has been conducted independently of these relationships. However, whilst many units and studies are affected by similar issues, research is always interpreted in the light of those who fund it. It is helpful that the subjects covered in this thesis are of widespread interest and other groups have corroborated some parts of the work presented here. In the longer term, the orthopaedic community as a whole needs to determine how to best use industrial sources to fund research whilst avoiding these issues. By the same token, other streams of research funding, independent of industry, must be maximised.

10.2.1. Part one: mechanisms of failure in UKR and TKR

This Part, and indeed the whole work, is built on the basis of large, observational datasets. The size of the study cohorts allows detailed investigation of multiple variables whilst retaining the sample size and statistical power to allow meaningful comparisons. The use of observational datasets also suggests that the external validity of the study is likely to be high; the diversity of the patients, surgeons and units studied reflects the overall use of TKR and UKR in England and Wales.

Having said that, observational study designs suffer from a number of drawbacks. Whilst all recorded confounders were included in the models given in Chapters 3, 4, 5, and 9, there is a high likelihood of unmeasured confounding. Unmeasured confounders include patient factors (such as degree of pre-operative activity, and pre-operative expectations); factors related to disease (such as the ACL status, the presence of

patellofemoral disease, or previous non-arthroplasty surgical procedures); factors related to the surgery (detailed prosthesis brand and model information was not available); and factors related to the surgeon (such as their place on the learning curve, or their threshold for revising poorly-functioning implants). Whilst many of these are unlikely to have made a material impact on the outcomes described, some are potentially important.

The most important unmeasured confounder is likely to be disease status. Joint replacement for partial thickness disease has a very poor outcome, and it has been suggested that such patients are more likely to receive UKR than TKR as it is a less invasive procedure[69]. Even in the single-group comparisons (of patient factors in Chapter 4, and surgical caseload and usage in Chapter 5), the influence of disease state may be important. It is plausible that lower-volume surgeons may favour UKR in young patients with partial-thickness disease, considering it a temporary solution until TKR is indicated at a later age. Likewise, the poor results reported for young patients with severe pre-operative symptoms (Chapter 4) may represent a group of patients with partial thickness disease but severe symptoms from other, undiagnosed, sources. This may be addressed as part of future work, which may involve the analysis of pre-operative, post-operative and pre-revision radiographs from revised UKRs to determine the effect of pre-operative disease stage, surgical technique, and revision diagnosis.

Another source of unmeasured confounding due to disease status concerns the eligibility of patients for UKR. Using registry data, it is not possible to define whether patients receiving TKR would have been suitable for UKR. Whilst one can be sure that a large proportion of the patients studied would have been suitable for either procedure, at least 50% of patients undergoing TKR are likely to have disease which is considered unsuitable for UKR[66]. The extent to which this affects the outcomes observed is not clear. In the propensity-score calculations, patients were matched on pre-operative symptom

severity (using the OKS and EQ5D), as well as multiple demographic covariates. It appears unlikely that a patient with unicompartmental disease, and an intact ACL, will fare substantially differently following TKR than one with tricompartmental disease of equal severity. However, to assess the relative results of TKR and UKR in patients eligible for both, either observational studies with detailed pre-operative radiographic information or a large RCT is needed. Of these, the latter would appear to be more feasible, and indeed, such an RCT is currently in progress[292].

The PROM data presented here is only in the short term, and it is not clear how these change over the lifetime of a knee replacement, or how they affect revision risk. Short-term PROMs may represent a suitable surrogate for revision into the medium-long term, and this is an aspect which should be explored. In the same way, study of the natural history of PROMs following TKR and UKR over the lifetime of the prosthesis would provide further insights. As the PROM dataset becomes more mature, the proportion of patients excluded due to issues with data quality (missing pre- or post-operative questionnaires, for instance) should improve.

Another unexplored area concerns the relative cost-effectiveness of TKR and UKR. The datasets used in this thesis contain most of the data required to produce a detailed cost-effectiveness analysis of the two procedures, which would be a great deal more comprehensive than those previously produced. Further information on the relative cost-effectiveness of the two procedures would further inform the decision-making of surgeons when deciding which procedure to offer their patients.

Whilst surgical usage and caseload have been studied extensively in this thesis, the datasets used provide little information about the true learning curve for UKR. To address this, it would be helpful to study surgeons performing UKR for the first time, to

determine how many cases are needed before competence is achieved, and whether there are any specific factors concerning surgical training which need to be improved.

10.2.2. Part two: fixation in unicompartmental knee replacement

The limitations of the second Part of the thesis largely concern external validity. Both of the clinical studies were conducted entirely, or in part, in large units with great expertise in UKR. This has different effects depending on the study. In Chapter 7, the survival and PROM outcomes reported may be superior to that which may be expected in the general population; by the same token, complication rates may be underestimated due to the expertise of the surgeons performing the surgery. The opposite effect is observed in Chapter 6: the likelihood of a difference in survival or function is reduced as both cemented and cementless cases are performed by highly-experienced surgeons who may expect to attain excellent results with either fixation method.

It is this effect that encouraged the NJR-based study in Chapter 9 to be undertaken. However, even outside those contributing to the clinical studies, the early adopters of cementless OUKR have tended to be experienced surgeons who are familiar with the cemented OUKR (as demonstrated by the high values observed for surgical caseload in the cementless group). As a result, the external validity of this study may again be called into question. Unfortunately, this poses a quandary for those tasked with introducing the cementless OUKR. Whilst one may be reluctant to encourage less experienced surgeons to switch to cementless OUKR in the absence of clear evidence of safety and reproducibility in inexperienced hands, such evidence is impossible to accrue without such surgeons switching. In an ideal world, the introduction of the cementless OUKR would be accompanied by a change in the general use of UKR to reflect the findings of Chapters 4 and 5. In the meantime, a detailed analysis of data from other joint registries (as suggested in Section 9.4.2) will go some way to providing support for less

experienced surgeons who wish to switch to cementless fixation. After all, it is less experienced surgeons for whom the cementless implant was designed, and it is less-experienced surgeons (who have the poorest outcomes from UKR) who stand to benefit the most from the cementless OUKR.

The studies presented in Chapter 8 represent a more detailed examination of fixation in cementless OUKR. The six patients presented in Chapter 8 represent all such patients who have come to the attention of the manufacturers of the OUKR. However, this series cannot be assumed to be exhaustive; to know the true incidence of such appearances, radiographs of the population of cementless OUKRs would have to be examined. Those patients who have not undergone revision have a minimum follow-up of two years, and their long-term outcomes remain unknown; they continue to be followed-up. Likewise, the quality of the fixation achieved in cementless OUKR cannot be estimated accurately without retrieval analyses of the bone-implant interface.

The mechanical study presented in Chapter 8 is a very simplified model, and limitations are discussed in detail in the Chapter itself. Future studies should attempt to more completely recreate anatomy, particularly in terms of the lateral buttress of bone and the presence of a cortex. As discussed in Section 8.3.4.3, modifications to the prosthesis itself may be useful in avoiding this type of case, and future studies may be useful in examining such modifications. Finally, a retrieval study examining revised cementless implants may be helpful in understanding the quality of fixation in cementless OUKR.

10.3. Conclusions

- Unicompartmental Knee Replacement has been demonstrated to have clear and important advantages over TKR in terms of morbidity, mortality and post-operative function.
- Important factors, in terms of patient selection and surgical practice, have been identified to reduce the revision rate to an acceptable level so that more patients can benefit from these advantages whilst minimizing the chance of undergoing revision.
- Surgical caseload has been demonstrated to have an important effect on the revision rate and patient-reported outcome of UKR. Surgeons can improve their caseload by increasing their UKR usage: surgeons with usage in the optimal range, around 50% of cases, can achieve revision/reoperation rates similar to those achieved in matched patients undergoing TKR.
- The cementless OUKR has been demonstrated to provide superior fixation when compared to the cemented OUKR, with a similar rate of complications in the short term. The technical aspects leading to suboptimal fixation in cementless OUKR have been identified. Early results from the NJR have demonstrated superior patient-reported outcomes in cementless OUKR, with similar implant survival in the first three postoperative years.

Appendices

Appendix 1: Publications associated with this thesis

Liddle AD, Judge A, Pandit H, Murray DW. Adverse outcomes after total and unicompartmental knee replacement: a study of 101,330 patients from the National Joint Registry for England and Wales. *Lancet 2014; published online ahead of print.*

Liddle AD, Judge A, Pandit H, Murray DW. Determinants of revision and functional outcome following unicompartmental knee replacement. *Osteoarthritis and Cartilage 2014; published online ahead of print.*

Liddle AD, Pandit H, Jenkins C, Lobenhoffer P, Jackson WFM, Dodd CAF, Murray DW. Valgus subsidence of cementless Oxford Unicompartmental Knee Replacement. *Bone Joint J 2014;96-3:338-42*

Pandit H, Liddle AD, Kendrick BJ, Jenkins C, Price AJ, Gill HS, Dodd CA, Murray DW. Improved fixation in cementless unicompartmental knee replacement: five-year results of a randomized controlled trial. *J Bone Joint Surg Am 2013;95-15:1365-72.*

Liddle AD, Pegg EC, Pandit H. Knee replacement for osteoarthritis. *Maturitas 2013;75-2:131-6.*

Liddle AD, Pandit H, O'Brien S, Doran E, Penny ID, Hooper GJ, Burn PJ, Dodd CA, Beverland DE, Maxwell AR, Murray DW. Cementless fixation in Oxford unicompartmental knee replacement: A multicentre study of 1,000 knees. *Bone Joint J 2013;95-B-2:181-7.*

Liddle AD, Pandit H, Murray DW, Dodd CA. Cementless unicondylar knee arthroplasty. *Orthop Clin North Am 2013;44-3:261-9.*

Liddle AD, Pandit H, Jenkins C, Price AJ, Dodd CA, Gill HS, Murray DW. Preoperative pain location is a poor predictor of outcome after Oxford unicompartmental knee arthroplasty at 1 and 5 years. *Knee Surg Sports Traumatol Arthrosc 2013;21-11:2421-6.*

Liddle AD, Pandit H, Murray DW, Dodd CAF. Unicompartmental knee arthroplasty: state of the art and future developments. *Archivio di Ortopedia e Reumatologia 2012;123-3:31-3.*

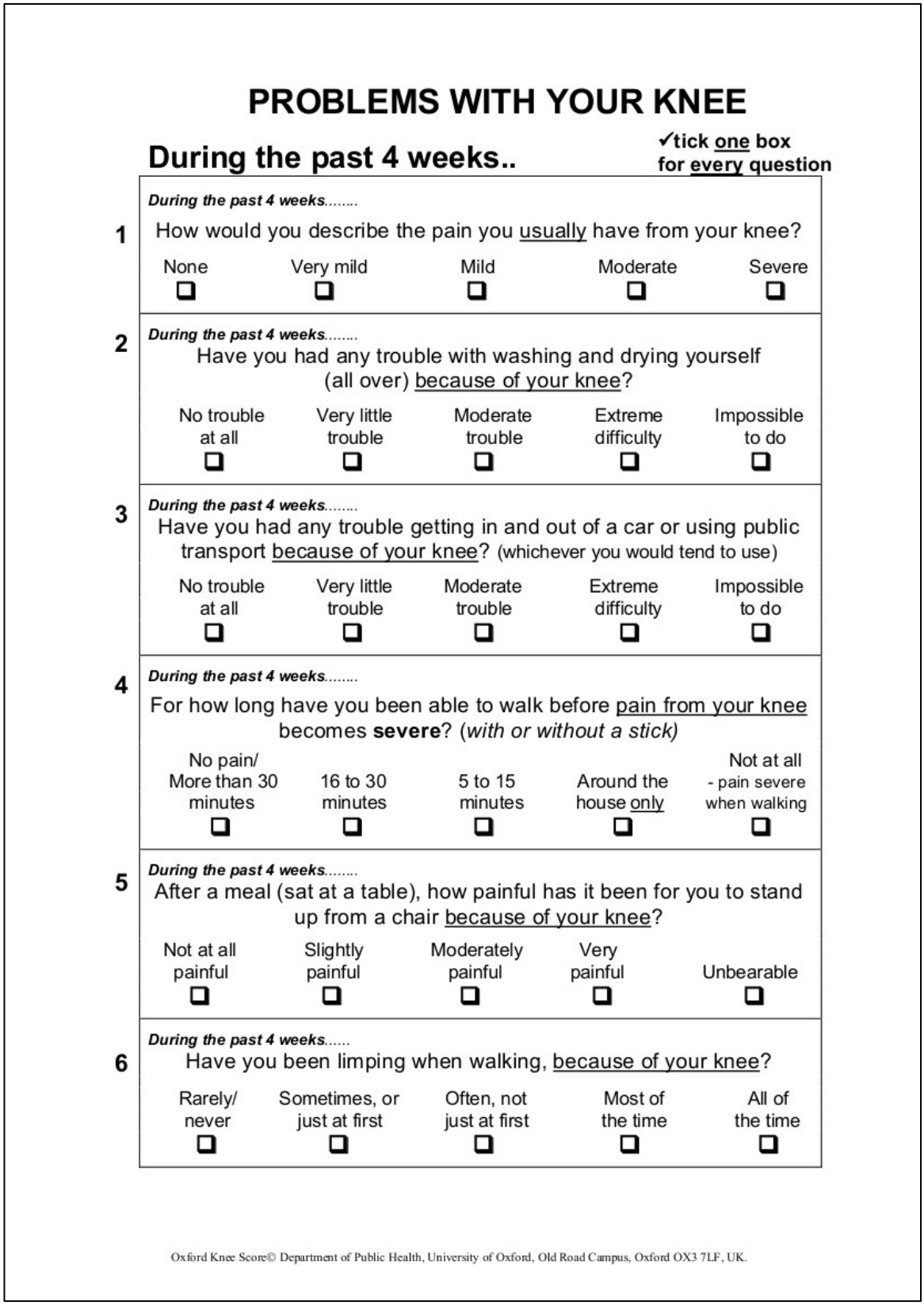
Appendix 2: Scoring systems

A2.1. Tegner Activity Scale

Please circle the number which best describes the activity you are able to do:

Level 10	Competitive sports: football/rugby – national and international elite
Level 9	Competitive sports: football (lower divisions), ice hockey, wrestling, gymnastics
Level 8	Competitive sports: bandy, squash/badminton, athletics (jumping etc.) downhill skiing
Level 7	Competitive sports: tennis, athletics (running), motocross, speedway, handball, basketball Recreational sports: football, badminton, ice hockey, squash, athletics (jogging), cross-country
Level 6	Recreational sports: tennis, badminton, handball, basketball, downhill skiing, jogging at least five times per week
Level 5	Work: heavy labour (e.g. building, forestry) Competitive sports: Cycling, cross-country skiing Recreational sports: jogging on uneven ground at least twice a week
Level 4	Work: moderate heavy labour (e.g. lorry driving, heavy domestic work) Recreational sports: cycling, cross-country skiing, jogging on even ground at least twice a week
Level 3	Work: light labour e.g. nursing Competitive and recreational sports: swimming, walking in forest possible
Level 2	Work: light labour Walking on uneven ground possible but walking in forest impossible
Level 1	Work: sedentary. Walking on even ground possible
Level 0	Sick leave or disability pension due to knee problems

A2.2. Oxford Knee Score



PROBLEMS WITH YOUR KNEE

During the past 4 weeks.. ✓tick one box for every question

1 *During the past 4 weeks.....*
How would you describe the pain you usually have from your knee?

None	Very mild	Mild	Moderate	Severe
❑	❑	❑	❑	❑

2 *During the past 4 weeks.....*
Have you had any trouble with washing and drying yourself (all over) because of your knee?

No trouble at all	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
❑	❑	❑	❑	❑

3 *During the past 4 weeks.....*
Have you had any trouble getting in and out of a car or using public transport because of your knee? (whichever you would tend to use)

No trouble at all	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
❑	❑	❑	❑	❑

4 *During the past 4 weeks.....*
For how long have you been able to walk before pain from your knee becomes **severe**? (*with or without a stick)*

No pain/ More than 30 minutes	16 to 30 minutes	5 to 15 minutes	Around the house only	Not at all - pain severe when walking
❑	❑	❑	❑	❑

5 *During the past 4 weeks.....*
After a meal (sat at a table), how painful has it been for you to stand up from a chair because of your knee?

Not at all painful	Slightly painful	Moderately painful	Very painful	Unbearable
❑	❑	❑	❑	❑

6 *During the past 4 weeks.....*
Have you been limping when walking, because of your knee?

Rarely/ never	Sometimes, or just at first	Often, not just at first	Most of the time	All of the time
❑	❑	❑	❑	❑

Oxford Knee Score© Department of Public Health, University of Oxford, Old Road Campus, Oxford OX3 7LF, UK.

Continued on next page

During the past 4 weeks...

✓tick one box for every question

7 *During the past 4 weeks.....*

Could you kneel down and get up again afterwards?

Yes, Easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, Impossible
❑	❑	❑	❑	❑

8 *During the past 4 weeks.....*

Have you been troubled by pain from your knee in bed at night?

No nights	Only 1 or 2 nights	Some nights	Most nights	Every night
❑	❑	❑	❑	❑

9 *During the past 4 weeks.....*

How much has pain from your knee interfered with your usual work *(including housework)*?

Not at all	A little bit	Moderately	Greatly	Totally
❑	❑	❑	❑	❑

10 *During the past 4 weeks.....*

Have you felt that your knee might suddenly 'give way' or let you down?

Rarely/ never	Sometimes, or just at first	Often, not just at first	Most of the time	All of the time
❑	❑	❑	❑	❑

11 *During the past 4 weeks.....*

Could you do the household shopping on your own?

Yes, Easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, Impossible
❑	❑	❑	❑	❑

12 *During the past 4 weeks.....*

Could you walk down one flight of stairs?

Yes, Easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, Impossible
❑	❑	❑	❑	❑

A2.3. Knee Society Score

Knee Society Score: For Doctor/Clinician to Complete

DIAGNOSIS: Date:

Evaluator (Surname) ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ Centre:

Pain	points
None	50
Mild or Occasional	45
Mild - Stairs only	40
Mild Walking and Stairs	30
Moderate - Occasional	20
Moderate - Continual	10
Severe	0

Stability: (maximum movt in any position)

AP	*points*	*Med-lat*	*points*
< 5 mm	10	<5°	15
5-10 mm	5	6-9°	10
>10 mm	0	10-14°	5
		15°	0

ROM degrees	points
≥125	25
120	24
115	23
110	22
105	21
100	20
95	19
90	18
85	17
80	16
75	15
70	14
65	13

degrees	points
60	12
55	11
50	10
45	9
40	8
35	7
30	6
25	5
20	4
15	3
10	2
5	1
0	0

Extension: ☐☐ Maximum Flexion ☐☐☐

subtotal ☐☐☐/100

Flexion contracture:		Extension Lag		Alignment	
	points		points	ASIS – Knee - Ankle	points
0	0	0	0	5-10°Valgus (normal)	0
5-9°	2	0-9°	5	0-4°Valgus	10
10-15°	5	10-20°	10	11- 15°Valgus	10
16-20°	10	>20°	15	Other	20
>20°	15				
				Measurement	degrees
				Note varus / valgus	

DEDUCTIONS (minus)

Deductions Total

☐☐/50

Knee Score

☐☐☐/100

FUNCTION SCORE

Walking		Stairs		Support (deductions)	
	points		points		points
Unlimited	50	normal	50	Stick	5
500m-1km	40	down with rail	40	2 sticks	10
100-500m	30	up & down with rail	30	crutches/walker	20
<100m	20	unable down	15		
Housebound	10	unable	0		
Unable	0				

Function Total

☐☐☐/100

A2.4. EuroQol 5-Domain score

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about ❑
I have some problems in walking about ❑
I am confined to bed ❑

Self-Care

I have no problems with self-care ❑
I have some problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

Usual Activities (*e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities ❑
I have some problems with performing my usual activities ❑
I am unable to perform my usual activities ❑

Pain/Discomfort

I have no pain or discomfort ❑
I have moderate pain or discomfort ❑
I have extreme pain or discomfort ❑

Anxiety/Depression

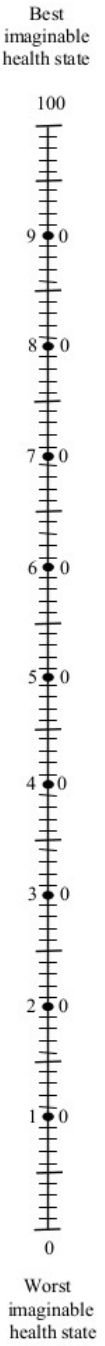
I am not anxious or depressed ❑
I am moderately anxious or depressed ❑
I am extremely anxious or depressed ❑

Continued on next page

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today



Appendix 3: Data collection forms

A3.1 Oxford UKR surgical data collection form

OXFORD UKA OPERATION FORM

Patient's name **Hospital Number** **Side: R / L** **Medial / Lateral**

Operation Date: / / 201 Operation type: Primary / Revision Diagnosis:

Operating surgeon: Operating surgeon grade:

Assistant surgeon: Assistant surgeon grade:

Consultant surgeon: Operation approach: MIS UKA Funded: NHS

Aanesthesia: 1.GA 2.Femoral block 3.Sciatic block 4.Single shot spinal 5.Epidural 6.Combined spinal and epidural 7.Intra-articular infiltration 8a.Intra-articular epidural catheter top-up with saline 8b.Intra-articular epidural catheter top-up with 0.5% bupivicaine

---

SURGICAL FINDINGS

ACL: N / Synovial Damage / Longitudinal splits / Friable and Fragmented / Absent / Absent and Reconstructed simultaneously / Absent and staged Reconstruction

	PTCL *	Focal (<2cm^2) FTCL**	Extensive (>2cm^2) FTCL	Bone loss < 5 mm	Bone loss > 5mm
Involved Femur					
Involved Tibia					

* Partial thickness cartilage loss ** Full Thickness cartilage loss

	Normal	Superficial Damage	PTCL*	Focal (<2cm^2) FTCL**	Extensive (>2cm^2)FTCL
Lateral facet patella					
Medial facet patella					
Trochlea					
Uninvolved femur (Non-weight bearing)					
Uninvolved femur (Weight bearing)					

IMPLANT PARAMETERS

Bearing: Phase 2 /3 Bearing thickness: 0 /1/ 2/ 3 /4 /5 /6 /7 /8 /9
Bearing type: Mark 1 /Mark 2/ Anatomic / Lateral domed /Lateral Fixed

---

Femur: Phase 3 / Phase 3 Hiflex/Cementless femur
Femur Size: Ex-Small / Small / Medium (Standard) / Large / Ex-Large

Last Spigot Size: 0 / 1 / 2 / 3 / 4 / 5 / 6 / 7

Tibia: Phase 3 (new) / Phase 3 (old) / phase 2

Tibia Size: AA / A / B / C / D / E / F or 26x38 / 26x41 / 28x44 / 30x47 / 32x50 / 34x53 0r 28x40 / 28x44 /28x48 /31x48 /31x52

Cement: CMW1 / CMW3 / Palacos **CEMENTED** **CEMENTLESS**

Additional procedures: 1. RSA Y / N **2. Mosaicplasty** Y / N

Comments:

PLEASE ATTACH IMPLANT STICKERS ON REVERSE - THANK YOU

A3.2: National Joint Registry patient consent form

National Joint Registry
www.njrcentre.org.uk

Patient Consent Form

What is the National Joint Registry?

The role of the National Joint Registry (NJR) for England, Wales and Northern Ireland is to improve patient safety and monitor the results of joint replacement surgery. The information held on the Registry helps to find out which are the best performing artificial joints and the most effective types of surgery.

How does the NJR help patients?

The NJR helps patients by:

- Helping surgeons choose the best artificial joints (commonly known as implants)
- Improving patient safety by checking how well implants, surgeons and hospitals perform and taking action where it is needed.
- When implant problems are found, helping surgeons to decide quickly whether a patient needs to come back to hospital
- Giving hospitals and implant manufacturers feedback about their performance to help them improve patient care

Research

Data in the NJR may only be used for medical research in orthopaedics, and scientifically-related studies. We do not pass on patients' personal details to researchers.

What information is collected?

Details of your operation and your implants will be recorded on the NJR by your hospital. However, your personal details such as your name and address will only be recorded if you give your consent.

Why does the NJR need my personal details?

Your personal details allow the NJR to link you to the implant(s) you received during surgery. If, for instance, you need another operation in the future, the NJR can measure the time between the operations. Adding together this time from all patients' operations tells us how well different implants and surgeons are doing. Without using personal details to link operations, the NJR cannot find out about problems with implants or surgeons.

Personal details needed by the NJR are:

- Name
- Date of birth
- Postcode
- NHS/National Patient number

The NJR Centre might also give you the opportunity to take part in patient feedback surveys in the future, to give your views on whether the surgery has made your life better. Shoulder patients will be routinely invited to take part. Patients receiving other joint replacements may also be invited. You do not have to take part in any surveys.

Whether you choose to consent or not, please sign this form on the back.

Page 1 of 2

Do I have to give my consent?

No. If you do not consent, your operation details will be stored on the NJR without any personal details, so you cannot be identified. If you change your mind about consenting to the NJR holding your personal details, please contact the NJR Centre (see 'Finding out more').

Is my information safe?

Your personal details are kept confidential at all times. Very strict rules and secure procedures are in place to ensure that your information is kept safe. You can ask for a copy of your personal data held on the NJR by writing to the NJR Centre.

Finding out more

NJR Website

www.njrcentre.org.uk

NJR Helpline

Tel: 0845 345 9991
Mon-Fri 9am to 5pm
(excluding public holidays)
Fax: 0845 345 9992

E-mail:

health_servicedesk@northgate-is.com

NJR Centre

Peoplebuilding 2, Peoplebuilding Estate,
Maylands Avenue,
Hemel Hempstead HP2 4NQ

Patient Details (all mandatory)

Surname _____

Forename _____

Date of birth _____

Postcode (home) _____

To be completed by the hospital

Hospital _____

NHS number _____

Height _____ cm & Weight _____ kg

or BMI _____

I CONSENT to my personal details being recorded within the NJR. I understand that the NJR will not release my personalised data unless required by law or where there is a clear overriding public interest in disclosure. However, where possible, I will be told if any disclosure is to take place.

Signature _____ Date _____

I DO NOT CONSENT to my personal details being recorded within the NJR.

Signature _____ Date _____

To be completed by the hospital (person accepting patient consent)

Name _____ Signature _____

Position _____ Date _____

Version 4.0 October 2012

This form should be kept as part of the patient record. DO NOT send this form to the NJR Centre

A3.3 NJR data collection form: Knee Primary

National Joint Registry www.njrcentre.org.uk	MDS VERSION 4.0 Knee Operation Form: MDSv4.0 K1 v1.0
K1 Knee Primary	Patient Addressograph
Important: Please tick relevant boxes. All component stickers should be affixed to the accompanying 'Minimum Dataset Form Component Labels Sheet'. Please ensure that all sheets are stapled together.	

All fields are Mandatory unless otherwise indicated

REMEMBER! MAKE A NOTE OF THE NJR REFERENCE NUMBER WHEN YOU ENTER THIS DATA	NJR REF:

PATIENT DETAILS				
Patient Consent Obtained	Yes ☐	No ☐	Not Recorded ☐	
Patient Hospital ID				
Body Mass Index (enter either H&W OR BMI OR tick Not Available box)	Height (IN CM) Weight (IN KG)	BMI	Not Available ☐	

PATIENT IDENTIFIERS				
Forename				
Surname				
Gender	Male ☐	Female ☐	Not Known ☐	Not Specified ☐
Date of Birth	DD/MM/YYYY			
Patient Postcode			Overseas Address ☐	
NHS Number (if available)				

OPERATION DETAILS					
Hospital					
Operation Date	DD/MM/YYYY				
Anaesthetic Types	General ☐ Regional - Epidural ☐		Regional – Nerve Block ☐ Regional – Spinal (Intrathecal) ☐		
Patient ASA Grade	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
Operation Funding	NHS ☐	Independent ☐			

SURGEON DETAILS					
Consultant in Charge					
Operating Surgeon					
Operating Surgeon Grade	Consultant ☐	SPR/ST3-8 ☐	F1-ST2 ☐	Specialty Doctor/SAS ☐	Other ☐
First Assistant Grade	Consultant ☐	Other ☐			

KNEE PRIMARY PROCEDURE DETAILS							
Side	Left ☐	Right ☐					
Indications for Implantation (select all that apply)	Osteoarthritis	☐	Rheumatoid Arthritis	☐			
	Avascular Necrosis	☐	Previous Trauma	☐			
	Other Inflammatory Arthropathy	☐	Other	☐			
	Previous Infection	☐					
PRE OPERATIVE RANGE OF MOVEMENT							
Fixed Flexion Deformity (degrees)	Less than 10 ☐	10 to 30 ☐	Greater than 30 ☐	Not Available ☐			
Flexion (degrees)	Less than 70 ☐	70 to 90 ☐	91 to 110 ☐	Greater than 110 ☐	Not Available ☐		

SURGICAL APPROACH							
Patient Procedure	Primary Total Prosthetic Replacement Using Cement ☐						
	Primary Total Prosthetic Replacement Not Using Cement ☐						
	Unicondylar Knee Replacement ☐						
	Patello-Femoral Knee Replacement ☐						
	Primary Total Prosthetic Replacement Not Classified Elsewhere (eg Hybrid) ☐						
Consultant in Charge – Default Technique used?	Yes ☐	No ☐	If Yes, ensure the relevant Surgeon Default Technique is recorded on the Data Entry system. The Surgeon's Default Technique is made up of several data fields.				
Approach	Medial Parapatellar	☐	Mid-Vastus	☐			
	Lateral Parapatellar	☐	Other	☐			
	Sub-Vastus	☐					
Minimally Invasive Technique Used?	Yes ☐	No ☐					
Computer Guided Surgery Used?	Yes ☐	No ☐					
THROMBOPROPHYLAXIS REGIME (intention to treat)							
Chemical	Aspirin	☐	Warfarin	☐	None ☐		
	LMWH	☐	Direct Thrombin Inhibitor	☐			
	Pentasaccharide	☐	Other	☐			
Mechanical	Foot Pump	☐	Other	☐			
	Intermittent Calf Compression	☐	None	☐			
	TED Stockings	☐					
BONEGRAFT USED							
Femur	Yes ☐	No ☐					
Tibia	Yes ☐	No ☐					
SURGEON'S NOTES							

INTRA OPERATIVE EVENT				
Untoward Intra Operative Event	None	☐	Ligament Injury	☐
	Fracture	☐	Other	☐
	Patella Tendon Avulsion	☐		

A3.4. NJR data collection form: Knee Revision

National Joint Registry
www.njrcentre.org.uk

MDS VERSION 4.0 Knee Operation
Form: MDSv4.0 K2 v1.0

K2

Knee Single Stage Revision
Knee Stage 1 of 2 Stage Revision
Knee Stage 2 of 2 Stage Revision
Knee Conversion to Arthrodesis
Knee Amputation

Patient Addressograph

Important:
Please tick relevant boxes. All component stickers should be affixed to the accompanying 'Minimum Dataset Form Component Labels Sheet'. Please ensure that all sheets are stapled together.

All fields are Mandatory unless otherwise indicated

REMEMBER! MAKE A NOTE OF THE NJR REFERENCE NUMBER WHEN YOU ENTER THIS DATA	NJR REF:

PATIENT DETAILS				
Patient Consent Obtained	Yes ☐	No ☐	Not Recorded ☐	
Patient Hospital ID				
Body Mass Index (enter either H&W OR BMI OR tick Not Available box)	Height (IN CM) Weight (IN KG)	BMI	Not Available ☐	

PATIENT IDENTIFIERS				
Forename				
Surname				
Gender	Male ☐	Female ☐	Not Known ☐	Not Specified ☐
Date of Birth	DD/MM/YYYY			
Patient Postcode			Overseas Address ☐	
NHS Number (if available)				

OPERATION DETAILS				
Hospital				
Operation Date	DD/MM/YYYY			
Anaesthetic Types	General ☐ Regional - Epidural ☐		Regional – Nerve Block ☐ Regional – Spinal (Intrathecal) ☐	
Patient ASA Grade	1 ☐	2 ☐	3 ☐	4 ☐ 5 ☐
Operation Funding	NHS ☐	Independent ☐		

SURGEON DETAILS					
Consultant in Charge					
Operating Surgeon					
Operating Surgeon Grade	Consultant ☐	SPR/ST3-8 ☐	F1-ST2 ☐	Specialty Doctor/SAS ☐	Other ☐
First Assistant Grade	Consultant ☐	Other ☐			

KNEE REVISION PROCEDURE DETAILS		
Procedure Type	Single Stage Revision ☐ Stage 1 of 2 Stage Revision ☐ Stage 2 of 2 Stage Revision ☐	Conversion to Arthrodesis ☐ Amputation ☐
Side	Left ☐ Right ☐	
Indications For / Findings at Time of Revision (select all that apply)	Aseptic Loosening Femur ☐ Tibia ☐ Patella ☐ Infection ☐ Dislocation / Subluxation ☐ Lysis Femur ☐ Tibia ☐	Instability ☐ Wear of Polyethylene Component ☐ Component Dissociation ☐ Pain (undiagnosed) ☐ Malalignment ☐ Peri-Prosthetic Fracture ☐ Implant Fracture ☐ Stiffness ☐ Progressive Arthritis Remaining Knee ☐ Other ☐

PRIMARY OPERATION DETAILS		
Primary Operation Date OR Year	DD/MM/YYYY Please enter Date if known	Not Available ☐
Primary Operation Hospital		Not Available ☐

COMPONENTS REMOVED (Do not complete for Stage 2 of 2 Stage Revision)		
Brand of Knee Removed		Not Available ☐

SURGICAL APPROACH (Used for Single Stage Revision & Stage 2 of 2 Stage Revision)				
Patient Procedure	Revision Using Cement ☐ Revision Not Using Cement ☐ Revision Not Classified Elsewhere (eg Hybrid) ☐			
Approach	Medial Parapatellar ☐ Lateral Parapatellar ☐ Sub-Vastus ☐ Mid-Vastus ☐		Quadriceps Turn-Down ☐ Tibial Tubercle Osteotomy ☐ Other ☐	
THROMBOPROPHYLAXIS REGIME (intention to treat)				
Chemical	Aspirin ☐ LMWH ☐ Pentasaccharide ☐		Warfarin ☐ Direct Thrombin Inhibitor ☐ Other ☐	None ☐
Mechanical	Foot Pump ☐ Intermittent Calf Compression ☐ TED Stockings ☐		Other ☐ None ☐	
BONEGRAFT USED				
Femur	Yes ☐	No ☐		
Tibia	Yes ☐	No ☐		
SURGEON'S NOTES				

INTRA OPERATIVE EVENT		
Untoward Intra Operative Event	None ☐ Fracture ☐ Patella Tendon Avulsion ☐	Ligament Injury ☐ Other ☐

Appendix 4: Cementless OUKR - results from other Joint Registries

A4.1. Background

Following the publication of the studies reported in Chapters 6 and 7, an assessment of the results of the cementless OUKR was undertaken using data from the NJR (the results of which are given in Chapter 9). During the conduct of this study, it was noted that the early adopters of the cementless implant were generally high-volume surgeons and a high proportion were from Oxford. In the conclusions of Chapter 9, it was suggested that this problem could be addressed by the use of NJR data from other countries using the cementless OUKR. This work is ongoing and forms part of the 'further work' described in Chapter 10.

As an initial response to a research request, the Australian Orthopaedic Association released to us unpublished data regarding the cementless OUKR. These data are unadjusted for patient and surgical characteristics, and the individual records have not at the time of writing been released to us for detailed analysis; hence there is a limit to the conclusions that can be drawn from these data. However, it is published here to provide context for the interpretations placed upon the results presented in Chapter 9. Likewise, some unadjusted data from the New Zealand joint registry have been obtained from the registry reports and through personal communication with Mr Rod Maxwell, Consultant Orthopaedic Surgeon in Christchurch.

A4.2. Results of the cementless OUKR

A4.2.4. Numbers of cementless OUKRs implanted

As in the UK, the cementless OUKR has been in use for a much shorter period of time than the cemented implant. However, in Australia, its popularity has increased at a much faster rate relative to the cemented OUKR and in 2012 its use overtook that of the cemented OUKR. The figures in the graph in Figure A4-1 are taken from the annual reports from the AOANJRR; this can be compared with Figure 9-1. Whilst the usage of the OUKR has remained constant in England and Wales since 2008, the use of the OUKR and UKR in general has declined in Australia during that time-period.

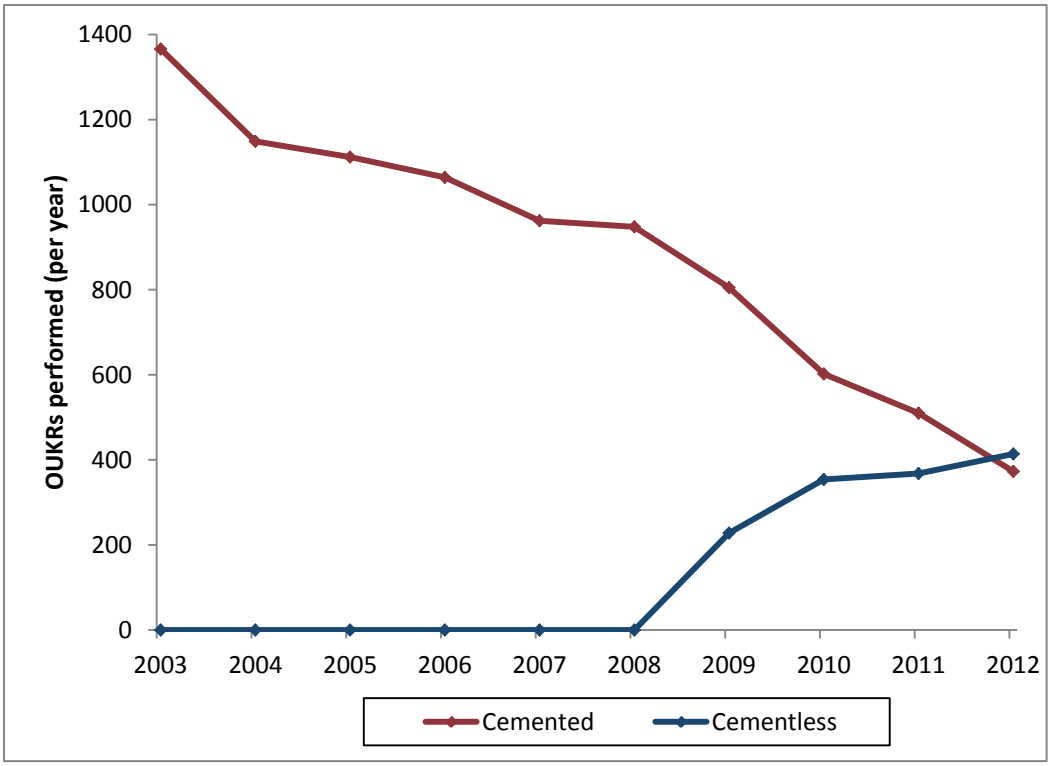


Figure A4-1: Use of cemented and cementless OUKR in Australia
Figures taken from published annual reports

In New Zealand, the use of UKR has remained relatively constant since figures were first published in 2005. Again, use of the cementless OUKR has overtaken that of the cemented OUKR (Figure A4-2).

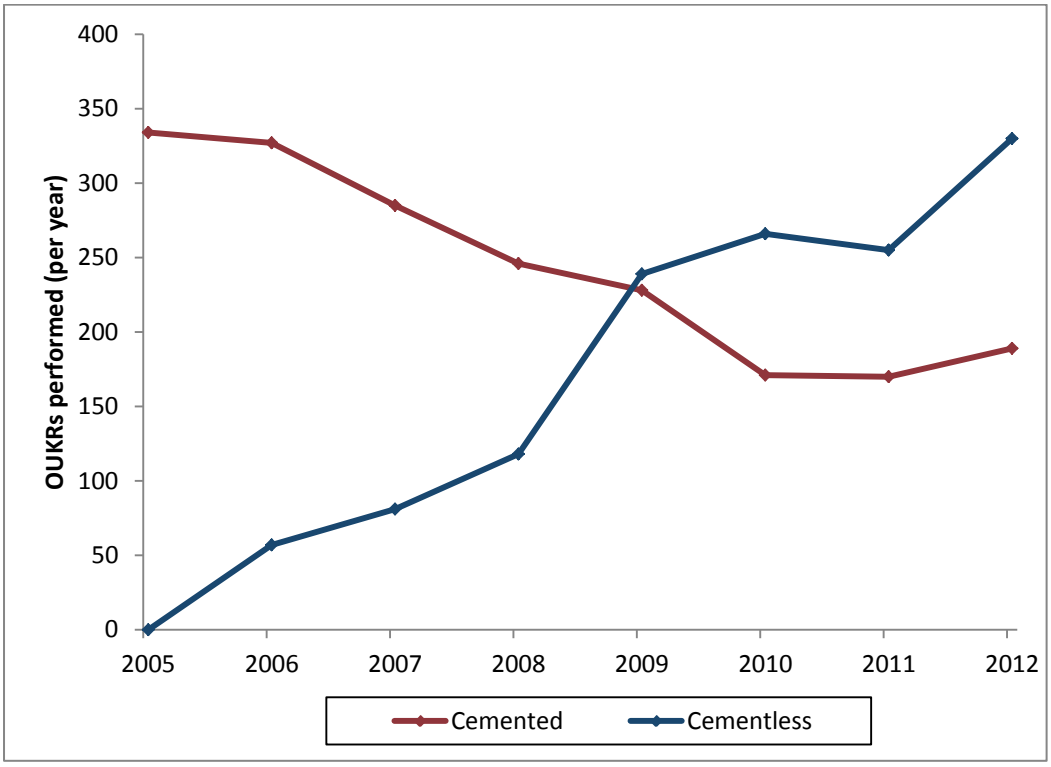


Figure A4-2: Use of cemented and cementless OUKR in New Zealand
Figures taken from published annual reports.

A4.2.5. Revision rates of cemented and cementless OUKR

A4.2.5.4. Australia

The following data were provided as part of a research request to the AOANJRR in January 2013 and cover the period between September 1999 and the end of December 2011.

Cement	Implanted	Revised	Revisions/100 Obs. Yrs (95% CI)
Cemented	10940	1095	1.73 (1.63-1.84)
Cementless	1235	46	1.74 (1.28-2.33)

Table A4-1: Revision rates for cemented and cementless OUKR in Australia

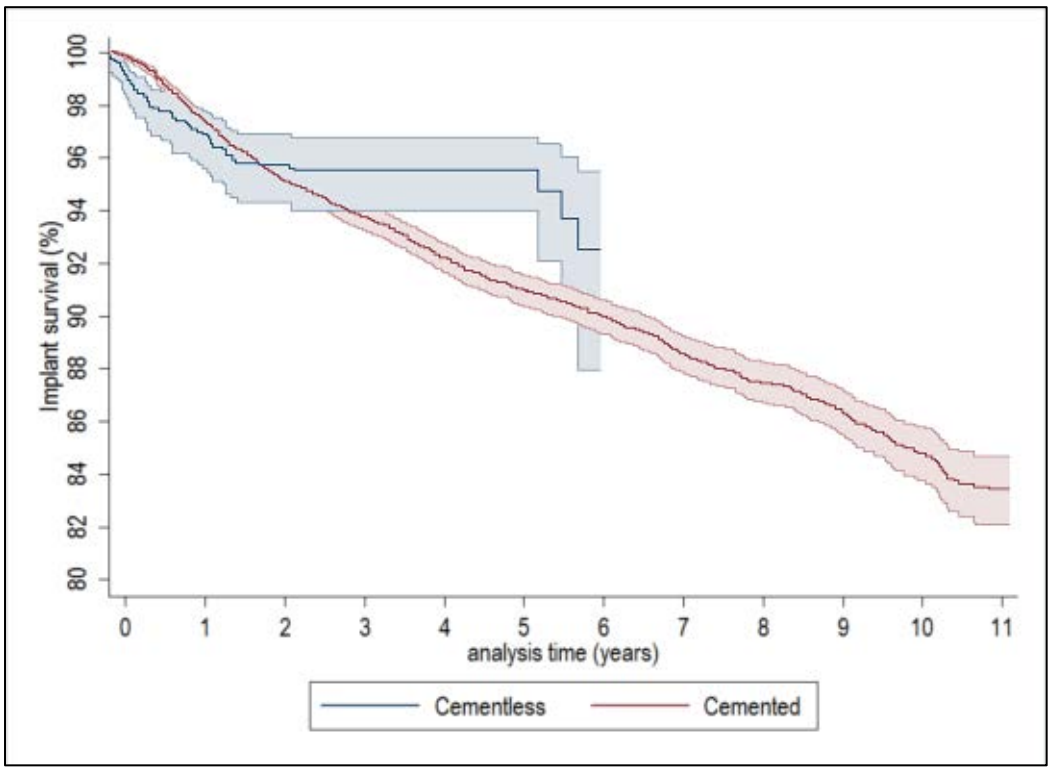


Figure A4-3: Cumulative revision rates for the cemented and cementless OUKR

	1 Yr	3 Yrs	5 Yrs
Cemented	2.2 (2.0, 2.5)	6.1 (5.6, 6.6)	8.8 (8.3, 9.4)
Cementless	2.9 (2.1, 4.1)	4.4 (3.3, 6.0)	4.4 (3.3, 6.0)

Table A4-2: Cumulative revision rates per year for cemented and cementless OUKR

Whilst revision rates are observed to be similar overall (Table A4-1), there is a trend to higher rates of early revision after the cementless OUKR (Figure A4-3, Table A4-2).

A4.2.5.5. New Zealand

Revision rate figures are published in the NZJR annual reports. The Kaplan-Meier curve was provided by Dr Maxwell on request. A significantly superior revision rate is given for the cementless OUKR overall. However, the number of cementless OUKRs with longer-term follow up is very limited (Figure A4-4) and there is no adjustment made for patient or surgical factors. Unlike the graphs from England and Wales and Australia, the

revision rate for the cementless OUKR appears to be superior to that of the cemented prosthesis throughout the time-period recorded (Table A4-3).

	Implanted	Revised	Revisions/100 Obs. Yrs (95% CI)
Cemented	3626	315	1.37 (1.22-1.53)
Cementless	1380	26	0.74 (0.48-1.08)

Table A4-3: Revision rates for cemented and cementless OUKR in New Zealand

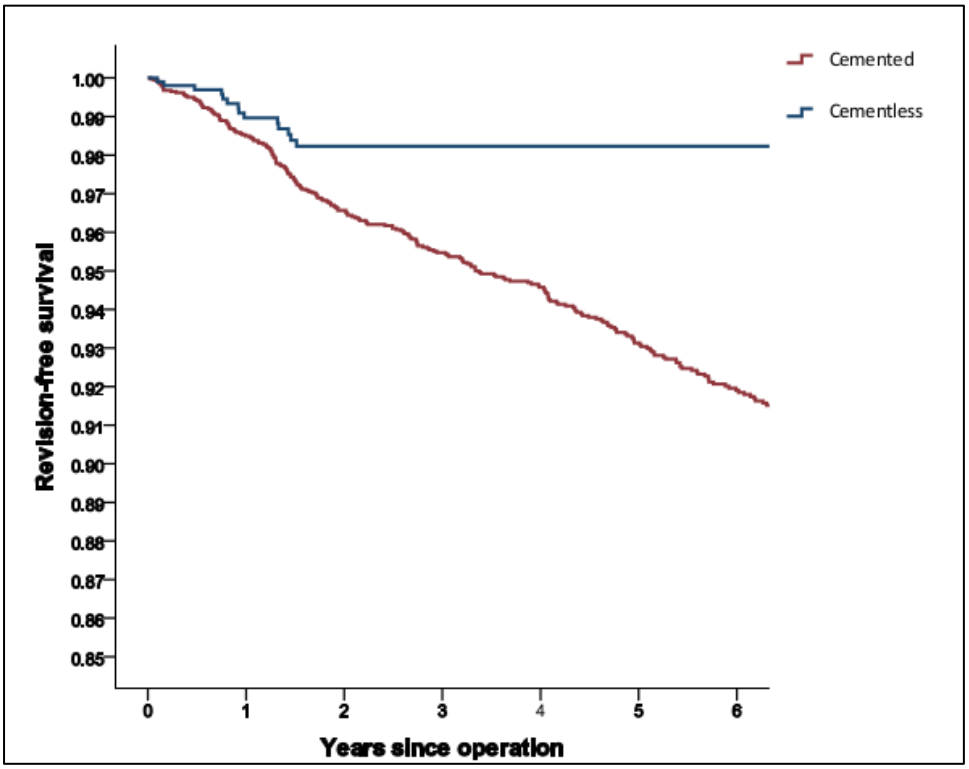


Figure A4-4: Cumulative survival - cemented and cementless OUKR (New Zealand)

A4.2.5.6. Reasons for revision (Australia)

Reasons for revision have been provided as part of the research request from the AOANJRR and are given in Table A4-4. A smaller proportion of the revisions in the cementless group are for aseptic loosening, but this may be a result of the different follow-up times of the two cohorts. As seen in the data from England and Wales in Chapter 9, there are fewer revisions for pain. However, more revisions are reported due

to peri-prosthetic fracture. This is a concern with the cementless UKR (see Chapter 7), but a similar effect has not been observed in the England and Wales data.

	Cemented			Cementless		
Reason for revision	Number	% Revision	% Primary	Number	% Revision	% Primary
Loosening/Lysis	486	43.9	4.4	14	30.4	1.1
Progression Of Disease	243	22.0	2.2	7	15.2	0.6
Pain	132	11.9	1.2	3	6.5	0.2
Infection	58	5.2	0.5	2	4.3	0.2
Bearing Dislocation	48	4.3	0.4	4	8.7	0.3
Fracture	25	2.3	0.2	8	17.4	0.6
Malalignment	17	1.5	0.2	2	4.3	0.2
Wear	22	2.0	0.2			
Instability	13	1.2	0.1	1	2.2	0.1
Patellofemoral Pain	13	1.2	0.1			
Incorrect Sizing	11	1.0	0.1	3	6.5	0.2
Prosthesis Dislocation	10	0.9	0.1			
Implant Breakage	10	0.9	0.1	1	2.2	0.1
Synovitis	5	0.5	0.0			
Arthrofibrosis	4	0.4	0.0			
Osteonecrosis	2	0.2	0.0	1	2.2	0.1
Other	9	0.8	0.1			

Table A4-4: Reasons for revision of OUKR by fixation (Australian registry data)

A4.2.5.7. Comparison of crude revision rates

As both the number of revisions and the number of implant years are available for all three NJRs, it is possible to combine the crude survival figures from each and calculate an overall incidence rate ratio (Table A4-5). These figures must be treated with caution given that they are unadjusted for patient and surgical characteristics.

Country	Cemented		Cementless		IRR	significance
	N	RR	N	RR		
Australia	10,940	1.73 (1.63-1.84)	1,235	1.74 (1.28-2.33)	1.01 (0.73-1.35)	0.95
New Zealand	3,626	1.37 (1.22-1.53)	1,380	0.74 (0.48-1.08)	0.54 (0.35-0.81)	<0.01
England & Wales	25,882	1.36 (1.29-1.43)	1,838	0.98 (0.68-1.41)	0.72 (0.48-1.04)	0.07
Combined	40,448	1.49 (1.43-1.54)	4,453	1.11 (0.90-1.31)	0.74 (0.60-0.91)	<0.01

Table A4-5: Comparison and synthesis of crude revision rates for the three registries
RR – revision rate per 100 implant years; IRR – incidence rate ratio

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