

OPTIMISING THE OUTCOMES OF THE OXFORD UNICOMPARTMENTAL KNEE REPLACEMENT

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ABSTRACT

OPTIMISING THE OUTCOMES OF THE OXFORD UNICOMPARTMENTAL KNEE REPLACEMENT

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The two main surgical options for knee arthritis are total knee replacement (TKR) and unicompartmental knee replacement (UKR). UKR has advantages over TKR but has higher revision rates. As a result, UKR only forms 10% of all primary knee replacements. The broad aims of this thesis were to determine; the long term implant survival of the Oxford UKR and to assess current and develop new evidence based strategies to reduce revision rates.

A systematic review investigating the long term outcomes of 8,658 Oxford UKRs found the 10 year implant survival was 93% with leading revision causes including aseptic loosening, pain and bearing dislocation. There was a lack of cementless studies.

A large prospective cementless Oxford UKR cohort study (n=1000) in Oxford allowed the assessment of long term clinical outcomes using various endpoints; reoperation, revision and revision to TKR. The respective 10 year survivals were 96.6%, 97.5% and 98.9%.

A retrospective observational study from the National Joint Registry (NJR) was used to compare the long term outcomes of 14,814 matched cemented and cementless UKRs. The cementless group has significantly reduced revision rates (HR=0.76) given rates of revision for aseptic loosening, pain and lysis decreased. However the revision rate for peri-prosthetic tibial fracture increased. These results were mirrored by a systematic review comparing fixation types for all UKR types (n=10,736).

Other retrospective observational studies from the NJR were used to investigate the effect on revision rates of (1) increasing surgeon caseload, (2) Microplasty (new guiding surgical instrumentation) and (3) adding a second femoral peg on revision rates. All three were associated with lower revision rates.

A radiostereometric study of polyethylene wear was undertaken to determine why an increased rate of bearing fracture has been observed. The wear rate for the current bearings are 57 $\mu\text{m}/\text{year}$ which is substantially higher than in previous studies. Although moulded bearings were found to have less wear than machined, no factors studied including recent changes to the bearing resin or manufacture accounted for the increased wear.

An experimental study found that new wider surgical saw blades halved the force required to seat the tibial component whilst maintaining fixation achieved. This should reduce the risk of periprosthetic fractures and is now used clinically.

This thesis has characterised the performance of the Oxford UKR and has highlighted strategies to lower UKR revision rates, to levels similar of TKR. If this is achieved the only real disadvantage of UKR compared to TKR will have been addressed.

This thesis is dedicated to my inspiration, Ali Ibn Abu Talib, whose dedication to knowledge, truth and justice inspired me to manage the reigns of academia and stretch myself to new heights. Verily without him I would be lost.

“Do not let your difficulties fill you with anxiety, after all it is only in the darkest nights that the stars shine ever more brightly”

Ali Ibn Abu Talib

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ABBREVIATIONS

ACL – Anterior cruciate ligament

AKSS-O/F – American Knee Society Score (Objective/Functional)

AMOA – Anteromedial osteoarthritis

ANOVA – One way analysis of variance

ASA – American society of anaesthesiologist's score

AVN – Avascular necrosis

BMI – Body mass index

CAD – Computer aided design

CENTRAL – Cochrane controlled register of trials

CI – Confidence interval

DCM – Direct compression moulded

DVT – Deep vein thrombosis

ECM – Extracellular matrix

EQ-5D – EuroQol Five Dimension Scale

HC10 – Dartec testing machine

HES – Hospital Episode Statistics

HR – Hazard ratio

HSS – Hospital for Special Surgery Knee Score

HTO – High tibial osteotomy

IQR – Interquartile range

KOOS – Knee injury and Osteoarthritis Outcome Score

LMWH – Low molecular weight heparin

MCID – Minimally clinically important difference

MCL – Medial collateral ligament

MINOR – Methodological Index for evaluation of Non-randomised Studies

MUA – Manipulation under anaesthesia

NHS – National Health Service

NJR – National Joint Registry of England, Wales, Northern Ireland and Isle of Man

NSAID – Non-steroidal anti-inflammatory drug

NZJR – New Zealand Joint Registry

OARSI – Osteoarthritis Research Society International

OKS – Oxford Knee Score

ONS – Office for National Statistics

PA – Per annum

PCL – Posterior cruciate ligament

PE – Pulmonary embolism

PRISMA – Preferred reporting items for systematic reviews and meta analyses

PROM – Patient Reported Outcome Measure

RCT – Randomised controlled trial

REC – Research Ethics Committee

RSA – Radiostereometric analysis

SD – Standard deviation

SMD – Standardised mean difference

TKR – Total knee replacement

UK – United Kingdom

UKR – Unicompartmental knee replacement

USA – United States of America

VTE – Venous thrombo-embolism

WOMAC – Western Ontario and McMaster Universities Arthritis Index

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1. INTRODUCTION

1.1 Overview

Arthritis is one of the commonest forms of joint disease and ranks amongst the leading causes of disability worldwide¹. It has a profound effect on quality of life affecting both psychological and physical function², particularly when involving the knee or hip joint. Affected individuals and their families often have to adapt their lifestyles, occupation and home in order to minimise its impact. Pain and restricted range of motion particularly cause dependence for ambulation, climbing stairs and lower extremity functions³. This inevitably results in a significant socioeconomic burden of approximately 1.0 - 2.5% of gross domestic product in developed countries⁴.

Knee arthritis is particularly troublesome, given its higher prevalence compared to other arthropathies with a lifetime risk of approximately 50%⁵. This is only expected to increase, given an increasingly ageing⁶ and obese population⁷, particularly in Western countries.

Patients who fail to respond to non-operative management are offered knee replacement surgery to restore function with over 100,000 procedures performed annually in the United Kingdom (UK)⁸, and this number is projected to only increase at an alarming rate⁹.

The three main surgical options which exist for end stage knee osteoarthritis are total knee replacement (TKR), unicompartmental knee replacement (UKR) and knee osteotomy surgery. In TKR the whole articulating surface of the knee joint are replaced whereas in UKR only the disease affected portion of knee is replaced, which usually is the medial compartment. Knee

osteotomy surgery refers to resecting part of the tibial or femoral bone to relieve pressure on the arthritic joint.

UKR offers several clinical advantages over TKR including faster recovery, superior functional outcomes, reduced medical complication rates and mortality¹⁰⁻¹³. Economically UKR is associated with lower resource utilisation and higher quality of life, with lower lifetime costs^{14, 15}.

However several joint registries^{8, 16, 17} report UKR revision rates are several times higher than TKR. Additionally there is significant variability in UKR results reported¹⁸ when compared to TKR, secondary to inconsistent selection criteria^{19, 20}, variable surgeon caseloads²¹ and different UKR revision thresholds²².

As a result UKR currently only forms approximately 10% of primary knee replacements in the UK⁸ despite eligibility studies suggesting they should be used in up to 50% of cases¹². In the UK, each operating surgeons' practice is audited by the National Joint Registry of England, Wales, Northern Ireland and Isle of Man (NJR) to monitor their joint replacement revision rates, with outliers detected an early stage and forced to change their practice. Therefore, it is logical for surgeons to avoid an implant with higher reported revision rates, given this can potentially adversely affect a surgeons' practice. Given this, many patients will not be presented with the benefits of UKR when considering treatment for their knee arthritis.

The purpose of this thesis is to investigate UKR revision rates, evaluate current methods employed and to develop new strategies to reduce revision rates. Only by reducing revision

rates can surgeons' confidence in UKR surgery improve and their proportion of primary knee replacements being UKRs improve.

This chapter will discuss the underlying pathophysiology of arthritis and its management. Then the concept of knee replacement surgery will be discussed with current data sources and methods of evaluating joint replacement performance. After this a review of existing TKR and UKR comparative studies will be presented. To conclude, the overall objectives and structure of this thesis will be discussed.

1.2 Pathophysiology of knee osteoarthritis

The principle indication for knee replacement surgery is osteoarthritis in over 97% of cases⁸ and therefore its pathophysiology will form the focus of this section.

The knee is the largest synovial joint and is composed of osseous, cartilage, ligaments and a synovial membrane (Figure 1.1). The osseous structures consist of the tibia, femur and patella. The synovial membrane produces synovial fluid which helps to lubricate the joint and provides nutrition to the relatively avascular cartilage. Given the high usage and loading of this joint, it is rather susceptible to developing osteoarthritis.

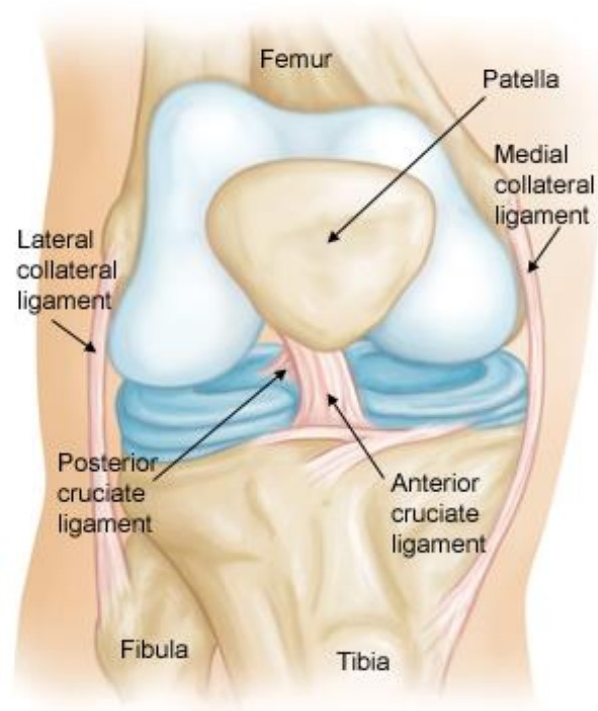


Figure 1.1. Anatomy of the human knee joint. Taken from ²³.

The precise aetiology of osteoarthritis remains unknown although is likely to involve both biomechanical and biochemical stresses. Osteoarthritis used to be regarded as simply a disease of mechanical degradation secondary to wear and tear but is now known to be a much more complex disease, primarily involving the cartilage, subchondral bone and synovial membrane²⁴. Each will be discussed in turn.

Cartilage is produced by chondrocytes and consists of an extracellular matrix (ECM) comprising mainly of type two collagen and proteoglycans including aggrecan. Type two collagen provides a template which is supported by other types of collagen providing tensile strength. Aggrecan is embedded into this template and is hydrophilic, drawing water into the ECM providing compressive resistance.

This ECM normally is in a dynamic state of remodelling where synthetic and degradative enzymatic processes are equivalent. In osteoarthritis the matrix degrading enzymes are upregulated often a result of inflammatory cytokine release after insult to the joint or as part of the ageing process^{24, 25}. This results in a net loss of collagen and proteoglycans. Initially the chondrocytes are able to compensate for this by increasing the amount of ECM produced, but eventually the degradation rates outweigh the generative capacity of chondrocytes. Given the cartilage is subject to various biomechanical and biochemical insults this results in fibrillation and erosions first in the superficial cartilage layers, but later these extend into deeper layers and eventually spread to the entire joint²⁶.

Subchondral bone lies between the calcified cartilage and underlying trabecular bone and is highly innervated²⁴. In osteoarthritis features of endochondral ossification and vascular ingrowth occur resulting in osteophyte and subchondral cyst formation²⁷. Given its innervation, it most likely contributes to the development of pain observed in osteoarthritis.

The synovium consists of synoviocyte cells which produce hyaluronic acid and lubricin which helps to lubricate the articulating surfaces of the knee joint^{28, 29}. These cells can also produce ECM degradative enzymes after joint insult helping to shift the ECM into a net catabolic state³⁰. Additionally synoviocytes have also been shown to reduce lubricating synthesis in osteoarthritis³¹.

1.3 Clinical diagnosis of knee osteoarthritis

According to work from the European League Against Rheumatism³² typical presenting complaints of knee osteoarthritis are disability from; pain which is worse towards the end of the day, pain relieved by rest, the knee joint feeling like giving way and mild morning stiffness. Typically pain increases gradually over time³³. Initially it presents during high level activity and resolves with rest. It then progresses to constant pain on use of the joint and then finally causes pain even at rest. However it is important to note that symptoms can vary widely amongst patients but there is generally little tenderness outside of the knee joint³³.

A clinical diagnosis of osteoarthritis involves a history, examination and usually imaging to confirm the findings. Osteoarthritic features in each are discussed over the next few paragraphs.

Cardinal features in the medical history that help to distinguish osteoarthritis from inflammatory arthropathies include asymmetric joint involvement, morning stiffness lasting less than thirty minutes, lack of systemic symptoms (e.g fatigue, weakness) and pain which is worse on motion but eases at rest³⁴.

On physical examination bony tenderness along the joint line, crepitus, bony enlargement at the joint line and warmth have been identified as key diagnostic findings according to the American College of Rheumatology^{32, 35}. There is also often limited range of motion and pain at extremes of motion.

General hallmark radiographic features of osteoarthritis include joint space narrowing, osteophyte formation, bony cysts and subchondral sclerosis, although all these findings may not all be present on the radiograph^{36, 37}.

Radiographic assessment of the knee usually involves orthogonal plain radiographs (anteroposterior and lateral), whilst the patient is weightbearing. Knee joint osteoarthritis in the majority of cases where the cruciate and lateral collateral ligaments are intact commences in the anteromedial aspect of the tibiofemoral joint with joint space narrowing^{38, 39} (Figure 1.2). As long as the anterior cruciate ligament (ACL) remains intact there is rarely posterior involvement of the medial aspect of the tibiofemoral joint. However as the disease progresses the ACL may rupture from biomechanical strain or trauma. This allows the tibia to sublux laterally and posteriorly, with the disease spreading to involve the posterior tibiofemoral joint with prominent osteophyte formation^{40, 41}. Following this the lateral compartment can also narrow but this is usually less marked than in the medial aspect of the joint³³.

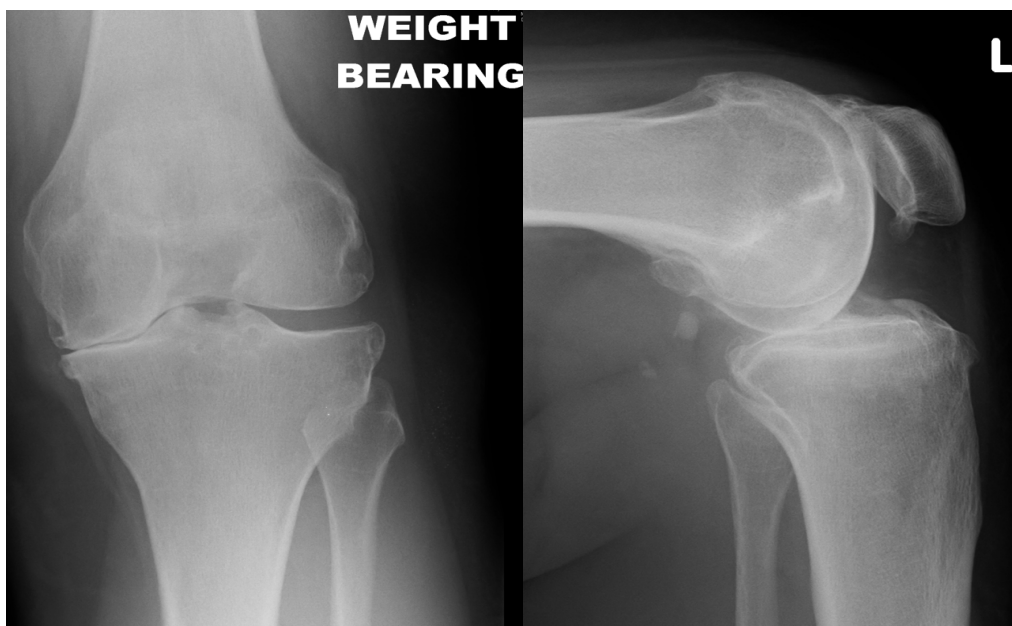


Figure 1.2. Anteroposterior and lateral radiographs of patient with medial compartment osteoarthritis.

1.4 Non-surgical management of knee osteoarthritis

Non-surgical management of knee osteoarthritis can be divided into non pharmacological and pharmacological treatment. The Osteoarthritis Research Society International (OARSI) published recommendations^{42, 43} for each treatment subcategory, based on systematic review evidence.

1.4.1 Non pharmacological treatment

Patient education about knee osteoarthritis, its prognosis, and how to self-manage the condition has been shown to provide moderate benefits for patients^{44, 45}. Self-management refers to the patient's ability to manage the symptoms, treatment, physical and psychological consequences of the condition.

Obese patients with knee osteoarthritis should be recommended to lose weight, given reductions in pain and disability have been reported after a moderate weight reduction regime⁴⁶. Obesity is strongly associated both with osteoarthritis development and the need for knee replacement surgery⁴⁷. Evidence exists that obesity increases the risk of developing knee osteoarthritis five times and twice if overweight⁴⁸. Options include lifestyle modification with a low calorie diet, increased physical activity and anti-obesity medication⁴⁹.

Exercise helps to improve mobility and knee function and can strengthen the muscle around the joint itself. OARSI recommend land based, water based and strength training with all being shown to be effective in improving function⁴².

The role of biomechanical adjuncts in knee osteoarthritis is less clear. Knee braces, sleeves and foot orthoses as directed by a specialist are recommended by OARSI although the systematic review used suffered from significant heterogeneity⁵⁰. There is currently a lack of evidence assessing the impact of crutches and the use of a walking stick has been shown to help reduce pain and improve function in some patients⁵¹. However a walking stick is not recommended for patients with multiple joint osteoarthritis where inappropriate loading on other affected joints may adversely affect these joints⁴².

1.4.2 Pharmacological treatment

Paracetamol is only recommended for individuals without co morbidities given it has been shown to slightly relieve osteoarthritic pain but had increased risk of adverse events related the gastrointestinal tract⁵².

Both topical and oral non-steroidal anti-inflammatory drugs (NSAIDs) are estimated to significantly reduce pain and OARSI guidelines suggest these as first line therapy⁴². Topical NSAIDs have a lower risk of gastrointestinal side effects but increased risk of dermatological adverse events when compared to oral NSAIDs⁵³.

Intra articular corticosteroids have been shown in systematic reviews to offer short term pain relief^{54, 55} but for longer term pain relief OARSI recommends alternative treatment options are sought.

1.5 Conservative surgical treatments for knee osteoarthritis

Surgical treatments are indicated when non-surgical management options fail to improve symptoms and relieve pain. They can be broadly categorised into conservative management where the damaged cartilage is left in situ and radical treatments where the cartilage is replaced. In this section conservative surgical treatment options are discussed.

Knee arthroscopy has rather limited indications, given its effect has not been demonstrated to be beneficial compared to placebo surgery⁵⁶ or medial management⁵⁷. On this basis arthroscopic surgery and lavage is not useful unless there is a structural lesion such as a meniscal tear. However even arthroscopy for meniscal tears has been shown to offer similar results to physical therapy⁵⁸ and increases the risk of needing a knee replacement compared to the general population⁵⁹.

Malalignment is a recognised risk factor for the development of knee osteoarthritis.

Osteotomy involves removing or inserting a wedge in the bone to help to correct the alignment of the knee joint to relieve pain and delay osteoarthritis progression. For example in medial compartment osteoarthritis a high tibial osteotomy (HTO) is performed removing a wedge of bone from the lateral proximal tibial bone. This helps to put the knee joint into a less varus alignment and transfer the load from the medial to lateral compartment. In lateral compartment disease the opposite is true. However it is not known whether osteotomies delay the onset or progression of knee osteoarthritis given there have been no direct trials with appropriate control groups⁶⁰. There have been various studies comparing the clinical outcomes of HTO and UKR surgery. Cao et al.⁶¹ in their systematic review included 10 comparative studies and found that UKR offered lower revision rates, less postoperative pain and fewer complications. However HTO patients benefited from greater range of motion.

1.6 Radical surgical treatments for knee osteoarthritis

The main surgical option for end stage knee arthritis which has failed to respond to non-operative management is knee replacement surgery. Knee replacements have been inserted for the last 40 years and are effective in helping to reduce pain and improve long term function⁹.

Over 100,000 primary knee replacements are performed annually in the United Kingdom alone⁸, with this number projected to increase several fold by 2030⁶² given an increasingly ageing and overweight population⁶³.

The most common indication for knee replacement surgery is knee osteoarthritis with the numbers of replacements for inflammatory arthropathies remaining relatively constant given the success of disease modifying anti-rheumatic drugs⁶⁴.

There are two well established types of knee replacement suitable for end stage medial compartment knee osteoarthritis, total knee replacement (TKR) and unicompartmental knee replacement (UKR) (Figure 1.3).

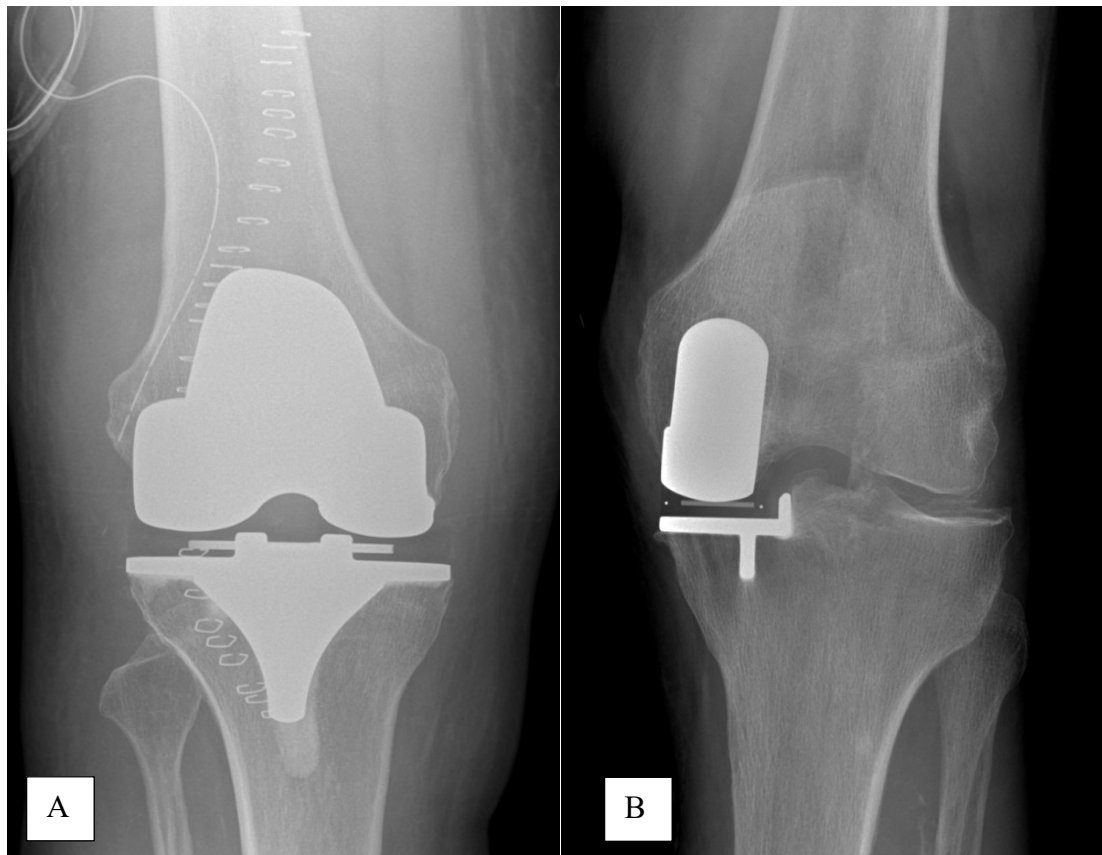


Figure 1.3. Anteroposterior radiographs of knee replacement types. A) Total knee replacement B) Unicompartamental knee replacement.

1.6.1 Total knee replacement (TKR)

TKR involves replacing the whole articulating surface of the knee with a prosthesis and constitutes approximately 90% of all knee replacements performed⁸. The prosthesis usually consists of a metal alloy. In TKR the distal femur and superior surface of the tibia are replaced with metal alloy components. Sometimes the posterior aspect of the patella is also resurfaced with polyethylene. Most TKRs have a fixed polyethylene bearing which is firmly attached to the upper surface of the tibial component. This allows the femoral component to roll on its surface.

The knee joint is much more complex than a simple hinge joint. Its articulating surfaces both roll and glide during flexion and rely on certain ligaments to help stabilise it through these composite motions. As a result there are different types of TKR which either attempt to mimic or retain these ligamentous structures⁶⁵.

In most TKRs the cruciate ligaments are removed to allow more accurate positioning of the implant. The two main types are posterior stabilised and cruciate retaining TKRs and each will be discussed in turn⁶⁵.

In posterior stabilised TKRs the cruciate ligaments are removed but the tibial component has an internal post which fits into a bar in the femoral component to help mimic the function of the posterior cruciate ligament (PCL).

Cruciate retaining TKRs preserve the PCL but remove the ACL and do not have an internal post or bar in the femoral component. These are more appropriate for patients with a healthy posterior cruciate ligament.

Bi-cruciate retaining TKRs are relatively new TKR design and retain both the anterior and posterior cruciate ligaments and evidence on their outcomes is sparse.

1.6.2 Unicompartamental knee replacement (UKR)

UKR involves only replacing the disease affected portion of the knee joint, rather than the complete surfaces of the distal femur and proximal tibial bone. The two main types of UKR are medial and lateral UKRs reflecting whether the medial or lateral aspect of the knee joint are affected⁶⁵.

They consist of a femoral component, tibial component and a polyethylene bearing. The bearing can either be mobile or fixed to the underlying tibial component. The medial knee compartment is most commonly replaced, but rarely when the lateral compartment is also replaced, this is referred to as a bicompartamental knee replacement.

UKR currently constitutes approximately 10% of all primary knee replacements with significant variation in practice throughout the UK⁸ with some surgeons using them in a high proportion of their practice and others not utilising them at all.

The most commonly used UKR is the Oxford UKR and therefore logically will form the focus of this thesis and will be discussed in detail in the subsequent section.

1.7 The Oxford Unicompartamental Knee Replacement

1.7.1 History

The Oxford UKR was first introduced in 1976 by Professor Goodfellow and Professor John O'Connor and introduced the concept of a congruous mobile bearing to knee replacement surgery⁶⁶. This iteration is referred to as the Phase 1 Oxford UKR and consisted of a metal femoral component with aspherical surface and flat metal tibial component. In between the femoral and tibial component was a mobile polyethylene bearing which had a flat inferior surface and a concave superior surface⁶⁷.

The Phase 1 Oxford was initially as a bicompartamental knee replacement, but it was observed that the majority of cases with an intact ACL suffered from anteromedial osteoarthritis and since 1982 was used predominantly as a medial UKR which will form the focus of this thesis⁶⁷. Surgeons struggled with femoral component positioning in relation to the ligamentous structures and matching the flexion and extension gap.

In 1987, the Phase 2 implant was introduced specifically for unicompartamental disease⁶⁷. The non-articulating surfaces of the femoral component had a flat posterior facet and concave inferior facet. This Phase also introduced a femoral mill allowing incremental amounts of bone to be removed from the inferior surface of the femoral condyle. This allowed for the gaps in flexion and extension to be matched intraoperatively and helped to restore ligament tension to normality⁶⁷.

The Phase 3 Oxford UKR was introduced in 1998 and is the most recent iteration. The surgical approach was significantly modified. The Phase 1 and 2 were implanted through an

open approach with patella dislocation. The Phase 3 on the other hand is designed to be implanted using a minimally invasive approach through a medial parapatellar arthrotomy without eversion or dislocation of the patella⁶⁸.

Since the Phase 3 UKR, a cementless Oxford UKR has also been introduced, a Twin Peg cemented UKR and new guiding instrumentation (Microplasty) to try and improve outcomes. However the clinical results from these interventions have not been thoroughly assessed.

1.7.2 Design

Most current knee replacements approximate the shape of the distal femur and proximal tibial bone and usually consist of a convex femoral component surface and flat or concave tibial component which articulate. The issue with this design is that they are not a perfect fit and at any specific time only a small portion of their surfaces are in contact⁶⁷.

Most femoral components are polyradial with the shortest radius posteriorly, meaning less area for contact in flexion than extension. This is problematic given it is known that loads are greatest in flexion and can reach six times that of a human's body weight⁶⁹. Additionally contact pressures are inversely proportional to the contact area and polyethylene wear is said to increase exponentially with increasing contact pressures^{70, 71}. Therefore the less congruous two surfaces are, the higher the contact pressures.

The natural meniscus consists of two congruous surfaces which not only change position on the tibial plateau as needed during flexion, extension and axial rotation, but also their shape, to accommodate the polyradial femoral condyle thereby maximising contact area⁷². In knee extension the greatest radius of the femoral condyle stretches the meniscus in the

anteroposterior direction. The reverse occurs in knee flexion where the smallest radius of the femoral condyle reduces the anteroposterior dimensions of the meniscus. This maximises the articulating contact area with the meniscus transmitting between 45-70% of the load and the other 30-55% being transmitted by the femoral and tibial articular cartilage⁷³. This division of load allows the articular cartilage to withstand these forces. Where the meniscus is damaged osteoarthritic changes of the affected compartment result^{59, 74}.

The Oxford UKR offers two congruent joint interfaces allowing for the advantages of the natural meniscus. The femoral component is spherical, tibial component flat and the polyethylene bearing has a concave superior surface and flat inferior surface⁶⁷. The femoral bearing interface allows angular movements whereas the tibial bearing interface allows for translation. The mobile bearing does not limit movements from surrounding soft tissues. Given the forces are predominantly compressive it is thought that this should minimise the chances of aseptic loosening of the components⁷⁵.

The femoral component used in the Oxford UKR is spherical rather than poly radial given that the bearing cannot change shape like the normal meniscus and accommodate the several radii offered from a polyradial condyle⁶⁷. The only shapes which can maintain congruency throughout are spherical surfaces in a spherical socket and two flat surfaces.

This design is supported from various retrieval, radiostereometric analysis and wear simulation studies which suggest wear rates of about 20 $\mu\text{m}/\text{year}$ which is lower than other reported non-congruent designs in the literature⁷⁶⁻⁷⁹.

1.7.3 Current surgical indications

The precise indications and contraindications for UKR have been controversial. Kozinn and Scott⁸⁰ advised that UKR should not be used in patients under 60, those over 82 kg, heavy labourers and those with exposed bone in the patellofemoral joint as these patients had poorer outcomes.

However these recommendations were based on their experience of fixed bearing UKR surgery. Goodfellow et al.'s experience of mobile bearing Oxford UKR was that as long as the surrounding ligaments remained intact, the majority of patients suffered from anteromedial osteoarthritis (AMOA) and were ideal candidates for UKR surgery⁸¹.

However the surgical indications for the Oxford UKR have become more refined since and define the changes satisfied to make the diagnosis of AMOA. These are bone on bone contact medially, an intact functional ACL, full thickness cartilage laterally and that the medial collateral ligament (MCL) is functionally intact⁸². Studies suggest that up to 50% of patients suitable for knee replacement satisfy these eligibility criteria⁸³.

The contraindications from Kozinn and Scott's work⁸⁰ do not apply as several clinical studies since their seminal paper have shown that age, weight, high activity and patellofemoral osteoarthritis do not adversely affect clinical outcomes⁸⁴⁻⁸⁶.

1.7.4 Clinical results

The first reported results of the Phase 1 Oxford were from Goodfellow et al.'s bicompartmental cohort in 1986⁶⁶. 125 knees had osteoarthritis and the other 74 knees had rheumatoid arthritis. In this cohort PCL deficiency was a contraindication but ACL deficiency was not. Failure was defined as when the Oxford prosthesis was no longer functioning. There were six failures for tibial component loosening (n=4), recurrent bearing dislocation (n=1) and infection (n=1) giving a five year survival of 89%. All failures occurred in knees with damaged or absent ACLs but no differences in outcomes existed between patients presenting with osteoarthritis or rheumatoid arthritis. Goodfellow et al.⁶⁶ also reported eight revisions for five dislocated bearings treated with thicker bearings, and two loose tibial components and one loose femoral component which needed recementing. At mean follow up of four years 89% of knees were reported pain free or had mild pain during activity.

This was followed up in 1992 with a study⁸⁷ of 301 consecutive Oxford UKRs (205 bicompartmentals, 65 medial UKRs and 31 lateral UKRs). Goodfellow et al.⁸⁷ found that six year survival of ACL intact patients was 95% compared to 83% for the ACL deficient knees. Again no differences were found in implant survival of patients with osteoarthritis and rheumatoid arthritis. Given the results of these studies it was decided that an intact ACL was a prerequisite for receiving an Oxford UKR.

In 1993 the first Oxford UKRs (Phase 1 and 2) implanted with intact ACLs and full thickness cartilage were published⁸⁸ and reported a nine year implant survival of 99%. The only revision was for tibial component loosening with bearing displacement five months postoperatively which was revised to a TKR. 75% of patients had no pain on activity, 22%

had mild pain and 3% reported moderate pain. The ten year results were subsequently published as 97.7% (95% confidence interval (CI) 92.7-100)⁸⁹.

The Phase 3 Oxford UKR was introduced in 1998 with the Oxford knee team reporting 10 year implant survivals of 98% (95% CI 93-100)⁶⁸, similar to those reported from previous iterations. However Labek et al.¹⁸ concluded in their literature review that these results were not reproducible outside of Oxford, revision rates three times higher in non-Oxford centres and four times higher in the national registries. Given this there is currently no surgical consensus on what the long term outcomes of the Oxford UKR are.

1.8 Data sources for analysis of outcomes

Data pertaining to the outcomes knee replacements can be obtained from four main data sources; joint registries, individual cohort studies, randomised controlled trials (RCTs) and systematic reviews and meta analyses⁹⁰.

The Oxford Centre for Evidence-based Medicine⁹¹ published guidance in 2009 ranking the level of evidence for each study design, with systematic reviews and meta analyses at the top, followed by RCTs and then individual cohort studies (Figure 1.4).

A sound understanding of the strengths and weaknesses is crucial in understanding the relevance of implant outcomes reported using such data. Each data source will be discussed in turn.

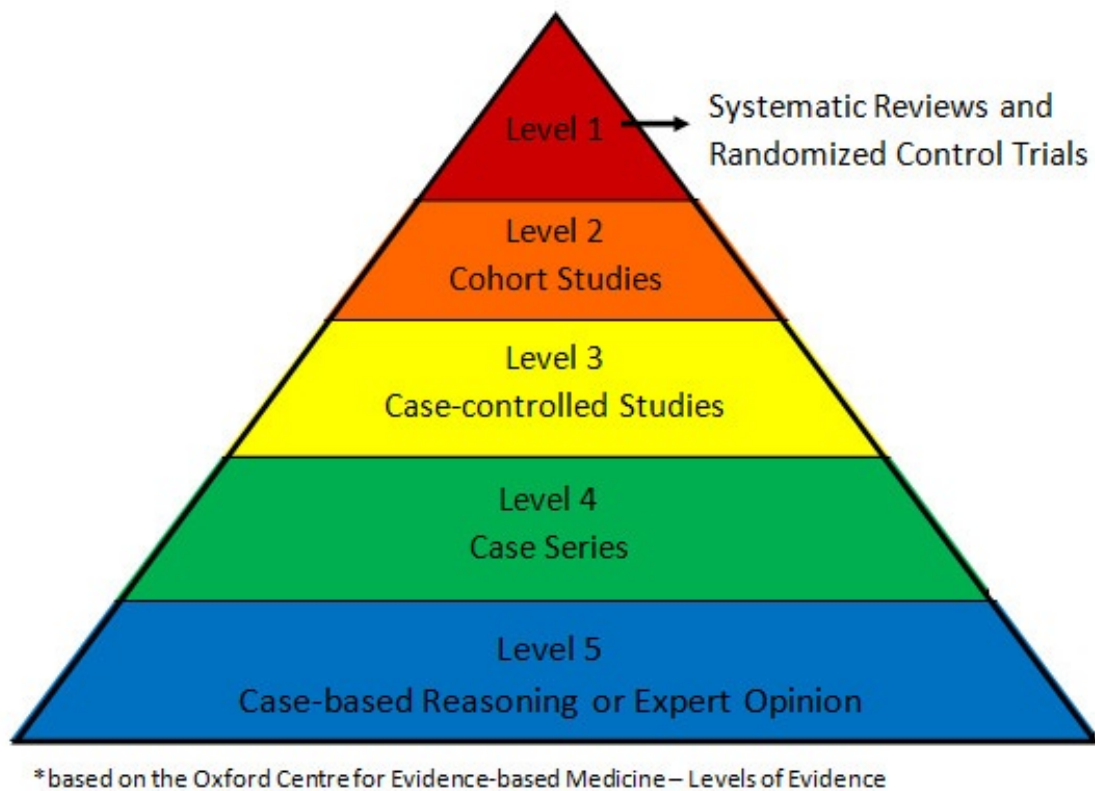


Figure 1.4. The Oxford Centre for Evidence-based Medicine pyramid of Evidence-based Medicine.

1.8.1. Joint Registries

Registries are a critical part of any healthcare system and collect pre specified relevant raw data longitudinally. This helps improvements in the levels of care provided to patients and promotes an evidence based approach to healthcare⁹². They allow monitoring of changes in outcomes over time, the distribution of healthcare in their respective regions and analysis of rare adverse events⁹³.

Specifically the first concept of a joint registry was first developed from Sir John Charnley who in 1972⁹⁴ recommended that a central joint registry should be created to monitor joint replacements on a national level so that surgical outcomes could be scrutinised. Interestingly

he also stated that this would be fiercely opposed by the Orthopaedic community as this would bring them under scrutiny, but if their outcomes were good there would be no reason to refuse participation.

Patients expect their joint replacements to provide a long term functional and pain free outcome with the procedure being complication free, tissue sparing with appropriate follow up postoperatively^{95, 96}. Given the influence of industry in implants used for joint replacements, a joint registry should be presented in a fashion that allows both clinicians and patients to distinguish truth from false claims whilst simultaneously protecting the patients' confidential data⁹⁷⁻⁹⁹.

The principle aims of a registry are to identify poorly performing implants at an early stage to prevent them being implanted at a larger scale and to allow surgeons to compare their results with colleagues⁶⁷. The first national joint replacement registry was established in Sweden (1975), followed by Finland (1980), Norway (1987), Denmark (1995) and Australia/New Zealand (1998)⁶⁷.

Specifically in the UK the Trent Regional Arthroplasty Study¹⁰⁰ and North West Arthroplasty Register¹⁰¹ were established in the 1990s and although it was recommended that a National Registry was established in 1996¹⁰², this did not happen. In 1997 the 3M Capital Hip was found to have much higher rates of femoral component loosening¹⁰³ resulting in the Medical Devices Agency recommending that all patients with the device implanted be called for clinical review¹⁰⁴. This created significant problems given many patients with the Capital Hip could not be traced¹⁰⁵ and resulted in significant public distress and media attention. The Royal College of Surgeons of England concluded that if a hip registry was in place then these

poorly performing hip replacements could have been detected earlier and recommended the formation of a joint registry¹⁰⁶. In 2002 under Lord Hunt's recommendation the National Joint Registry of England, Wales, Northern Ireland and Isle of Man (NJR) was formed in the UK and started collecting data from April 2003.

Most registries produce an annual report and have a process by which data can be requested for research purposes. The advantages of registries are that they collect data on a large number of patients over an extended period of time. Given participation is obligatory in many countries¹⁰⁷ this minimises publication and reporting bias. As the data collected related to the whole population this allows for a large diversity of cases in terms of implant type, surgical technique, surgical experience, patient selection and postoperative regimens.

Registries are a powerful resource for three main type of analyses⁹³. The first is descriptive purposes such as in a cross sectional manner like the number of replacements performed each year and correlation of covariates. The second is longitudinally for trends in such as patient characteristics over time and analytically to investigate risk factors for revision surgery and for implant comparative studies. The large numbers also allow for subgroup analyses with appropriate power. The third is for the evaluation of public health efforts.

However registries are not without their limitations. Given they collect data on a large scale and rely on operating centres for information, this significantly limits the amount of data which is obtained for each case. Registries only collect outcome data on revision and mortality^{8, 16, 17}. Although revision outcomes are relatively straightforward to collect, they have several limitations. Given revision surgery is regarded as a failure, if it has not been revised it is considered a success even if the implant is painful and does not offer good

function to the patient¹⁰⁸. Registries do not record outcomes such as reoperations and complications (such as amputations or fusions) and do not assess functional or pain outcomes.

Additionally registries record the reasons for revision at the time of surgery, even if these subsequently change from later available histopathology and microbiology results. There is also evidence that registries can under report the revision rate¹⁰⁹. Furthermore registries do not typically collect pre and postoperative radiographs, the specific indications for surgery and the volume of the operating surgeon performing the procedure. These potential confounders can influence raw results for each implant type reported in the registry reports.

1.8.2. Individual cohort studies

A cohort study is when information is collected on a group of patients over a period of time and comparisons made to determine whether risk factors occur more or less frequently in those which develop the adverse outcome⁹⁰. The design of these studies can be retrospective or prospective in nature. The outcome measures are chosen prior to the inclusion of patients.

These studies can be used to study trends and monitor the outcomes of patients over an extended period of time and are relatively cost effective as the patient data can be collected as they attend their routine clinical follow up. Additionally they can benefit from relatively large sample sizes of patients who meet specific inclusion criteria allowing a more homogenous population than registries can provide. Furthermore specific data on outcomes other than revision can be obtained including radiographs, blood results, reoperations, complications and patient reported outcome measures (PROMs).

However prospective study designs have the potential for selection bias unless a consecutive series of patients with a certain diagnosis are included. Retrospective study designs are often limited by the data fields captured, as these were not captured for the specific study in mind. Both prospective and retrospective designs are also prone to bias from various confounders. Examples include if the study centre has a particular referred patient demographic, overly specific diagnostic criteria excluding relevant patients and having a non-representative clinical team. These factors can all limit the generalisability and relevance of the results. Finally these studies may simply be case series with no comparative arm to compare treatments and when cohorts are compared to others this must be done with caution as other confounders may explain differences observed.

1.8.3. Randomised controlled trials

A RCT randomly allocates patients to a treatment arm and a control group which can be positive in which the patient receives treatment or negative with a placebo where no active treatment is received⁹⁰. The randomness of allocation helps to evenly distribute confounders between groups allowing fair comparison of outcomes¹¹⁰.

It is also important that the trial is free from systematic subjectivity and treatment bias. If the clinician believes the treatment arm is superior this can lead to assessment bias of the outcomes of interest. Or the clinician could withdraw patients from the study with prior knowledge constituting attritional bias. A single blinded study would have one of the clinician, patient or investigator blinded. If two of the three are blinded this becomes double blinded and if all three are blinded this becomes triple blinded which is the gold standard¹¹⁰. The blinding should be maintained until the end of the study after all the analysis is performed.

Advantages of RCTs include that the randomisation process minimises selection bias and control over confounding factors is enhanced with even unknown factors being evenly distributed between comparative groups. Additionally the studies are prospectively adequately powered for their specific question of interest¹¹⁰.

However, RCTs are not without their limitations. First of all if an RCT is not adequately blinded they are no better than observational studies (individual cohorts and registries). In fact this is mostly the case in Orthopaedics with reports that over 50% of RCTs¹¹¹ have poor randomisation, blinding, outcome measurements and are inadequately powered¹¹².

Additionally if they are not adequately powered they may be susceptible to type two error and not detect a real difference between groups⁹⁰. They are not ideal for detecting rare events such as revision or to conduct subgroup analyses, as these would require very large numbers of patients impractical for an RCT. Finally they are very expensive to run and often do not continue in the long term, meaning long term outcomes are rarely studied. Additionally given they often take considerable time to publish, practice has often progressed since their inception limiting their relevance¹¹³.

1.8.4. Systematic reviews and meta analyses

Systematic reviews and meta analyses are regarded as the highest level of evidence as per the Oxford Centre for Evidence-based medicine⁹¹. They bring together existing published studies to synthesise results and have the advantage of pooling together large numbers of patients from studies all across the world whilst not losing the ability to analyse several relevant outcomes of interest.

However systematic reviews are subject to systematic error and publication bias⁹⁰.

Additionally they are only as reliable as the quality of studies that they are combining. If the primary studies are poor quality the systematic review will not yield useful results although they can help direct where future research is needed from unanswered questions.

Inevitably the studies brought together in a systematic review will have variation also known as heterogeneity. There are three types of heterogeneity, clinical, methodological and statistical heterogeneity¹¹⁴. Clinical heterogeneity refers to differences in patients, interventions and outcomes between studies. Methodological heterogeneity refers to variability in study design and risk of bias. Statistical heterogeneity refers to variations in the intervention effects being analysed in the different studies more than what one would expect from random chance. This is often a consequence of clinical or methodological heterogeneity or in some cases both.

Therefore it is crucial that a systematic review assesses a specific question, uses a comprehensive search strategy, appropriate inclusion and exclusion criteria, assesses studies risk of bias, evaluates heterogeneity and discusses the limitations of its findings¹¹⁵.

1.9 Comparison of TKR and UKR

The two most common types of knee replacement are TKR and UKR. It is estimated that up to 50% of patients in the UK present with isolated unicompartamental osteoarthritis and hence would be eligible for either treatment option⁸³.

Therefore it is of utmost importance that these two replacements are compared in order to offer the best treatment options for patients. Decisions should be shared between clinician and patient and made once both parties recognise the benefits and risks of both treatment options available¹¹⁶⁻¹¹⁸.

The current gold standard assessment of knee replacement outcomes, is the implant's revision rate²². Revision is defined as the removal, addition or exchange of components used for the knee replacement^{8, 16, 17}. On its own, it is a limited outcome measure as it does not assess the function obtained from the replacement, the quality of life, medical complications, mortality and other operative procedures not meeting the strict definition of revision such as manipulations under anaesthesia (MUA) and washouts. Hence a patient suffering any of these outcomes but not revisions are classically regarded as successful¹⁰⁸.

These other outcome measures are essential to be discussed with the presenting patient, otherwise their decision would not be deemed as fully informed^{119, 120}. The James Lind Alliance is an organisation which brings together clinicians, patients and carers to discuss the priorities for research. The leading research priority for knee and hip replacements identified by the James Lind Alliance was the most important clinical outcomes¹²¹.

In the next few sections a review of the literature comparing TKRs and UKRs is presented using various data sources and clinical outcome measures to understand each knee replacements' advantages and disadvantages.

1.9.1 Current usage in the United Kingdom

The NJR is the largest dataset in the world⁸ with over one million knee replacements recorded with a maximum follow up of 15 years. 97.4% of knee replacements are performed for osteoarthritis as the only indication⁸.

Despite up to half of patients presenting with knee osteoarthritis being eligible for either TKR or UKR, there are large differences in the usage of UKR and TKR. The 2019 NJR annual report⁸ shows that of the 1,193,830 primary knee replacements recorded between 1st April 2003 and 31st December 2018, 1,070,873 (89.7%) were TKRs and 122,910 (10.3%) were UKRs. Although these proportions have remained fairly constant there has been a recent increase in UKR use which rose to 10% for the first time in 2017.

However enormous variations exist in usage of UKR both geographically and between centres in the same region. Liddle et al.²¹ calculated the average surgeon caseload for each surgeon in the NJR (n=2589) using their unique surgeon ID between 2004 and 2012. Surgeons who used UKR (n=1272, 49%) performed an average of only 5.4 cases (standard deviation (SD) 9.3) per year with the most common mean UKR caseload being 1 case/year. However several surgeons had UKR caseloads ≥ 30 cases/year. Surgeons who used TKR (n=2536, 98%) performed a mean of 33.6 procedures/year (SD 32.5).

In terms of the patient demographic receiving knee replacements, the median age of patients receiving TKR was 69 years (interquartile range (IQR) 63-76) and those receiving UKR were on average 5 years younger at 64 years (IQR 57-70)⁸. Additionally for TKR the majority of patients are female (56.8%) compared to UKR where the majority of patients are male (53.1%)⁸.

1.9.2 Revision rates

As discussed in section 1.9, revision is defined as the removal, addition or exchange of components used for the knee replacement^{8, 16, 17}. This is currently the gold standard outcome measure for a knee replacement.

All large national registries^{8, 16, 17} report that the revision rates for UKR are overall on average about three times higher than TKR using raw data collected (Table 1.1). As a result most surgeons believe that UKR has poorer results and should not be used. However this is an oversimplification as raw data does not take into consideration various confounding factors including indications for surgery, revision threshold, surgeon volume, patient demographics and surgical technique. There is obvious disparity in the caseload of surgeons performing UKR and TKR and the average age of patients undergoing UKR is 5 years younger⁸.

Registry	TKR survival	95% CI	Oxford UKR survival	95% CI
National Joint Registry of England, Wales, Northern Ireland and Isle of Man (2019) ⁸	96.6	96.5 - 96.6	88.7	88.3 – 89.0
Australian Joint Registry (2019) ¹⁶	94.7	94.7 - 94.8	85.2 (Cemented) 87.8 (Cementless)	84.5 - 85.8 (Cemented) 85.6 - 89.7 (Cementless)
New Zealand Joint Registry (2019) ¹⁷	95.2	95 - 95.3	86.0 (Cemented) 92.3 (uncemented)	84.7 - 87.1 (Cemented) 90.9 - 93.5 (uncemented)
Dutch Joint Registry (2019) ¹²²	94.1	94.0 – 94.3	85.4 (Cemented) 86.5 (Cementless)	84.4 - 86.4 (Cemented) 80.6 - 91.8 (Cementless)

Table 1.1. 10 year TKR and Oxford UKR implant survivals reported in the Joint Registries.

Another issue is that given UKR is more bone conserving, most surgeons will have a lower threshold to revise than they would if a patient had a TKR⁶⁷. A UKR revision is a relatively straightforward conversion to a TKR whereas a TKR revision often involves the use of stems, wedges and augments¹²³. Additionally patients who undergo a UKR revision report more satisfaction with their knees than those who undergo a TKR revision¹²⁴.

An example of this was in the Trent Regional Replacement Registry which found that the lowest knee replacement revision rate was for the Sheehan knee which is no longer available given its poor performance^{125, 126}. However because of the implant size, surgeons would rarely revise the implant given the surgery would be so complex.

There are a few RCTs comparing the revision rates of UKR to TKR with conflicting results. Ackroyd et al.¹²⁷ conducted the first RCT comparing the St Georg Sled UKR to Kinematic modular TKR and found that at five years there were no differences in failure but at 15 years the implant survival for UKR (90%) was better than TKR (79%). Sun et al.¹²⁸ randomised patients to the Oxford UKR or the AGC TKR and found at four years that (7/52) needed a revision in the UKR group for tibial loosening/subsidence compared to 0 in the TKR group. Costa et al.¹²⁹ inserted UKR and TKR as simultaneous bilateral replacements in the same patient and found implant survivals of 85% and 100% respectively with this difference being significantly different. More recently the five years results of TOPKAT¹³⁰, the largest RCT comparing TKR and UKR were published. This large multi-centre RCT found fewer revisions in the UKR group although the differences were not statistically significant. However the authors state that the study was underpowered to detect differences in revision and only looked at mid rather than long outcomes.

The most powerful comparison to date was a matched study performed by Liddle et al.¹⁰ Liddle et al.⁷⁴ performed a matched comparison of 25,334 UKRs and 75,996 TKRs using NJR data linked to Hospital Episodes Statistics (HES) database which holds all the medical records of a patients admissions to hospitals in England. Patients were propensity matched on patient demographics, implant factors and surgical factors. They found that at eight years the revision rate for UKR was 2.12 (95% CI 1.99 - 2.26) times higher with UKR than TKR.

Wilson et al.¹² performed a meta-analysis of comparative studies of UKR and TKR. They stratified their analysis based on the study type into RCTs, health databases and cohort studies. They found significantly higher revision rates for UKR in all study types with risk ratios of 5.95 (95% CI 1.29 - 27.59), 2.50 (95% CI 1.77 - 3.54) and 3.13 (95% CI 1.89 - 5.17) respectively.

Therefore UKR revision rates are currently problematic, given they are several times higher than TKR. This will form the focus of this thesis.

1.9.3 Reoperation rates

Reoperation is defined as any surgery performed on the replaced joint. This includes arthroscopies, MUAs and washouts.

Reoperation data is not currently collected in the Joint Registries^{8, 16, 17} and therefore this outcome can only be assessed looking at existing clinical studies. On review of the literature outcomes using the endpoint reoperation are poorly reported. This is surprising given this is an important outcome for patients as they would want to know the probability of returning to theatre for further interventions after primary surgery.

Wilson et al.'s¹² meta-analysis of comparative studies found no significant differences in reoperations rates of UKR and TKR in included RCTs and health database groups. However a lower reoperation rate for UKR was reported on comparison of included cohort studies.

More recently the TOPKAT study¹³⁰ reported five year reoperation rates of 9% and 10% in the UKR and TKR comparative groups with this difference not being significant although the study was not powered to detect differences in reoperations.

1.9.4 Mortality

An understanding of the rates of mortality in UKR and TKR is crucial to help facilitate the discussion between the clinician and patient in determining which type of replacement is most appropriate considering all the risks and benefits. Without a sound understanding of this outcome, consent cannot be truly informed.

The NJR⁸ do not place much emphasis on this in their annual reports. In their 2018 report⁹⁰ this is reported over a couple of pages with the analysis only being stratified by age and gender and not by implant type.

Liddle et al.¹⁰ in their large propensity matched comparison of UKR and TKR found significantly lower mortality at 30 days, 90 days, one year, four years and at eight years for UKRs. This difference was statistically significant. Additionally the rates of intraoperative complications, blood transfusion, thromboembolism, stroke and myocardial infarction were all significantly lower in the UKR group.

Wilson et al.'s¹² meta-analysis supported these findings. They assessed early mortality within the first 45 days of surgery and found significantly reduced mortality in the UKR group with a risk ratio of 0.27 (95% CI 0.16-0.45). Additionally the rates of myocardial infarction, cerebrovascular and thromboembolic events were significantly lower in the UKR group.

This was further supported in the TOPKAT RCT study¹³⁰ which found from the 17 deaths reported six were in the UKR group and 11 were in the TKR group. However this study was not adequately powered to detect differences in mortality.

1.9.5 Patient reported outcome measures

PROMs are validated questionnaires completed by patients which assess their quality of life¹³¹. They offer significant insight into the function and pain a patient experiences after surgery and have been routinely used by the National Health Service (NHS) since 2009 for assessing the outcomes of knee and hip replacements¹³². The most commonly used PROMs used for knee replacements are the Oxford Knee Score (OKS), American Knee Society Score – Objective (AKSS-O), American Knee Society Score – Functional (AKSS-F) and the Tegner activity score. A summary of commonly used PROMs are in Table 1.2.

It is important to emphasise that a statistically significant difference in PROMs between comparative groups is not necessarily meaningful. The minimally clinically important difference (MCID) is defined as the smallest change in score that an individual patient would regard as being important¹³³. Therefore any significant differences between comparative groups should also have a difference equal to or greater than the MCID to be clinically meaningful.

Patient reported outcome measure	Origin	Description	Scale	Minimally clinically important difference
Oxford Knee Score (OKS) ¹³⁴	Oxford, United Kingdom	12 questions on pain and function over the last four weeks. Each question is scored from 0-4. Each questions score is added to give overall final score.	0 (Worst) – 48 (Best)	4 points ¹³⁵
American Knee Society Score – Objective (AKSS-O) ¹³⁶	New York, United States	Series of questions assessing pain in 50 points, stability in 25 points and range of motion in 25 points.	0 (Worst) – 100 (Best)	5.9-7.8 points ¹³⁷
American Knee Society Score Functional – (AKSS-F) ¹³⁶	New York, United States	Series of questions assessing walking distance in 50 points and act of climbing and descending stairs in 50 points.	0 (Worst) – 100 (Best)	6.1-6.4 points ¹³⁷
Western Ontario and McMaster Universities Arthritis Index (WOMAC) ¹³⁸	Ontario, Canada	Five questions on pain (0-20 points), two questions on stiffness (0-8 points) and 17 questions on functional limitation (0-68 points).	0 (Worst) – 100 (Best)	10 points ¹³⁹
Knee injury and Osteoarthritis Outcome Score (KOOS) ¹⁴⁰	Lund, Sweden	Nine questions on pain, seven questions on symptoms, 17 questions on activities of daily living, five questions on sports and recreation, four	0 (Worst) – 100 (Best)	8-10 points ¹⁴⁰

		questions on quality of life.		
EuroQol Five Dimension Scale Visual Analogue Scale ¹⁴¹	Europe	Continuous scale from 0 to 100 where patient is asked to rate overall health.	0 (Worst) – 100 (Best)	9 points ¹⁴²
Tegner Activity Score ¹⁴³	Linkoping, Sweden	A question with 10 levels of activity patient is able to do. Level 0 refers to sick leave/disability from knee problems whereas 10 refers to competitive football.	0 (Worst) – 10 (Best)	N/A
Hospital for Special Surgery Knee Score (HSS) ¹⁴⁴	New York	Seven categories including pain, function, range of motion, muscle strength, flexion deformity, instability and subtractions.	0 (Worst) – 100 (Best)	8.3 points ¹⁴⁵

Table 1.2. Commonly used patient reported outcome measures used for knee replacements.

PROMs are not routinely collected in the registries^{8, 16, 17} and hence can really only be comprehensively analysed and compared using data from existing clinical studies and PROMs databases.

Wilson et al.'s¹² systematic review was designed to detect differences between UKR and TKR PROM scores. They found significantly better functional scores in for UKRs than TKRs although they did not find any differences in pain scores. However this analysis is limited as the authors combined all post-operative PROM scores after six months, rather than stratifying this over specific time periods. This would have contributed significant heterogeneity to their analysis evidenced by the I^2 statistic (percentage of variance in the meta-analysis attributable to study heterogeneity) reaching as high as 94%.

The KAT trial¹⁴⁶ reported the 10 year Oxford Knee Scores of TKR with and without patellar resurfacing as being 33.6 (SD 11.3) and 33.5 (SD 10.8) respectively. This is remarkably lower than those reported in the UKR which are commonly reported as being over 40 at 10 years^{68, 82, 147, 148}. This difference of 6.5 points is clearly larger than the MCID of four points and suggests that patients have better functional outcomes with UKR.

The TOPKAT study¹³⁰ found that although UKR had a higher 5 year OKS of 38 (SD 10.1) compared to 37 (SD 10.6), this difference was not statistically or clinically significant. However they found significantly higher ($p=0.004$) EuroQol Five Dimension Scale (EQ-5D) visual analogue scores in the UKR group suggesting better health status in UKR patients at five years follow up.

1.9.6 Cost effectiveness

Various studies have compared the cost effectiveness of TKR and UKR. Burn et al. performed a systematic review¹⁴ of comparative economic evaluation studies. They found that UKR was less costly than TKR and was associated with greater increases in quality adjusted life years. However the cost effectiveness was much better in UKR for older age groups and less certain in the younger demographics.

Burn et al.¹³ followed this up with a registry based comparison using NJR data using a lifetime Markov model factoring in the higher revision rates of UKR compared to TKR. The analysis included 25,334 and 75,996 propensity matched UKRs and TKRs respectively. They found significant cost savings throughout the patient's life across all age groups and genders, ranging from £601 to £1223 (Table 1.3).

Gender	Male			Female		
Age groups	<60 years	60-75 years	75+ years	<60 years	60-75 years	75+ years
Cost savings from UKR	£1223	£1355	£2005	£601	£935	£1102

Table 1.3. Costs savings from UKR in different age groups. Adapted from¹³.

This work has been additionally supported by the TOPKAT RCT study¹³⁰ that reports five year results showing cost savings of £910 (95% CI £317-£1503) during the study period. However work by Koskinen et al.¹⁴⁹ using the Finnish Arthroplasty Register found that although UKR was more cost effective in the short term, in the long term TKR was more cost effective given the higher revision rates in the UKR group.

1.10. Implications for the Oxford UKR

The comparison of existing literature clearly indicates that UKR offers significant advantages over TKR including improved functional outcomes, lower mortality, lower risk of major medical complications, better cost effectiveness and similar reoperation rates.

Given that currently UKR are only used in 10% of cases, despite being eligible for up to 50% of cases⁸³, this is concerning given there are several advantages over TKR. Additionally this raises questions over how informed patients' consent is for TKR. The only explanation for this disparity in usage must relate to UKR's revision rate, which is currently several times higher than those of TKR. It is therefore pertinent that these higher revision rates are addressed.

The most commonly used UKR is the Oxford UKR⁸ and hence it is logical to direct efforts to this implant in solving the UKR issue. Henceforth the Oxford UKR will form the focus of this thesis.

A consensus first needs to be reached on what the Oxford UKR long term outcomes actually are. Although the registries suggest higher revision rates, this needs to be investigated in clinical studies across the world. Registries are often limited to certain countries and have significant limitations including data quality issues¹⁰⁹ and were discussed in depth in section 1.8.1. To date there have been no reviews of the long term outcomes of the Oxford UKR. A review of all long term studies across the world would prove useful in understanding not only the Oxford UKR's revision rate, but its mechanisms of failure.

Several changes have been implemented to the Oxford UKR in an attempt to lower its revision rate including, cementless fixation, a new femoral peg design and new guiding instrumentation. However it is currently unknown whether these interventions have any effect on revision rates.

Therefore this thesis will assess the long term outcomes of the Oxford UKR, the effect of previously implemented interventions and then develop new strategies to improve the implant's performance. The structure of the thesis will be outlined in the next section.

1.11 Thesis objectives

The purpose of this thesis is to use an evidence based approach to optimise the outcomes of Oxford UKR by identifying modifiable factors associated with lower revision rates. To do this this thesis has three broad objectives.

- 1) To first assess the long term outcomes of the Oxford UKR and the mechanisms of implant failure. Only by a comprehensive understanding of this baseline can current and new interventions to developed.
- 2) To assess current strategies employed to reduce UKR revision rates
- 3) To develop new strategies to reduce UKR revision rates.

The null hypothesis of this thesis is that the current strategies employed do not currently lower revision rates and therefore new strategies need to be developed to lower these in order to increase the future usage of UKR.

1.12 Thesis scope and structure of thesis

The first experimental chapter (Chapter 2), investigates the global long term clinical outcomes reported of the Oxford UKR. This looks at various clinical endpoints including revision, reoperation, non-revision reoperation, medical complications, mechanisms of implant failure and patient reported outcome measures. The results from this chapter are critical and guide the other chapters of the thesis. Chapter 3 focuses on the clinical and radiographic results of cementless Oxford UKRs inserted under the recommended indications by the surgeons involved in the development of the current version of the Oxford UKR.

Given the promising results of the cementless Oxford UKR reported in Chapter 3, Chapter 4 consists of two parts comparing the outcomes of cemented and cementless Oxford UKRs. The first part compares cemented and cementless Oxford UKRs using data from the NJR. The second part makes the same comparison in a systematic review looking at all UKR brands across the world.

Chapter 5 analyses the effect of other critical factors on revision rates in the NJR. These include surgeon caseload, new guiding surgical instrumentation and modifying the design of the femoral component.

Chapters 6 and 7 focus on developing new strategies to lower UKR revision rates. Chapter 2 identifies bearing issues as leading causes for revision and Chapter 4 demonstrates that periprosthetic fractures are more common in cementless fixation. Therefore Chapter 6 involves comparing the long term wear rates of three different types of polyethylene used in the Oxford UKR, which helps select the most appropriate polyethylene. Chapter 7 is an

experimental study of new tibial cutting surgical instrumentation can reduce the risk of periprosthetic fracture in the cementless Oxford UKR.

Chapter 8 summarises the key findings and conclusions of this thesis and recommends future work based on any unanswered questions or limitations.

2. SYSTEMATIC REVIEW OF THE LONG TERM OUTCOMES OF THE OXFORD UKR

2.1 Introduction

The first step of this thesis is to calculate the long term revision rate of the Oxford UKR.

Although excellent results within Oxford are frequently reported for the Oxford UKR with implant survivals frequently exceeding 95% at 10 years, this has not been reproduced in Joint Registries^{8, 16, 17} across the world (Table 1.1). This has led to some¹⁸ understandably raising concerns regarding the validity of these results, thereby resulting in uncertainty of what the outcomes of the Oxford UKR are. As a result many surgeons avoid the implant given this uncertainty.

Variability in outcomes can be from patient, implant or surgical factors. Patient factors include the selection criteria for surgery outlined in section 1.7.3 as per Goodfellow et al.⁸¹ Implant factors refer to the actual design of the prosthesis and surgical factors refer to the operating surgeons' ability and technique.

* This chapter has been published¹⁴⁷ as: Mohammad HR, Strickland L, Hamilton TW, Murray DW. Long-term outcomes of over 8,000 medial Oxford Phase 3 Unicompartamental Knees—a systematic review. *Acta Orthop* 2018; 89(1): 101-107. (Appendix 1).

In helping to bring a consensus on an implants performance it is important to recognise the limitations of registry data to help interpret results appropriately. The data is often significantly limited from not having radiographs and detailed indications for primary surgery. However most importantly the majority of surgeons in the registries perform only a single UKR case per year²¹. Additionally no information is given on reoperation rate, PROMs and medical complications which are important outcomes for patients.

Kennedy et al.¹⁵⁰ performed a study in which they linked a subset of Oxford UKR revisions cases from the NJR to preoperative radiographs from various centres to analyse whether the specific indications for Oxford UKR surgery were appropriate. They found that the recommended indications were only satisfied in 70%, with major technical errors seen in 6%. However worryingly, no reason for revision indication was observed in 67% of revisions performed.

Additionally given the most common caseload from surgeons in the NJR is one UKR case/year compared to the 34 TKR cases/year, this would adversely affect UKRs' outcomes compared to TKR. Liddle et al.²¹ found that surgeon caseload significantly affected revision rates with caseloads greater than 30 UKR cases/year having the lowest revision rates. In addition less experienced surgeons performing UKR would be more likely to revise a UKR to TKR, simply because they would be more familiar with TKR surgery and the revision is fairly straightforward.

Therefore the results from the registries should be compared to those from cohort studies across the world to help bring a consensus on what the long term outcomes of the Oxford UKR actually are. This would satisfy critics of the Oxford UKR, given results from all over

the world outside of Oxford would all be included in the analysis. Currently there have been no systematic reviews of the Oxford UKR's long term performance. The objective of this chapter is to present a systematic review of the long term outcomes of the Phase 3 Oxford UKR reported across the world using various outcome measures.

2.2 Patients and methods

PROSPERO is an international database of registered systematic reviews investigating healthcare related issues and records key details of a research protocol "a priori" and forms a record of the review. This helps to prevent duplication of review articles.

This systematic review was prospectively registered on PROSPERO and given the identifier CRD42017058005 as per the preferred reporting items for systematic reviews and meta analyses (PRISMA) guidance¹⁵¹.

2.2.1 Inclusion and exclusion criteria

The inclusion criteria were all studies in the English language reporting the ≥ 10 year clinical outcomes of the Oxford Phase 3 medial UKR for patients equal to or over 18 years of age. Although no registry studies or reports were identified by our search, we did not intend to include them anyway, given their limitations in data pooling, potential to underestimate revisions¹⁰⁹ and to prevent duplication of patients. Furthermore, clinical studies provide more details about patient demographics and the specific implant type (for example the type of fixation and whether it is medial or a lateral UKR) allowing us to determine whether they should be included or not. We excluded case reports from our review.

2.2.2 Search strategy

Given the Oxford Phase 3 UKR was first introduced in 1998, this means that the 10-year outcomes of the implant can only be reported from studies published from 2008 and onwards. With the assistance of an expert information analyst (Eli Harris), the databases Medline, Embase, Cochrane Central Register of Controlled Trials (CENTRAL) were searched from January 2008 to December 2016.

Key words used in the search strategy included ‘knee replacement’, ‘partial’, ‘unicompartmental’, ‘unicondylar’ and all synonyms, abbreviations and variations in spellings of these terms. The full search strategies used are listed in Appendix 2. Additionally five abstracts from papers presented at the Oxford Partial Knee 40 Year Symposium were included. All five abstracts are available in Appendix 2.

Search results from the databases had titles and abstracts assessed for shortlisting based on the eligibility criteria specified in section 2.2.1 by two independent reviewers (Hasan Raza Mohammad and Louise Strickland). All shortlisted papers had full papers obtained and assessed to confirm eligibility. In cases in which more than one paper had been published on the same cohort of patients, the most recent paper using the entire cohort was used and the others excluded to prevent overpowering analyses by duplicating UKRs included. There was complete agreement between the two independent reviewers (Hasan Raza Mohammad and Louise Strickland) regarding the inclusion and exclusion of all papers for this review.

2.2.3 Outcomes of interest

The primary outcomes of interest were; (1) Revision rate (2) Non revision reoperation rate (3) Reoperation rate and (4) Implant survival at ≥ 10 years. Secondary outcomes of interest were; (1) Revision indications, (2) ≥ 10 year PROMs and (3) Medical complications.

Revision was defined as the removal, addition or exchange of any implant component from primary surgery as per the joint registries^{8, 16, 17}. Reoperation was defined as any sort of surgical intervention and included all revisions and surgical procedures which would not conventionally classify as revisions such as MUAs and arthroscopies. Non revision reoperation was defined as a reoperation which did not classify as a revision. Medical complications were defined as any adverse medical event postoperatively. This included myocardial infarctions, strokes, pulmonary embolisms (PE) and deep vein thromboses (DVT).

2.2.4 Risk of bias and data collection

All included studies were assessed for risk of bias using the methodological index for evaluation of non-randomised studies (MINORS)¹⁵² with an additional established scoring system based on the presence of reporting our primary outcome of interest^{153, 154} (A=clearly reported, B=non reported/unclear) and the number of cases in the studies (A>100, B=51-99, C=<50). Studies with a MINORS score over 80% were considered low risk of bias and those below 70% at high risk except those with 3 or more “A” in outcome reporting and study size¹⁵³.

All data was extracted independently by two reviewers (Hasan Raza Mohammad and Louise Strickland) and where data was missing authors were contacted in an attempt to obtain this information.

2.2.5 Data synthesis and analysis

The unit of analysis used in this review is the number of UKRs. The outcomes revision, non-revision reoperation and reoperation were calculated per 100 observed component years which is equivalent to the annual rate (% per annum (pa)) and is a well-established methodology of the joint registries^{16, 17}.

The total observed component years was calculated by multiplying the number of cases by the mean follow up for each study. Then the total number of revisions, non-revision reoperations or reoperations were respectively divided by the total observed component years and multiplied by 100¹⁵⁵. 95% CIs were calculated using the Clopper Pearson exact method and are presented¹⁵⁶.

The revision rate per 100 component years was transformed into 10-year survival by multiplying the rate by 10 and subtracting the resulting value from 100. To calculate the 15-year survival this revision rate per 100 observed component years was multiplied by 15 and the value subtracted from 100. Results are presented both in tables and in forest plots for clarity.

2.3 Results

The database search identified 958 manuscripts, which after duplicates were removed was reduced to 555 articles. After all the titles and abstracts were assessed by two independent reviewers this number was narrowed to 23. Full texts of these manuscripts were assessed for inclusion by two independent reviewers, of which 15 were deemed suitable (Figure 2.1).

Details of full text excluded papers (n=8) and their reasons for exclusion are listed in Appendix 2.

The total number of UKRs from the included studies was 8,658 cases. All 15 included studies were observational in design.

2.3.1 Risk of bias assessment

All studies scored low risk of bias except for Aly et al.¹⁵⁷ (Table 2.1). The primary outcomes of interest implant survival (13/15 manuscripts) and number of revisions (all manuscripts) were well reported. However reoperations/non revision reoperations were not as well reported (6/15 manuscripts).

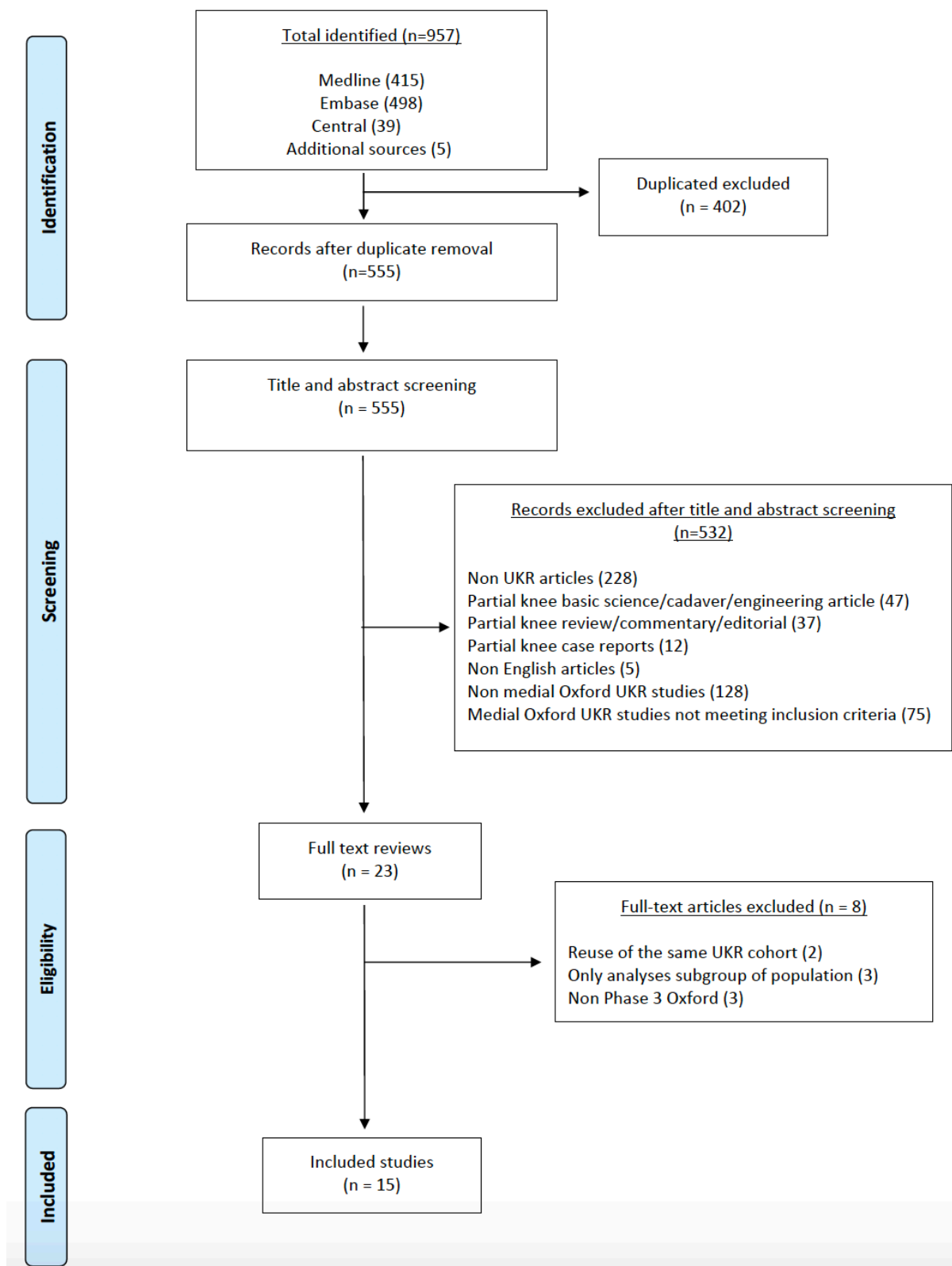


Figure 2.1. PRISMA flowchart.

Study	MINORS	Sample size	Survival outcome	Revision outcome	Reoperation outcome	Bias risk
Alnachoukati et al. ¹⁵⁸	10/16	A	A	A	B	Low
Aly et al. ¹⁵⁷	9/16	C	B	A	B	High
Bottomley et al. ¹⁵⁹	13/16	A	A	A	A	Low
Campi et al. ¹⁶⁰	13/16	A	A	A	A	Low
Edmonson et al. ¹⁶¹	11/16	A	A	A	A	Low
Emerson et al. ¹⁶²	12/16	A	A	A	B	Low
Faour-Martin et al. ¹⁶³	14/16	A	A	A	A	Low
Kendall et al. ¹⁶⁴	13/16	A	A	A	A	Low
Kim et al. ¹⁶⁵	12/16	A	A	A	B	Low
Kornilov et al. ¹⁶⁶	9/16	A	B	A	A	Low
Kristensen et al. ¹⁶⁷	13/16	A	A	A	B	Low
Lisowski et al. ¹⁶⁸	13/16	A	A	A	B	Low
Pandit et al. ⁸²	13/16	A	A	A	B	Low
White et al. ¹⁶⁹	11/16	A	A	A	B	Low
Yoshida et al. ¹⁷⁰	13/16	A	A	A	B	Low

Table 2.1. Risk of bias of included studies in the review.

2.3.2 Revisions

All 15 studies reported the number of revisions during their study period. There was a total of 460 revisions (5.3%) from the 8,658 UKRs. The summary of all revisions, reoperations and non-revision reoperations from each individual study are summarised in Appendix 2.

Fourteen studies reported the mean follow up which allowing the calculation of the revision rate pa (Table 2.2, Figure 2.2). From these 14 studies (n=8,406) there were 441 revisions and 59,656 component years. The overall revision rate was 0.74% pa (CI 0.67-0.81) which corresponds to a 10-year survival of 93% (CI 91.9-93.3) and 15-year survival of 89% (CI 87.9-90) (Table 2.2, Figure 2.2). The only study which did not report the mean follow up was Kornilov et al.¹⁶⁶ who reported 19 revisions from their 252 UKRs.

Analysis of the causes of revision was possible on all 15 papers giving a total of 8,658 cases. From these cases the most common reasons for revision were OA progression (n=130, 1.50%), aseptic loosening (n=108, 1.25%), bearing dislocation (n=50, 0.58%) and pain (n=49, 0.57%). For details for all revision indications see Figure 2.3.

Study	No of UKRs	No of revisions	Mean follow up in years	Observed component years	Annual revision rate (95% CI)
Alnachoukati et al. ¹⁵⁸	825	93	9.7	8003.5	1.16 (0.94-1.42)
Aly et al. ¹⁵⁷	45	2	8.8	393.8	0.51 (0.06-1.82)
Bottomley et al. ¹⁵⁹	1,084	46	5.2	5636.8	0.82 (0.60-1.09)
Campi et al. ¹⁶⁰	1,000	25	7	7000	0.36 (0.23-0.53)
Edmonson et al. ¹⁶¹	364	26	5.5	2002	1.30 (0.85-1.90)
Emerson et al. ¹⁵⁸	213	20	10	2130	0.94 (0.57-1.45)
Faour-Martin et al. ¹⁶³	511	29	10.4	5304.2	0.55 (0.37-0.78)
Kim et al. ¹⁶⁵	166	16	10	1660	0.96 (0.55-1.56)
Kristensen et al. ¹⁶⁷	695	51	4.6	3197	1.60 (1.19-2.09)
Lisowski et al. ¹⁶⁸	138	11	11.7	1614.6	0.68 (0.34-1.22)
Pandit et al. ⁸²	1,000	52	10.3	10300	0.50 (0.38-0.66)
White et al. ¹⁶⁹	563	16	6.6	3715.8	0.43 (0.25-0.70)
Kendall et al. ¹⁶⁴	523	29	3.9	2048.4	1.42 (0.95-2.03)
Yoshida et al. ¹⁷⁰	1,279	25	5.2	6650.8	0.38 (0.24-0.55)
TOTAL/OVERALL:	8,406	441		59,656	0.74 (0.67-0.81)

Table 2.2. Studies reporting the number of revisions and mean follow up period. These studies were used to calculate the total number of revisions and observed component years which were subsequently used to calculate the overall revisions per 100 observed component years.

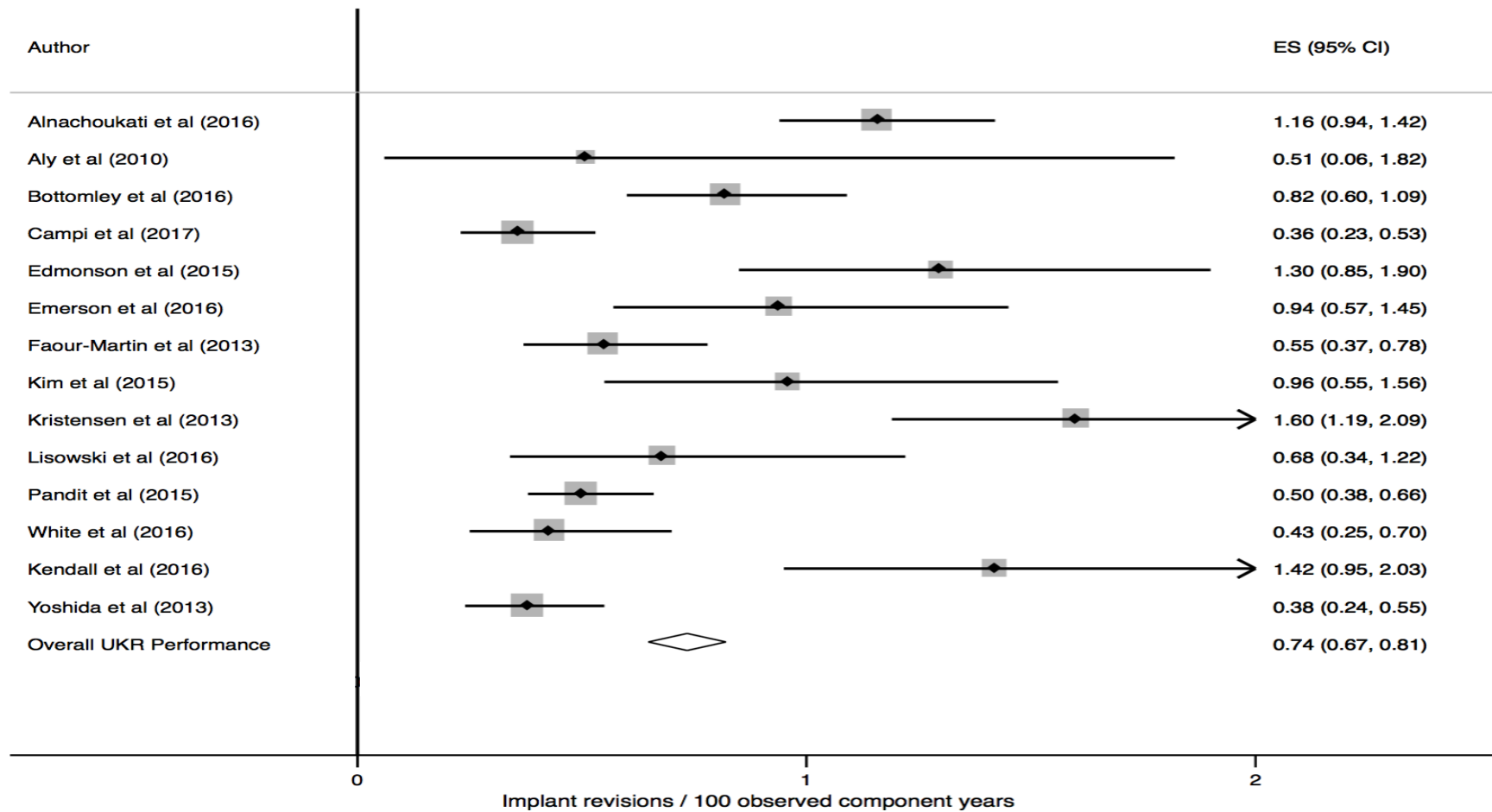


Figure 2.2. Forest plot of revision rate per 100 component years.

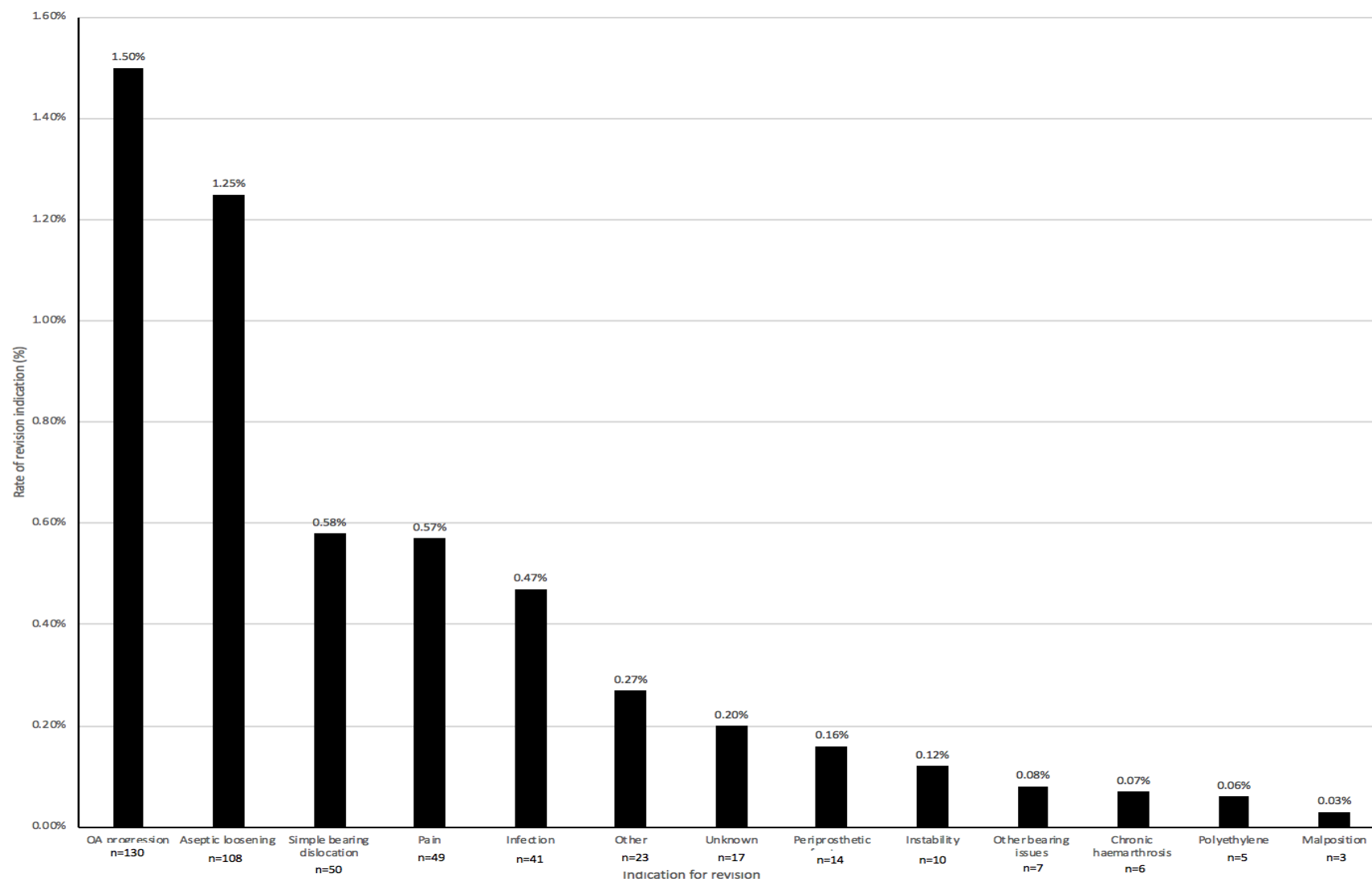


Figure 2.3. Bar chart of indications for revision from the 8,658 UKRs included in the systematic review.

2.3.3 Non revision reoperations

Six out of 15 studies ^{159-161, 163, 164, 166} (n=3,734) reported 43 non revision reoperations (1.2%).

From these six studies, five reported mean follow up time used to calculate the non-revision reoperation rate pa. From these five studies (n=3,482) there were 41 non revision reoperations and 21,988 component years giving a non-revision reoperation rate of 0.19% pa (CI 0.13-0.25) (Table 2.3). Kornilov et al.¹⁶⁶ did not report mean follow up time but report two non-revision reoperations from 252 cases.

Study (No of UKRs, mean follow up in years)	Reoperation	Non revision reoperation	Observed component years	Reoperation rate (95% CI)	Non-Revision Reoperation rate (95% CI)
Bottomley et al. ¹⁵⁹ (n=1,084, 5.2 years)	69	23	5636.8	1.22 (0.95-1.55)	0.41 (0.26-0.61)
Campi et al. ¹⁶⁰ (n=1,000, 7 years)	29	4	7000	0.41 (0.28-0.59)	0.06 (0.02-0.15)
Edmonson et al. ¹⁶¹ (n=364, 5.5 years)	29	3	2002	1.45 (0.97-2.07)	0.15 (0.03-0.44)
Faour-Martin et al. ¹⁶³ (n=511, 10.4 years)	31	2	5304.2	0.58 (0.40-0.83)	0.04 (0.00-0.14)
Kendall et al. ¹⁶⁴ (n=523, 3.9 years)	38	9	2044.9	1.86 (1.32-2.54)	0.44 (0.20-0.83)
TOTAL: (n=3,482)	196	41	21,988	0.89 (0.77-1.02)	0.19 (0.13-0.25)

Table 2.3. Studies reporting the number of reoperations and mean follow up period. These studies were used to calculate the total number of reoperations and observed component years which were subsequently used to calculate the overall reoperations/non revision reoperation rate.

2.3.4 Reoperations

Six out of 15 studies ^{159-161, 163, 164, 166} (n=3,734) reported 217 reoperations (5.8%). From these six studies, five reported mean follow up time used to calculate reoperation rate pa. From these five studies (n=3,482) there were 196 reoperations and 21,988 component years giving a reoperation rate of 0.89% pa (CI 0.77-1.02) (Table 2.3). Only Kornilov et al.¹⁶⁶ who reported 21 reoperations from 252 cases, did not report mean follow up time and therefore could not be included in this calculation.

2.3.5 Implant survival

Thirteen of 15 studies (n=8,361, Table 2.4) reported the 10 year or 15 year survival. Eleven out of 15 studies (n=7,700, Table 2.4) reported the overall 10-year survival of the implant using revision as the endpoint as between 85 and 97%.

Study	Location	No of UKRs	10 Year Survival reported (95% CI)	15 year Survival reported (95% CI)
Alnachoukati et al. ¹⁵⁸	Ohio/North Carolina/Texas, USA	825	85%	n.r
Bottomley et al. ¹⁵⁹	Oxford, UK	1,084	93% (86-100)	n.r
Campi et al. ¹⁶⁰	Oxford, UK/ Christ Church, New Zealand	1,000	97% (93-100)	n.r
Edmondson et al. ¹⁶¹	East Sussex, UK	364	88% (83-93)	n.r
Emerson et al. ¹⁵⁸	Texas, USA	213	88% (82-94)	n.r
Faour-Martin et al. ¹⁶³	Avenida Juan Carlos Primero, Spain	511	96%	n.r
Kendall et al. ¹⁶⁴	Canada	523	n.r	96%
Kim et al. ¹⁶⁵	Seoul, Korea	166	91% (86-95)	n.r
Kristenen et al. ¹⁶⁷	Vejle, Denmark	695	85% (79-90)	n.r
Lisowski et al. ¹⁶⁸	Amsterdam, Netherlands	138	n.r	91% (85-96)
Pandit et al. ⁸²	Oxford, UK	1,000	96% (93-100)	91% (83-98)
White et al. ¹⁶⁹	Oswestry, UK	563	95%	n.r
Yoshida et al. ¹⁷⁰	Japan	1,279	95% (91-100)	n.r

Table 2.4. Studies reporting 10 year and 15 year implant survival.

2.3.6 Medical complications

Four out of 15 studies ^{157, 161, 163, 164} reported medical complications of their cohorts. From the 1,443 UKRs 12 medical complications were reported corresponding to a medical complication rate of 0.83%. All medical complications were DVTs or PEs. No cases of myocardial infarction or stroke were reported.

2.3.7 PROMs

Nine out of 15 studies (n=5,177, Table 2.5) reported the PROMs of patients in their cohorts. All studies reported PROMs of either the OKS or AKSS except Aly et al.¹⁵⁷ who only reported the HSS. All studies reported improvements in PROMs at final follow up as compared to preoperatively (Table 2.5). The four studies (n=3,417) reporting 10-year OKS had average scores of 42, 42, 40, and 38 giving a weighted average of 40. The five studies (n=2,715) reporting 10-year AKSS-O all reported average scores of 90, 93, 90, 85 and 80 giving a weighted average of 86.

2.3.8 Search update

The database search was repeated on 23rd April 2019 to check for any new articles. Two additional articles were identified which utilised new cohorts of patients and met the inclusion criteria; (1) Mohammad et al.¹⁷¹ and (2) Campi et al.¹⁷². Both studies presented results similar to those presented in this chapter and their full results are presented in the second systematic review comparing fixation methods in Chapter 4.2.

Study	No of UKRs	Preop PROMS	10 year PROMS
Alnachoukati et al. ¹⁵⁸	825	n.r	AKSS-O 90, AKSS-F 77
Aly et al. ¹⁵⁷	45	HSS 74 (range 60-84)	HSS 177.6 (range 78-198)
Campi et al. ¹⁶⁰	1,000	OKS 23 (SD 8)	OKS 42 (SD 7)
Emerson et al. ¹⁵⁸	213	AKSS-O 50, AKSS-F 56	AKSS-O 93, AKSS-F 78
Faour-Martin et al. ¹⁶³	511	AKSS-O 52 (SD 12), AKSS-F 51 (SD 19)	AKSS-O 90 (SD 8), AKSS-F 89 (SD 18)
Kim et al. ¹⁶⁵	166	AKSS-O 54 (range 25-70), AKSS-F 56 (range 35-80)	AKSS-O 85 (SD 9), AKSS-F 81 (SD 12)
Lisowski et al. ¹⁶⁸	138	OKS 19 (SD 7), KSS 47 (SD 18)	OKS 42 (SD 6), KSS 81 (SD 20.7)
Pandit et al. ⁸²	1,000	OKS 25 (SD 9), Tegner 2 (SD 1), AKSS-F 69 (SD 18), AKSS-O 47 (SD 20)	OKS 40 (SD 9), AKSS-O 80 (SD 15), AKSS-F 76 (SD 22), Tegner 3 (SD 1)
Yoshida et al. ¹⁷⁰	1,279	OKS 22 (SD 8)	OKS 38 (SD 7)

Table 2.5. Studies reporting preoperative and postoperative PROMs in their cohorts

(N=5,177). AKSS-O American knee score objective, AKSS-F American knee score

functional, HSS Hospital for Special Surgery Knee Score, OKS Oxford Knee Score. n.r = not reported.

2.4 Discussion

This review has brought together existing evidence of the long term outcomes of the Oxford Phase 3 implant reported across the world for the first time. Through assessing approximately 8,500 UKRs the revision rate was 0.74% pa corresponding to an implant survival of 93% and 89% at 10 and 15-years respectively. This implant survival of 93% at 10 years is higher than those reported from the registries for the Oxford UKR which range between 86.0 to 92.3% (Table 1.1). However it still lags behind the 10 year TKR implant survival reported from the registries which range between 94.1 to 96.6% (Table 1.1).

A meta-analysis of the long term outcomes of TKR calculated the revision rate to be 4.4% over a mean follow up of 11 years¹⁷³. The predicted revision rate at 11 years using the data from this review (0.74% pa) is 8.1%. Therefore, the 11 year survival (92%), is lower than that reported for TKR (96%)¹⁷³. However, it is important to note that UKR revisions are more straightforward than TKR revisions, with most being simple conversions to TKR or exchanging the polyethylene bearing^{108, 123}. Whereas TKR revisions often require the use of augments or stems. Additionally patients are more satisfied after a UKR revision than a TKR revision¹²⁴. Both reoperation and non-revision reoperation rates are poorly reported for TKR from a literature search. However, Zmistowski et al.¹⁷⁴ reported the non-revision reoperation rate of 10,188 TKRs to be 3.8% at four years post operatively. This is much higher than the predicted non revision reoperation rate of 0.78% over the same period based on the data from this review. The KAT trial¹⁴⁶ reported 10 year TKR revision rate of 5.8%, non-revision reoperation rate of 7.5% and an overall TKR reoperation rate of 13.3%. In this review the 10-year revision rate was 7.8%, with a 10-year non-revision reoperation rate of 1.9% and the

overall reoperation rate was 8.9%. Therefore the Oxford UKR has a higher revision rate than TKR, but a much lower non revision reoperation and reoperation rate.

In terms of indications for revision surgery; lateral disease progression, aseptic loosening, bearing dislocation and pain were the commonest causes for revision for the Oxford UKR in this chapter. These indications were also leading causes for Oxford UKR revision in Kim et al.'s¹⁷⁵ systematic review of the implant's early-midterm outcomes. However, this review found that lateral disease progression was the commonest cause for revision which was not identified by Kim et al.¹⁷⁵, presumably given the included studies had a longer follow up than in their study. The most common causes for TKR revisions reported in the literature include aseptic loosening and polyethylene wear^{176, 177}.

The overall rate of medical complications in this review was 0.83% and all complications reported were either DVTs or PEs. Gandhi et al.¹⁷⁸ in their TKR systematic review, reported DVT rates in cemented and cementless groups as 8% and 7.7% respectively, which is nearly ten times higher than the results from this review. This higher rate of thromboembolism in TKR is supported from a large matched comparison of UKR and TKR using joint registry data linked to HES data¹⁰. The reported rates of stroke and myocardial infarction following TKR are 0.2%¹⁷⁹ and 2.2%¹⁸⁰ respectively and in this review no cases were reported.

The 10-year OKS for the Oxford UKR ranged from 38-42 in this review, with a weighted mean of 40. The KAT trial¹⁴⁶ reported a 10 year OKS of 34 for TKR. Other reports of long term reports of TKR's OKS are worse averaging 30 at 10 years¹⁸¹. This suggests functional outcomes are better in UKR.

The cementless Oxford UKR was introduced in 2004⁶⁷. There is a concern that cementless fixation may be worse than cemented potentially increasing the risk of loosening. From the long term papers included in the review only Campi et al.¹⁶⁰ exclusively reported cementless UKRs (n=1000). Although they demonstrated excellent long term implant survival and 10-year OKS suggesting a performance at least equivalent to the cemented implant, it is important to recognise that the data on the cementless Oxford UKR in this chapter is sparse with more studies required.

This review found only one study⁸² based solely on the data from the surgeons involved in the design of the implant. In this study of cemented components, reported by Pandit et al.⁸², the annual revision rate was 0.50% pa corresponding to a 10-year survival of 95%. In the non-designer studies, the revision rates ranged from 0.38 – 1.60% pa with most 10-year survival rates above 90%. Campi et al.¹⁶⁰ compared results of designer and non-designer surgeons with no differences identified. These comparisons suggest that all surgeons can achieve good results if they adhere to the recommended indications and techniques.

There are some limitations to this chapter. Some studies did not report all the outcomes of interest. Regardless of this, the numbers of UKRs for analysis of revision rates were approximately 8,500. Several studies lacked clear definitions of implant related outcomes. In most cases a formal definition of revision was given, but this was poorly reported for reoperation and complications. It was possible to work out the number of reoperations and medical complications using the a priori definitions specified in the section 2.2.3 with the data available. Most importantly there was only one study reporting the long term outcomes of the cementless Oxford UKR, indicating more work investigating its outcomes is required to understand its performance and how it compares to the cemented version. The overall rate of

revisions per 100 observed component years (% pa) and its subsequent survival calculation is based on the assumption that revision rate is constant and does not account for revision rates that may be higher earlier. This can overestimate revision rates in studies with shorter follow ups. This method does however offer the advantage of being able to compare studies with different lengths of follow up. Finally, all included studies were observational in nature, although only Aly et al.¹⁵⁷ was deemed at high risk of bias.

In summary this chapter has shown that excellent global long term implant survivals, PROMs and complication rates can be achieved for the Oxford UKR and are not exclusive to the surgeons involved in the design of the implant. Although, the PROMs, medical complication rate and non-revision reoperation/reoperation rate were better in the Oxford UKR than those found in the literature search of TKR, the revision rate was higher. Therefore it is important for interventions to be developed to lower this revision rate and therefore encourage more surgeons to use UKRs. One intervention developed was the introduction of the cementless Oxford UKR. Unfortunately in this chapter only one study reported its long term outcomes, which is insufficient to draw conclusions from.

The next chapter discusses the clinical and radiographic long term outcomes of a prospective cohort of 1000 cementless Oxford UKR procedures in Oxford to help better understand the implant's performance.

3. LONG TERM CLINICAL OUTCOMES OF THE CEMENTLESS OXFORD UKR

3.1 Introduction

Several observational studies have reported excellent implant survivorship of the cemented Oxford UKR with reoperation rates and functional outcomes being superior to TKR¹⁴⁷.

However unfortunately given the revision rates are several times higher than TKR^{8, 16, 17, 147} there has not been widespread acceptance of the implant, with UKR currently only forming approximately 10% of all primary knee replacements⁸.

The most common indication for revision for UKRs in the joint registries^{8, 16, 17} are aseptic loosening and pain. Most UKRs including the Oxford UKR are implanted with the use of bone cement to provide adequate primary stability. Given the Oxford UKR is implanted through a minimally invasive approach, cementation can be particularly challenging with errors leading to excessive polyethylene wear, loosening and pain^{67, 182}.

* This chapter has been published as two publications^{171, 183}

1) Mohammad HR, Kennedy JA, Mellon SJ, Judge A, Dodd CA, Murray DW. Ten-year clinical and radiographic results of 1000 cementless Oxford unicompartmental knee replacements. *Knee Surg Sports Traumatol Arthrosc* 2020; 28(5): 1479-1487 (Appendix 1)

2) Mohammad HR, Kennedy JA, Mellon SJ, Judge A, Dodd CA, Murray DW. The clinical outcomes of cementless unicompartmental knee replacement in patients with reduced bone mineral density. *J Orthop Surg Res* 2020; 15(1): 35. (Appendix 1)

In a loose knee replacement, the components at the bone cement interface can become replaced by a soft tissue layer which manifests as a thick, poorly defined and progressive radiolucency known as a pathological radiolucency¹⁸⁴. However often well-defined radiolucencies can form at the bone cement interface of well-functioning cemented implants, known as physiological radiolucent lines and represent fibrocartilage formation. Gulati et al.¹⁸⁵ found 63% of implanted cemented Oxford UKRs had evidence of physiological radiolucent lines. These physiological radiolucencies are not associated with pain or loosening although suggest that fixation could be of higher quality if this fibrocartilage did not exist¹⁸⁶. If a patient presents with pain following an Oxford UKR and has a physiological radiolucency many surgeons would attribute the pain to potential loosening and revise to a TKR¹⁸⁷. However this is unnecessary given anteromedial pain occurs frequently in the early post-operative period, likely secondary to changes in bone stresses following surgery and are self-limiting in nature¹⁸⁸.

Therefore in order to prevent these misinterpretations and the resulting errors which can arise from cement, the cementless Oxford UKR was introduced in 2004⁶⁷ (Figure 3.1). The cementless Oxford UKR is similar to its cemented counterpart, but has a coating of calcium hydroxyapatite and porous plasma sprayed titanium on its surface which contact the bone with an additional small anterior femoral peg⁶⁷. The surgical indications remain exactly the same as those for the cemented Oxford UKR⁸².

This chapter presents the long term clinical and radiological results of the first consecutive 1,000 cementless UKRs inserted by Professor David Murray and Mr Christopher Dodd who have both been involved in the design of the Oxford UKR implant.



Figure 3.1. The cementless Oxford UKR. With permission taken from¹⁴⁸.

3.2 Methods

3.2.1 Patient recruitment

Between June 2004 and November 2017, 1,000 cementless medial Oxford UKRs were implanted into patients through a minimally invasive approach by Professor David Murray and Mr Christopher Dodd using the recommended surgical indications developed from Goodfellow et al.⁶⁷.

These indications were based on knee pathoanatomy with the majority being AMOA and a few medial avascular necrosis (ANV) cases. Specifically these patients' knees all had bone on bone medial arthritis, fully intact functional ACLs and full thickness cartilage in the lateral compartment. There were no restrictions on age, weight, activity and patellofemoral status. Given the broad indications used, approximately 70% of both surgeons' primary knee replacement practice was UKR surgery.

3.2.2 Data collection

An intraoperative proforma (Appendix 3) was completed for each patient operated on during this period by the operating surgeon documenting the status of all of the knee structures as per Pandit et al.'s⁶⁸ cemented 1,000 Oxford UKR study. The ACL was classified as normal, synovial damage, longitudinal splits, friable fragmented, absent. ACLs reported as friable fragmented or absent were regarded as non-intact ACLs and not included in this case series. The weight bearing articular surfaces of the medial and lateral compartment (tibia and femur), medial and lateral patella facets and trochlea were graded for any cartilage defect. These were classified as normal, superficial damage, partial thickness cartilage loss (PTCL), focal (≤ 2 cm²) full thickness cartilage loss (FTCL), extensive FTCL (> 2 cm²), bone loss ≤ 5 mm or

bone loss > 5 mm. Bone on bone arthritis in the medial compartment required both the involved femur and tibia to show evidence of FTCL or bone loss. The lateral compartment was required to show either normal or superficial damage to be considered full thickness cartilage.

All patients were assessed both pre and post operatively by research physiotherapists who were independent of both the clinical and surgical teams involved in each patient's care. Patients were assessed clinically preoperatively and then at one, five, seven and ten years post operatively for the status of their knee joint and their functional outcomes. Additionally primary and secondary care records were screened for the status of the knee joint. Complications or further surgeries were recorded when they occurred or at each follow up appointment. Patients unable to attend were contacted by post or telephone to obtain the relevant clinical information. All data was recorded onto a prospective database which is maintained in real time by a full time data manager and research physiotherapist who are in regular contact with all patients from the cohort. Data was extracted from the prospective database on 14th August 2018.

3.2.3 Outcomes of interest

The primary outcome of interest in this study was implant survival. Failure was defined a priori with four different definitions in order to fully assess the performance of the implant. Each will be listed in turn; (1) Revision which was defined as the removal, addition or replacement of any implant component. (2) Reoperation which was defined as any surgical intervention to the knee joint and included arthroscopies, wash outs and MUAs. (3) Revision to TKR which was defined as the removal of the Oxford UKR and insertion of TKR

components. (4) Major revision which was defined as the usage of revision TKR components which included stems, wedges, augments or constraints.

Secondary outcomes were functional outcomes and radiological assessment. Each will be discussed in turn.

Functional outcomes were assessed using the OKS, AKSS-O, AKSS-F and Tegner scores preoperatively and at one, five, seven and ten years (Appendix 3). The AKSS-O was calculated without performing deductions for alignment given unlike in TKR the Oxford UKR aims to restore anatomical alignment and not a neutral alignment. Range of motion and lower limb alignment were measured using a long arm goniometer. The proportion of OKS scores classifying as excellent (>41) using the method by Kalairajah et al.¹⁸⁹ was calculated as a percentage.

Radiological assessment was performed at a minimum of five years and 10 years follow up using aligned images. Anteroposterior (AP) radiographs were conducted with the patient supine and knee flexed to 20 degrees and the image aligned parallel to both the under surface and vertical wall of tibial component. Lateral radiographs were performed with alignment to the posterior facet of the femoral component.

Postoperative radiographs were assessed by two independent surgeons (Hasan Raza Mohammad and James Kennedy) to assess for the presence of radiolucencies and to assess the lateral compartment. Radiolucencies were first classified as either pathological which are poorly defined, progressive and greater than 2 mm thick or physiological which are ≤ 2 mm thick, well defined with a sclerotic margin and non-progressive in nature⁸². Physiological

radiolucencies are otherwise regarded as radiolucent lines and are not associated with loosening¹⁸⁵.

The region under the tibial component from the anteroposterior radiographs were divided into six regions (Figure 3.2) which is a well-established method from Liddle et al.¹⁹⁰. Tibial radiolucencies were defined as completed if all six zones were involved and partial if less than six zones were affected. As in previous studies the border lateral to the vertical wall of the tibial component was not assessed given the component is not fixed in this position and is not deemed to be weight bearing.

The lateral radiographs were used to assess the femoral component by examining the flat region at the posterior femoral condyle and flat regions around the femoral pegs in seven zones which is a well-established method from Hooper et al.¹⁹¹ (Figure 3.3). Femoral radiolucencies were defined as completed if all seven zones were affected and partial if under seven zones were affected.

The lateral compartment was graded based on the Kellgren Lawrence grading scale¹⁹² as full thickness cartilage, slight narrowing, major narrowing or bone on bone contact of the proximal tibia and distal femur.

An ethical opinion was sought from the local ethics committee chair (Oxfordshire Research Ethics Committee C) who confirmed that given the clinical and radiological follow up was part of their routine assessment, this study did not require ethical approval (Appendix 3).

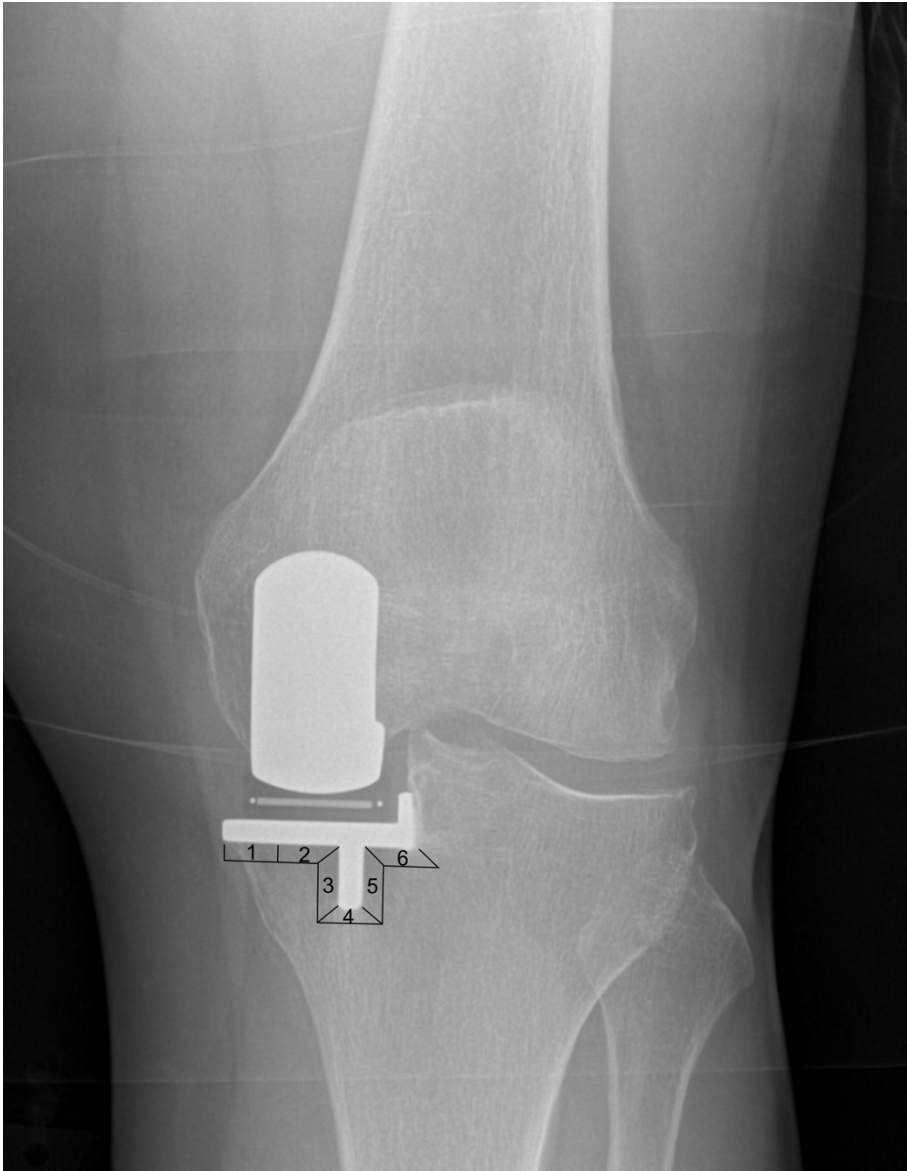


Figure 3.2. Six zones assessed for tibial radiolucencies from AP radiograph.

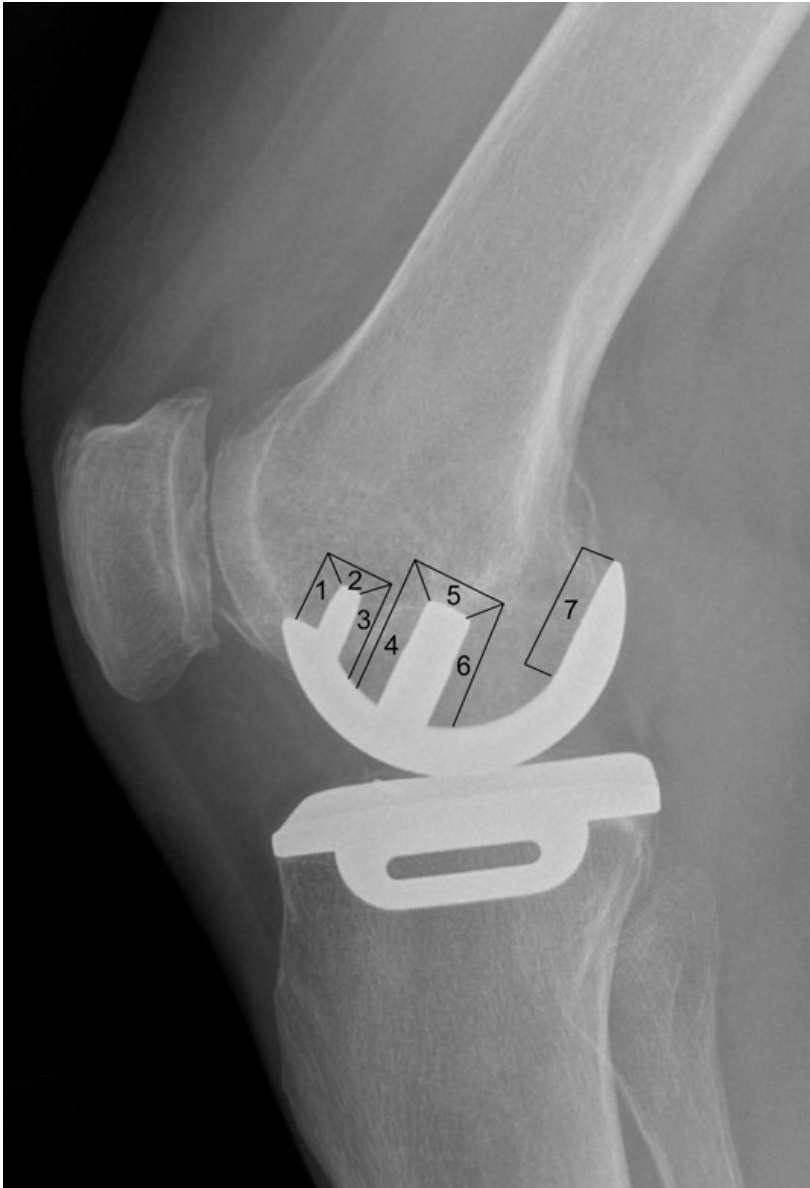


Figure 3.3. Seven zones assessed for femoral radiolucencies from lateral radiograph.

3.2.4 Statistical analysis

To assess cumulative implant survival using the various definitions specified in section 3.2 (Revision, reoperation, revision to TKR and major revision), the Kaplan-Meier method was utilised to calculate the 10 year implant survival.

Given the PROMs scores were not normally distributed comparisons of preoperative and most recent postoperative scores were conducted using nonparametric statistics, specifically the Wilcoxon sign rank test.

Inter and intra observer error was calculated between the two surgeons (Hasan Mohammad and James Kennedy) performing radiographic analysis using Cohen's kappa statistic.

Continuous data were described using means, SDs, medians and IQRs. Categorical variables were tabulated with absolute frequencies. All statistical analyses were performed in Stata version 14 (STATA Corp, Texas, United States of America (USA)). P values of 0.05 were considered significant and 95% CIs reported.

3.3 Results

3.3.1 Cohort characteristics

From the 1,000 UKRs implanted in this consecutive series, 748 were unilateral and 252 were bilateral. Of the 252 bilateral UKRs four were simultaneous. 536 UKRs (54%) were implanted into males and 464 (46%) implanted into females. The mean age of primary surgery in this cohort was 66.2 years (SD 10.0) and mean body mass index (BMI) was 29.2 (SD 5.0). 495 knees were left and 505 were right sided. 988 knees had a diagnosis of AMOA and 12 had AVN of the knee. All patients met the indications described in section 3.2.

The mean follow up of the cohort (n=1000) was 5.1 years (SD 2.6) with 262 patients having follow up of seven years and over and 29 knees with 10 years plus follow up. During the study period 33 knees withdrew from regular follow up; 22 knees from patients with poor health, four knees from patients going abroad and seven knees from patients requesting to leave the study. None of these knees were revised or re operated prior to their withdrawal.

3.3.2 Implant survival

There were 25 reoperations at a mean of 2.6 years (SD 2.6). Using reoperation as the endpoint 5 year implant survival was 97.3% (CI 95.9-98.2) and 10 year implant survival 96.6% (CI 94.8-97.8) (Table 3.1, Figure 3.4). From these 25 reoperations, 18 met the criteria for implant revisions at a mean of 3.0 years (SD 2.8) postoperatively. Using revision as the endpoint the 5 and 10 year implant survival was 98.1% (CI 96.9-98.9) and 97.5% (CI 95.7 - 98.5) respectively (Table 3.1, Figure 3.5). The minimum follow up was 0.84 years.

There were 12 patients with a known diagnosis of osteoporosis as per the World Health Organisation's definition¹⁹³. The mean age and BMI were 68 (SD 8.3) and 27.1 (SD 5.7) respectively. Subgroup analysis of this group revealed no reoperations or revisions recorded.

Leading indications for revision surgery in the whole cohort (n=1000) were bearing dislocation (7 knees, 0.98%), disease progression in the lateral compartment (4 knees, 0.4%) and pain (2 knees, 0.2%). For the full list of each reoperation and revision performed, these are summarised in Table 3.2.

Follow up (Years)	Number at risk for revision	Revision survival (95%CI)	Reoperation survival (95% CI)	TKR Survival (95% CI)
1	976	99.6 (98.9 – 99.9)	99.3 (98.5 – 99.7)	99.9 (99.3 - 100)
2	845	99.1 (98.2 – 99.5)	98.7 (97.7 – 99.2)	99.7 (99.0 – 99.9)
3	737	98.8 (97.9 – 99.3)	98.2 (97.1 – 98.9)	99.6 (98.8 – 99.8)
4	614	98.7 (97.6 – 99.2)	98.0 (96.9 – 98.8)	99.4 (98.6 – 99.8)
5	494	98.1 (96.9 – 98.9)	97.3 (95.9 – 98.2)	98.9 (97.7 – 99.4)
6	373	98.1 (96.9 – 98.9)	97.3 (95.9 – 98.2)	98.9 (97.7 – 99.4)
7	262	97.5 (95.7 – 98.5)	96.6 (94.8 – 97.8)	98.9 (97.7 – 99.4)
8	137	97.5 (95.7 – 98.5)	96.6 (94.8 – 97.8)	98.9 (97.7 – 99.4)
9	65	97.5 (95.7 – 98.5)	96.6 (94.8 – 97.8)	98.9 (97.7 – 99.4)
10	29	97.5 (95.7 – 98.5)	96.6 (94.8 – 97.8)	98.9 (97.7 – 99.4)

Table 3.1. Implant survival at each year for revision, reoperation and conversion to TKR endpoints.

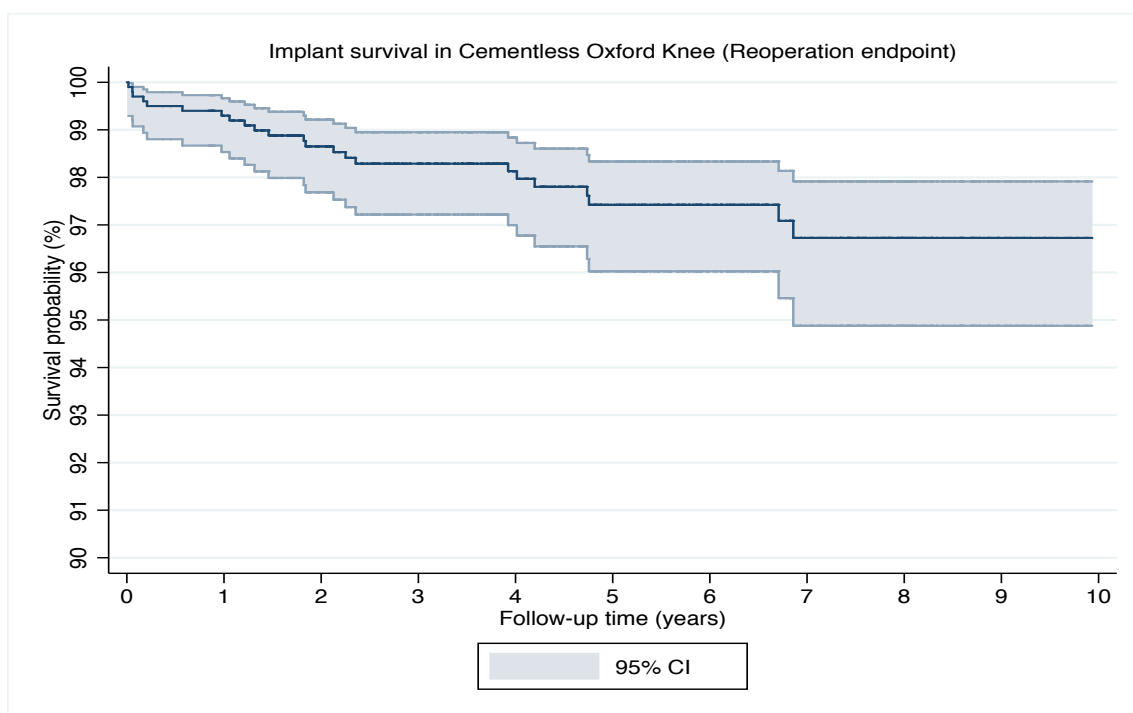


Figure 3.4. Kaplan Meier graph of cumulative implant survival with reoperation as the endpoint.

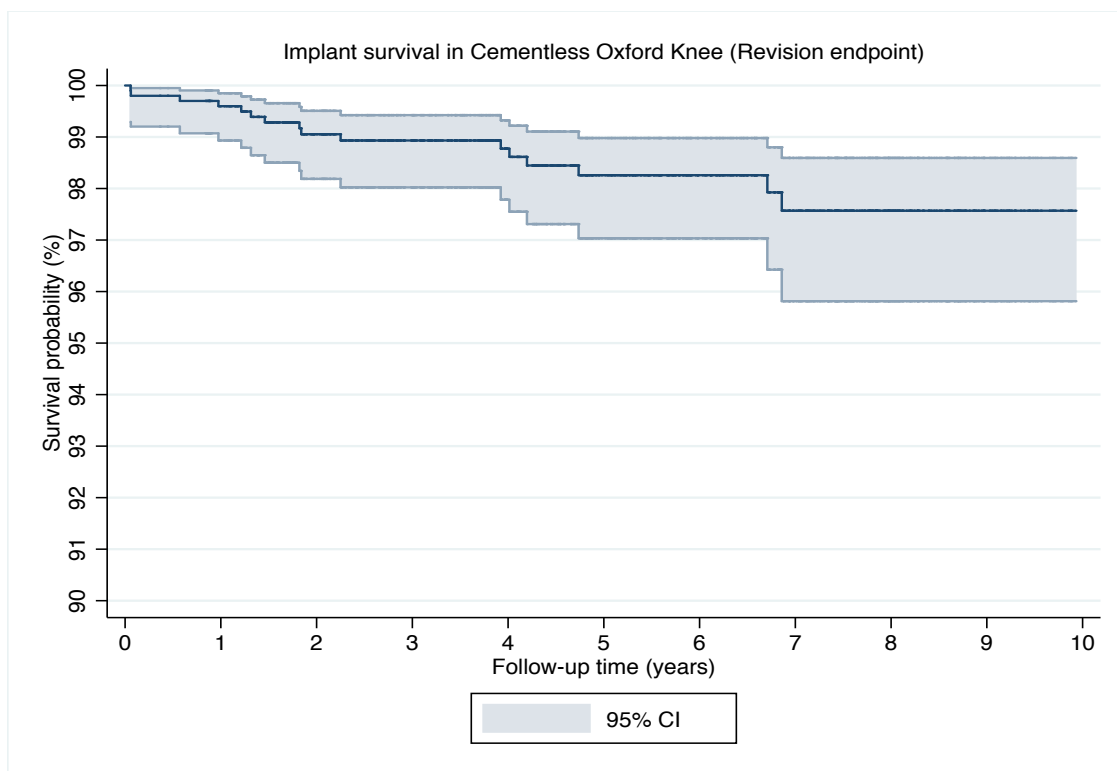


Figure 3.5. Kaplan Meier graph of cumulative implant survival with revision as the endpoint.

Indication	Number of UKRs	Surgical procedure conducted	Mean time from initial surgery (Years)	Number of reoperations	Number of revisions
Bearing dislocation	7	7 Bearing exchange	2.9 (SD 3.4)	7	7
Disease progression	4	2 TKRs 2 Lateral UKR	4.8 (SD 1.4)	4	4
Pain	5	2 Arthroscopies 1 Tibial revision 1 TKR 1 Aspiration and MUA	1.9 (SD 1.8)	5	2
Infection	3	1 Arthroscopy and washout 2 debridement, washout and bearing exchange.	0.04 (SD 0.02)	3	2
Avascular necrosis	1	1 Lateral UKR	6.7	1	1
Femoral component loosening	1	1 Cemented femoral component	0.6	1	1
Lateral meniscal tear	1	1 Arthroscopy	4.8	1	0
Wound dehiscence	1	1 Debridement and primary closure	0.2	1	0
Loose body	1	1 Arthroscopy and arthrotomy	2.1	1	0
Tibial plateau fracture (lateral)	1	1 TKR	2.2	1	1
Totals				25	18

Table 3.2. List of reoperations and revisions in the study cohort.

Using conversion to TKR as the endpoint implant survival at five and 10 years was 98.9% (CI 97.7 – 99.4) (Table 3.1). There was a total of eight conversions to TKR at a mean time of 3.0 years (SD 1.6). Four knees had a primary revision to TKR; two knees for lateral compartment arthritis, one knee for pain and one knee for a lateral tibial plateau fracture following a fall. The revision for pain was done in a different institution and the pain source is not clear. It was noted that both at the primary procedure, which had a good result and at the revision procedure, there was some patellofemoral osteoarthritis. Four knees were converted to TKR as a re-revision after a failed primary revision; two knees had re-revisions to TKR for infection after failed debridement, bearing exchange and washout (one single stage TKR and one dual stage TKR). One knee had a re-revision to TKR (single stage) after arthrotomy and bearing exchange for recurrent bearing dislocations with lateral compartment arthritis and one knee had a re-revision (single stage TKR) after a bicompartamental knee replacement due to lateral compartment bearing dislocation.

Using major revision as the endpoint survival at both five and 10 years was 99.6% (CI 98.8-99.9). There was a total of three major revisions at a mean of 2.4 years (SD 1.6). One knee was converted to a TKR with a stemmed tibial implant following a lateral tibial plateau fracture after a fall that did not improve with non-operative management, one knee was converted to TKR with tibial stem for lateral disease progression and one knee had a deep infection requiring a two-stage revision with a tibial stem and augment.

There were 28 deaths during the study at a mean 3.6 years (SD 2) postoperatively. This corresponds to a five and 10 year patient survival of 97.2% (CI 95.7-98.2) and 95.1% (CI 92.8 - 96.7) respectively (Figure 3.6). No death reported was related to the implant.

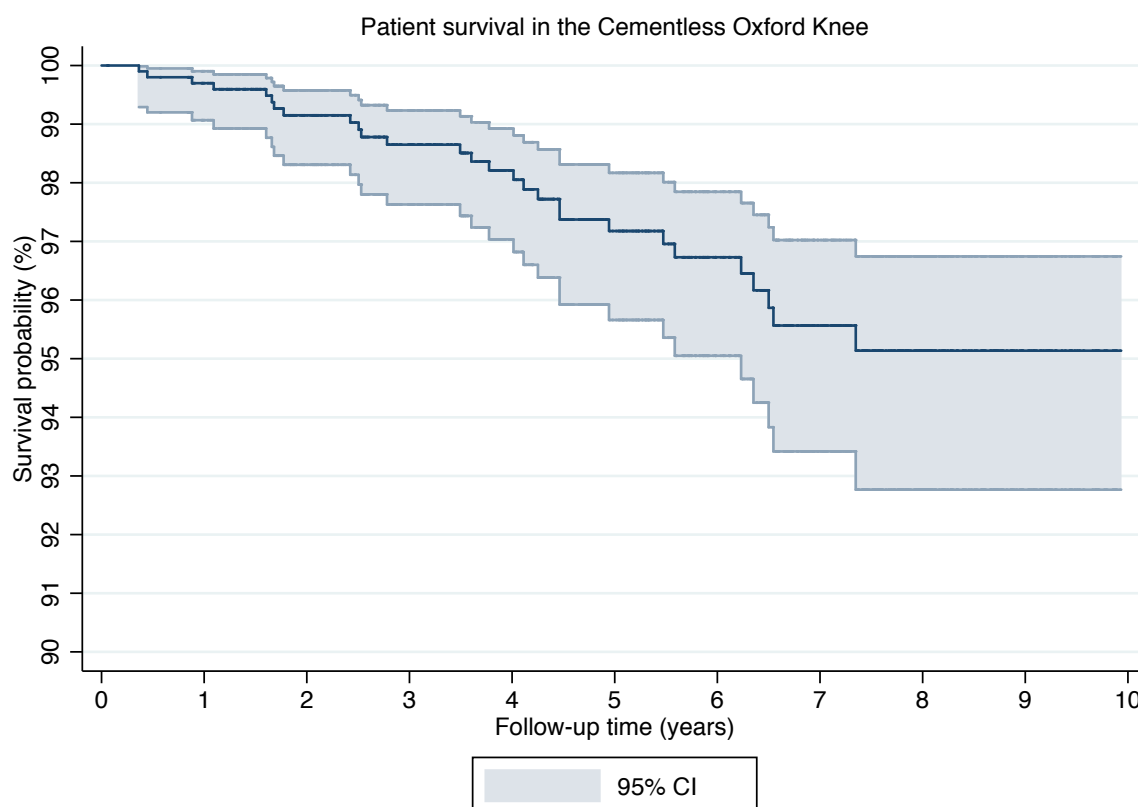


Figure 3.6. Kaplan Meier graph of cumulative patient survival during study.

3.3.3 Patient reported outcome measure results

The most recent outcome scores (OKS, Tegner, AKSS-O and AKSS-F) were all significantly better ($p < 0.001$) than their respective preoperative scores. The most recent mean and median flexion angle was 127.4 degrees (SD 10.3, range 80-152 degrees) and 128.5 (IQR 14). The most recent mean and median extension angle was -2.71 (SD 4.4, range -20 to 10 degrees) and -2 (IQR 5).

The mean and median preoperative OKS were 25.1 (SD 8.5) and 25.0 (IQR 12.0) which increased to 41.6 (SD 7.7) and 45.0 (IQR 8.0) at one year, 42.0 (SD 7.3) and 45.0 (IQR 8.0) at five years, 42.3 (SD 7.4) and 45.0 (IQR 6.0) at seven years and 41.2 (SD 9.8) and 45.0 (IQR 6.0) at 10 years (Figure 3.7). At one, five, seven and 10 years 68%, 69%, 74% and 73%

respectively had an excellent OKS (>41). 3.6% had worse OKS post operatively than preoperatively.

The mean and median preoperative Tegner score were 2.4 (SD 1.1) and 2 (IQR 1) which increased to 3.0 (SD 1.3) and 3.0 (IQR 2.0) at one year, 3.1 (SD 1.5) and 3.0 (IQR 2.0) at five years, 2.9 (SD 1.5) and 3.0 (IQR 1.0) at seven years and 2.8 (SD 1.3), 3.0 (IQR 1.0) at 10 years (Figure 3.8).

The mean and median preoperative AKSS – O were 60.2 (SD 15.4) and 60.0 (IQR 21.0) which increased to 91.7 (SD 11.4) and 95.0 (IQR 7.0) at one year, 93.6 (SD 9.0) and 95.0 (IQR 8.0) at five years, 88.5 (SD 16.7), 94.0 (IQR 9.0) at seven years and 89.1 (SD 13.0) and 93.0 (IQR 7.0) at 10 years (Figure 3.9). The mean and median preoperative AKSS – F were 70.8 (SD 16.8) and 70.0 (IQR 20.0) which increased to 82.3 (SD 17.7) and 80.0 (IQR 30.0) at one year, 83.6 (SD 19.4) and 90.0 (IQR 25.0) at five years, 83.3 (SD 18.2) and 90.0 (IQR 30.0) at seven years and 80.4 (SD 14.6), 80.0 (IQR 20.0) at 10 years (Figure 3.9).

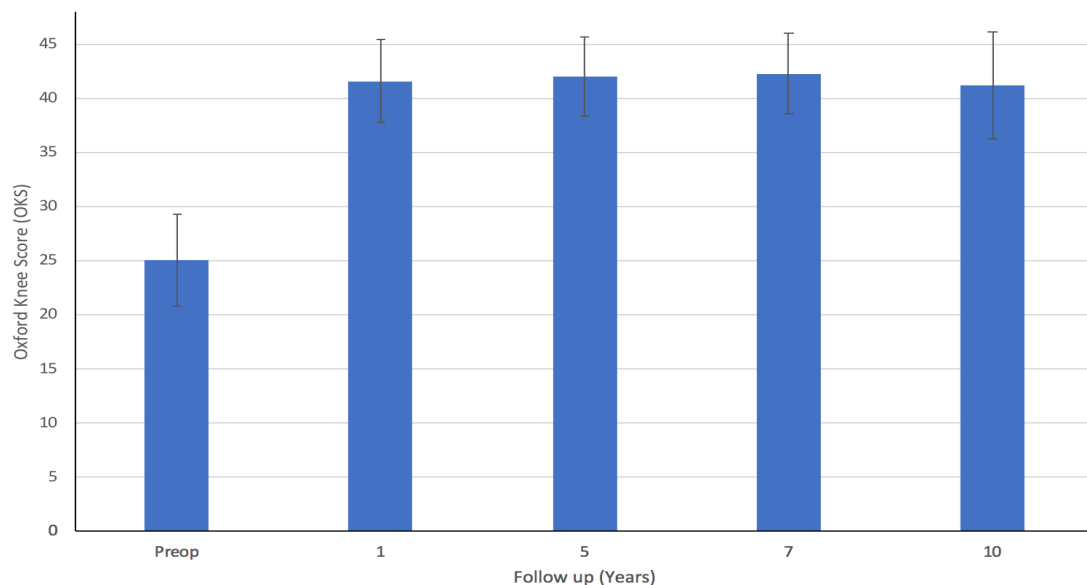


Figure 3.7. Mean Oxford knee score at different time points during the study. Error bars represent SDs.

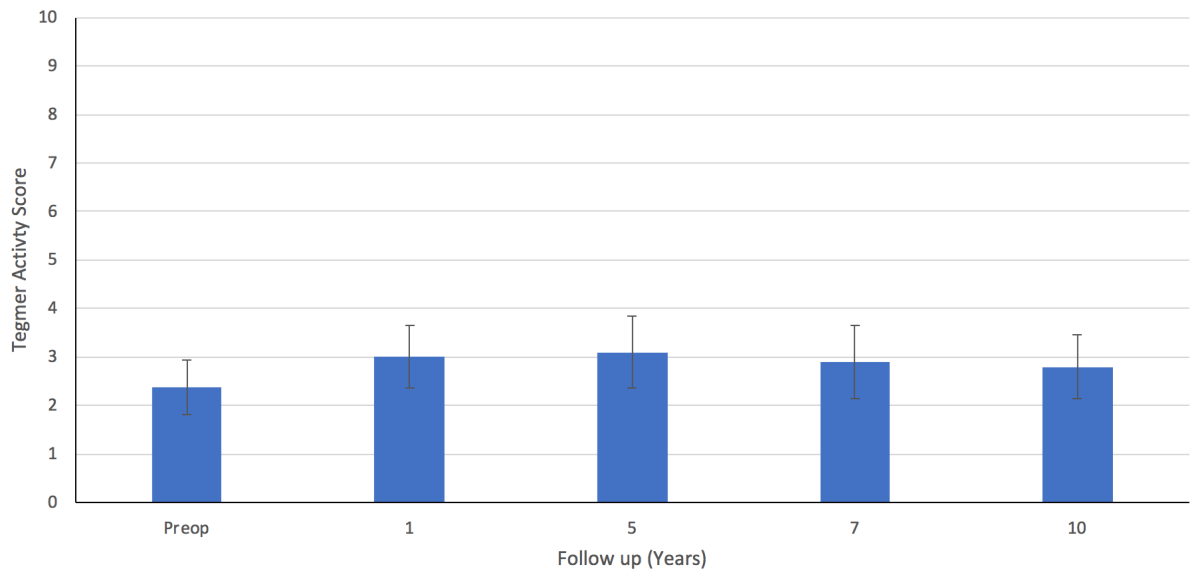


Figure 3.8. Mean Tegner activity score at different time points. Error bars represent SDs.

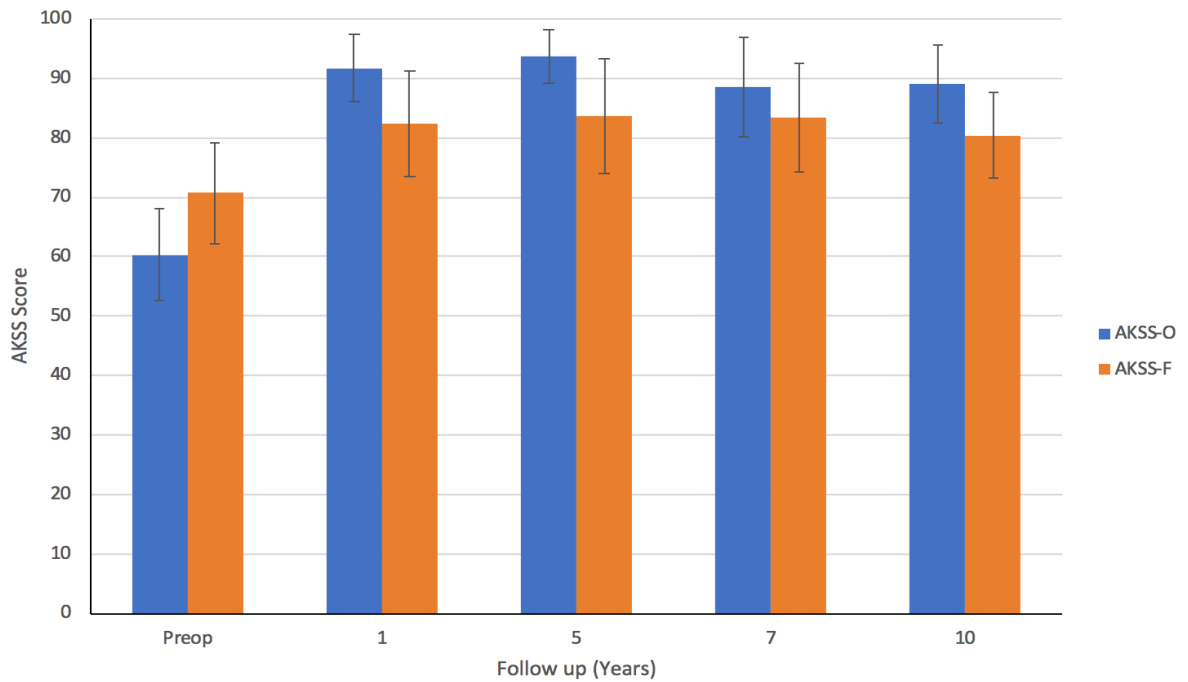


Figure 3.9. American knee society score at different time points. Error bars represent SDs.

3.3.4 Radiographic analysis

The inter and intra observer error for radiographic analysis was kappa = 0.80 ($p < 0.001$) and kappa = 0.90 ($p < 0.001$) which is acceptable and similar to those previously reported for this type of analysis^{190, 194}. 348 radiographs (70%) were available for patients with a minimum follow up of five years. On these radiographs there were no tibial or femoral pathological radiolucencies. There were 45 (13%) partial and zero (0%) tibial radiolucent lines (Figure 3.10). The sites for tibial radiolucencies were zone six (n=36), zone five (n=11), zone three (n=9), zone four (n=1) and zone one (n=1). There were four (1.1%) femoral radiolucent lines with one in zone one, three, four and six. Regarding the lateral compartment assessment, there were 309 (88.7%) knees with full thickness compartments, 24 (6.9%) knees showing slight narrowing, 12 (3.4%) knees showing marked narrowing and three (0.9%) knees demonstrating evidence of bone on bone contact (Figure 3.11).

22 radiographs (76%) were available for patients with follow up of 10 years and over and none showed pathological radiolucencies. There were two (9%) partial tibial radiolucent lines both of which were in zone six and no (0%) complete tibial radiolucent lines. There was one partial femoral radiolucent line in zone four. Regarding the lateral compartment there were 20 (91%) knees that had full thickness compartments, one with marked narrowing and one with evidence of bone on bone contact.

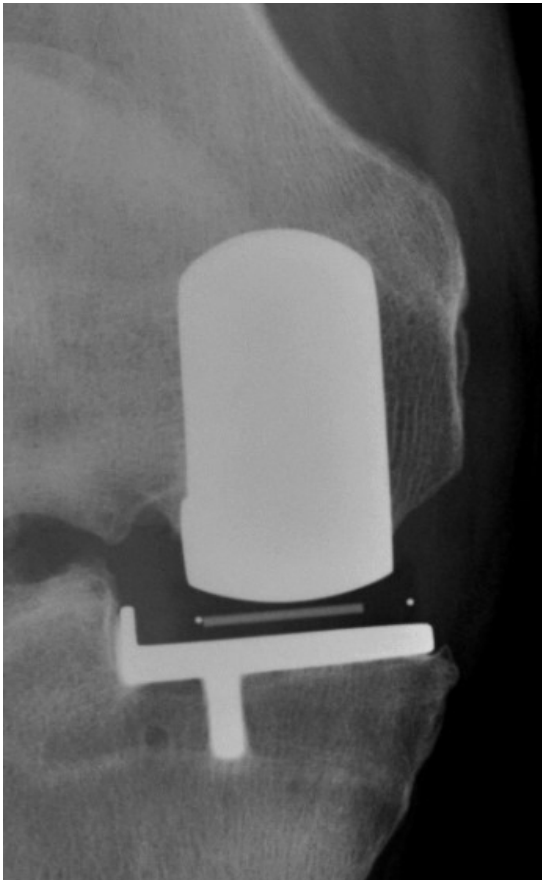


Figure 3.10. Radiograph example of tibial radiolucency in zone six.



Figure 3.11. Radiograph example of lateral compartment bone on bone contact.

3.4 Discussion

This chapter demonstrates that excellent long-term clinical and radiographic outcomes can be achieved using the cementless Oxford UKR and supports the work from Campi et al.'s¹⁶⁰ study identified from the systematic review¹⁴⁷ presented in Chapter 2. The primary and secondary outcomes measured were at least as good and potentially better than those previously reported for the cemented implant in an almost identical study by the same operating surgeons¹⁹⁵ using the same surgical indications. However the cementless does have advantages including a marked decrease in both radiolucent lines and revision for pain suggesting improved fixation. These results are likely to be generalisable given previous studies^{147, 148, 190, 196} and a meta-analysis¹⁴⁷ have shown that similar results can be achieved by designer and non-designer surgeons providing the recommended indications and techniques are adhered to.

When revision is considered to be a failure the 10-year survival of the cementless UKR is 97.5% (CI 95.7 - 98.5) which is similar to the survival of 96% (CI 92.5 - 99.5) in an almost identical study of cemented UKRs by Pandit et al.¹⁹⁵. When compared to TKR, its survival is similar to the 96% reported from a meta-analysis of 20,873 TKRs¹⁷³. However if reoperations are considered the endpoint, then the advantages for the cementless UKR compared to TKR are highlighted (96.6% vs 86.7%¹⁴⁶ respectively at 10 years).

Additionally revisions of TKR tend to be complex procedures with most requiring revision TKR components with stems and wedges. If revision requiring such components is considered the endpoint, then the cementless UKR also performed well with a 10 year survival of 99.6%. Patient mortality was low with no deaths related to the implantation and

the 10 year patient survival is 95.1% which is better than that reported for TKRs (88.5% at 8 years¹⁰) although this may in part be because TKRs are implanted in older patients than UKRs⁸ (69 vs 64 years) as discussed in section 1.9.1.

The main PROM score recorded was the OKS and did not change appreciably with time at one, five, seven and 10 years postoperatively ranging between 41.2 and 42.3 points. At each time point the mean OKS score classified as excellent (>41) according to Kalairajah et al.'s¹⁸⁹ classification. These scores are similar to those in the previously reported cemented cohort¹⁹⁵. The post-operative OKS appears better than those reported for TKR in the KAT trial¹⁴⁶ (at one, five, seven and 10 years ranging between 33.5 to 35). A patient would want to avoid being worse post-operatively than pre-operatively. In this chapter only 3.6% of knees had a worse post-operative score which is half that reported for TKR¹⁹⁷. A recent meta-analysis also found superior functional outcomes for UKR compared to TKR¹².

The leading causes for revision were bearing dislocation (n=7, 0.7%), disease progression (n=4, 0.4%) and pain (n=2, 0.2%) and were also the commonest reasons for revision reported in the similar cemented UKR cohort¹⁹⁵. However in the cemented cohort¹⁹⁵ pain (n=10, 1%) was the leading cause of revision followed by disease progression (0.7%, n=9), and then bearing dislocation (0.6%, n=6). The rate of revision for pain appears lower for cementless than cemented. In the cementless study six out of the seven bearing dislocations were successfully treated with a bearing replacement.

The main surgical concern about changing from cemented to cementless implants is an increased risk of aseptic loosening. The rate of aseptic loosening (0.1%) in this cohort was the same as to Pandit et al.'s¹⁹⁵ similar cemented cohort with the same operating surgeons. In this

study there was only a single case (0.1%) of femoral component loosening, treated by replacement with a cemented femoral component.

There was no radiographic evidence of tibial or femoral loosening, with no pathological radiolucencies. Additionally there were no complete radiolucent lines (physiological radiolucencies) and only 13% of tibial components and 1% of femoral components had had partial radiolucent lines. In contrast, evidence suggests one third of cemented tibial UKR components have complete radiolucent lines¹⁸⁵. Although not indicative of loosening, they suggest superior fixation for cementless components and that if patients have pain, they are less likely to be revised. This may go a long way to reduce UKR revision rates in the joint registries.

Peri-prosthetic fractures are a serious complication of UKR with concern that implanting press fit cementless components can increase the risk of fracture¹⁹⁸. Cadaveric work suggests that these fractures are more likely to occur with cementless than cemented implants¹⁹⁹. There was only one fracture in this study. A lateral tibial plateau fracture occurred after a traumatic fall over two years post operatively and is therefore not related to the implant or surgery. This study suggests that the risk of periprosthetic fractures is actually very low with adherence to the recommended surgical technique.

Many surgeons believe that following UKR, lateral compartment arthritis will inevitably progress requiring a revision procedure. This study shows that revision for disease progression is rare with only four knees (0.4%) requiring revision for lateral progression (two with TKR and two with lateral UKR), although at 10 years 10% (2/22) had radiographic evidence of lateral arthritis.

In general the UKR revision rates reported from the joint registries is higher than in large cohort studies from specialist centres. This is because most surgeons reporting results to registries do small numbers of UKR and only use UKR for a small proportion of their knee replacements²¹. Therefore there is likely to be poor adherence to the recommended indications and inappropriate criteria for revision surgery. Recent work by Kennedy et al.¹⁵⁰ investigated the preoperative radiographs of Oxford UKRs revised in the NJR and found that only 70% met the correct surgical indications and no reason for revision was found in 67% of cases. However despite these limitations, recent reports from the New Zealand Registry (NZJR)¹⁷ have shown that the revision rate of the cementless Oxford is about half that of the cemented. This may be because of the improved fixation or it may be because more experienced surgeons are using the cementless implant.

The main strengths of this study are that it is a large prospective consecutive series of 1,000 cementless Oxford UKRs using the recommended indications and techniques. Additionally the follow up was performed by staff independent of the clinical teams treating patients. A large variety of data was also collected providing both clinical radiographic outcome data. The main weakness is that the data pertains to a single centre with patients from one geographical location. Additionally the study is from the designers of the implant and suffered from a significant proportion of missing radiographs limiting its generalisability. Furthermore given this is a cohort study, it is not the best quality of evidence (Figure 1.4). Finally there was no cemented UKR comparative arm.

In summary this chapter has shown that excellent long term clinical and radiographic outcomes can be achieved with the cementless Oxford UKR, when used for the recommended surgical indications. The main concerns with cementless fixation are that it may lead to

increased rates of aseptic loosening or periprosthetic fractures, neither of which were observed in this cohort.

However it is important for a formal comparison to be made comparing the cementless and cemented Oxford UKR whilst controlling for confounding factors to confirm whether there are any real differences in implant performance and if the introduction of the cementless Oxford UKR will lower revision rates in the joint registries. Formal comparisons of cemented and cementless UKRs are presented in the next chapter.

4. THE EFFECT OF SURGICAL FIXATION ON LONG TERM UKR REVISION RATES

4.1 NJR comparison of cemented and cementless UKRs

4.1.1 Introduction

As discussed in Chapter 1, over 100,000 primary knee replacements are performed each year in the United Kingdom of which TKR and UKR are the main treatment options⁸. Although UKR offers significant advantages over TKR, its revision rate is several times higher in the joint registries^{8, 16, 17}. As a result UKR is only used in approximately 10% of cases⁸ despite it being suitable for use in 50% of presenting cases⁸³.

The most commonly used UKR is the Phase 3 Oxford UKR. The cemented Oxford UKR was introduced in 1998. Chapter 2 highlighted that its commonest reasons for revision include aseptic loosening and pain¹⁴⁷. Radiolucent lines, also known as physiological radiolucencies are indicative of fibrocartilage at the interface and are seen in over half of cemented UKR tibial components¹⁸⁵. These are often misinterpreted in the presence of pain for aseptic loosening, despite studies showing no relation¹⁸⁵, and lead to unnecessary revisions. In an attempt to counter this the cementless version was introduced in 2004 with the only changes to the implant being a porous coating of titanium and hydroxyapatite, and the femoral component having an additional peg⁶⁷.

* This chapter has been published^{200, 201} as two publications:

(1) Mohammad HR, Matharu GS, Judge A, Murray DW. Comparison of the 10-year outcomes of cemented and cementless unicompartmental knee replacements: data from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man. *Acta Orthop* 2020; 91(1): 76-81 (Appendix 1).

(2) Mohammad HR, Bullock G, Kennedy JA, Mellon SM, Murray DW, Judge AJ. Cementless unicompartmental knee replacement achieves better ten year clinical outcomes than Cemented – A systematic review. *Knee Surg Sports Traumatol Arthrosc.* 2020; 1:1-7 (Appendix 1).

RCTs^{187, 202} comparing cemented and cementless UKRs found no differences in functional outcomes but the prevalence of partial and complete radiolucencies were lower in cementless implants. These trials were too small to compare revision rates. However, raw data from the NZJR¹⁷ suggests that the cementless UKR has a lower revision rate than the cemented UKR. It is not currently clear whether the difference in revision rate seen in the NZJR is due to differences in the implants or to other factors. For example it could be that more experienced surgeons, who are doing larger numbers and therefore have lower revision rates are predominantly using cementless components. This is problematic given raw data reported from the joint registries does not control for these important confounders and could mislead many surgeons on what the actual relative performance of each implant was. Therefore any comparative analysis must adjust for these factors.

The NJR was established in 2002 by the Department of Health and Welsh Government as per Lord Hunt's recommendation and its history was extensively discussed in section 1.8.1. From 1st April 2003 all primary and revision knee replacements performed at both NHS and private hospitals have been routinely collected. Procedures performed in Northern Ireland and from the Isle of Man have also been collected from February 2013 and July 2015 respectively. It is now the world's largest arthroplasty register with over two million joint replacements recorded and is linked to the UK's Office of National Statistics (ONS) mortality data⁸.

The NJR's purpose is to collect joint replacement surgery data to provide early insight into issues pertaining to patient safety and in a continuous effort to improve the clinical and cost effectiveness of procedures performed and to support and enable research.

Unfortunately, the NJR does not report the revision rates of cemented and cementless UKR separately in their Annual Report. In this chapter NJR data is used to compare the revision rates following cemented and cementless Oxford UKRs. The null hypothesis was that there would be no difference between cemented and cementless UKR implant survival. To ensure that any difference in implant performance was due to the fixation rather than other factors, cemented and cementless cases were propensity matched on patient, surgeon (including caseload) and implant factors.

4.1.2 Methods

A retrospective observational study was performed using NJR records for all patients who had an Oxford UKR inserted. A formal application was submitted to the NJR Research Sub-Committee to access the relevant data and perform the work at the Musculoskeletal Research Unit at the University of Bristol. This application was approved on 5th July 2018 (Appendix 4).

4.1.2.1 NJR data collection

Informed and voluntary patient consent is required for joint replacement procedures to be included in the NJR database with identifiable information including surname, date of birth, NHS number and postcode. If consent is not obtained, then only anonymous surgical data can be included not allowing linkage to subsequent procedures. The 2019 Annual NJR Report⁸ states that 94% of all patients provided consent for their details to be recorded in the NJR.

Data collection forms are completed by every operating surgeon at the time of any primary or revision knee replacement surgery (Appendix 4). These forms collect data on patient demographics, the procedure performed, and the components implanted. Data from these forms is then electronically entered in the NJR data entry system through a portal by trained staff in each hospital. Each patient who has given consent to their data being used by the NJR is given a unique identifier which allows the primary replacement procedure to be linked to any subsequent revision procedures in which components are added, removed or replaced. Currently the most recent Annual NJR Report reports a linkability of 96%⁸.

The NJR collects data on patient factors (including age, sex, BMI, American society of

Anaesthesiologists (ASA) grade), implant factors (including component design, sizes and manufacturer type) and surgical factors (surgical approach, indication, caseload, operating surgeon grade) for each replacement procedure, which are provided by the operating surgeon. The NJR database is linked to the ONS which provides data on patient mortality.

4.1.2.2 NJR data extract

An extract of data was received from the NJR containing details of all primary Oxford UKRs recorded in the NJR for any indication between 1st January 2005 and 31st December 2016 (n=50,334). The former date was the first complete year of data the NJR could supply. The later date was chosen to provide a minimum 1-year follow up period for determining outcomes following primary joint replacement surgery. Prior to obtaining the dataset the entire NJR database was linked to the ONS database using unique patient identifiers for all cause patient mortality data.

4.1.2.3 Data cleaning

The data extract which contained 50,334 Oxford UKRs was loaded into Stata (Version 15.1, Texas, USA) and subsequently coded and cleaned. Each continuous, categorical and string variable was systematically assessed for inconsistencies and implausible/missing data.

Data cleaning involved the removal of lateral UKRs, hybrids, complex primaries, old tibial sizes and missing component data given our study was focussing on comparing the outcomes of cemented and cementless Oxford medial UKRs. After data cleaning there were 40,522

UKRs (30,814 cemented and 9,708 cementless) eligible for study inclusion (Figure 4.1).

After data cleaning the only variable with missing data was BMI. However this did not vary significantly between groups and was well balanced between comparative groups both before and after matching.

Following data cleaning all numerical variables distributions were assessed graphically for normality, with the data subsequently summarised based on the respective distribution. Binary categorical variables, such as sex, were maintained in their format. Multi-level categorical variables were made binary where possible to aid data processing and analysis. For example there are four main surgical approaches that can be used for medial Oxford UKR surgery, however the overwhelming majority are performed through a medial parapatellar approach. Therefore this multilevel categorical variable was converted into a binary variable (i.e medial parapatellar approach and other). The remaining multilevel categorical variables were grouped to retain the minimum number of levels required to clinically differentiate them from each other. For example ASA grade is graded as one to five in the NJR although it is standard nomenclature in NJR studies to code this variable at one, two and three plus, as little is gained from the categories four and five being separate. This is as per several other published registry studies^{203, 204}.

Every surgeon in the NJR has a unique identifier, which was used to calculate each operating surgeons' UKR caseload for each calendar year. The mean caseload (cases per year) was then calculated for each surgeon, with the exclusion of years in which surgeons were inactive (to prevent artificial reductions for surgeons who started operating in later years or who subsequently stopped performing UKR procedures). Each patient was allocated a value

representing the caseload of the operating surgeon. Surgeon caseloads were grouped into three categories: low-volume (<10 cases/year), medium-volume (10 to <30 cases/year), and high-volume (≥ 30 cases/year). These thresholds were described by Liddle et al.²¹ and are evidence-based, unlike other thresholds. Liddle et al.²¹ found that revision rates fell steeply with increasing caseload up 10 cases/year. Thereafter, revision rates decreased at a slower rate until they plateaued at ≥ 30 cases/year.

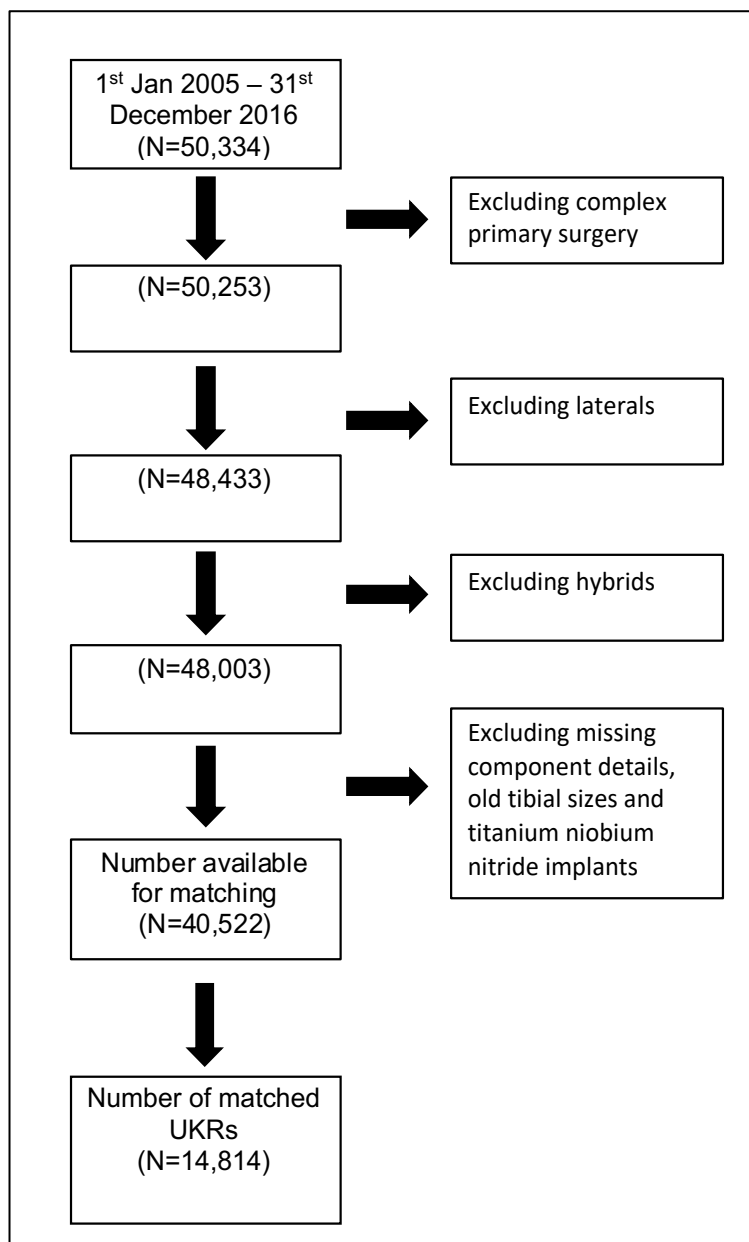


Figure 4.1. Data cleaning flowchart for NJR UKR fixation dataset

4.1.2.4 Outcomes of interest

The primary outcome of interest for this comparative study was the 10 year implant survival of cemented and cementless UKRs. The secondary outcomes for this study were a comparison of (1) indications for revision surgery and (2) long term patient survival.

4.1.2.5 Identification of confounding factors

As will be discussed in section 4.2.2.1 the NJR collects data on patient factors (including age, sex, BMI, ASA grade), implant factors (including component design, sizes and manufacturer type) and surgical factors (surgical approach, indication, operating surgeon grade) for each replacement procedure. A literature search was conducted to identify published studies showing whether certain variables collected by the NJR could influence the primary outcome, the revision rate. The potential confounders are summarised in Table 4.1.

Identified potential confounder	Evidence in literature
<u>Patient factors</u>	
Age	Bayliss et al. ²⁰⁵ Murphy et al. ²⁰⁶
Gender	Lim et al. ²⁰⁷
Primary diagnosis	Hamilton et al. ²⁰⁸
Unilateral/Bilateral replacements	Mementsoudis et al. ²⁰⁹
ASA grade	Prempeh et al. ²¹⁰ Elmallah et al. ²¹¹ Lenguerrand et al. ²¹²
<u>Surgical factors</u>	
Thrombo mechanical prophylaxis	Selby et al. ²¹³
Surgeon caseload	Liddle et al. ²¹
Surgical approach	Picard et al. ²¹⁴
Bone graft usage	Hosaka et al. ²¹⁵
<u>Implant factors</u>	
Implant design	Deere et al. ²¹⁶
Component size	Judge et al. ²¹⁷

Table 4.1. Identified potential revision confounders from literature search

4.1.2.5 Propensity score matching

The unmatched cohort consisted of 40,522 UKRs (30,814 cemented and 9,708 cementless). Given the potential for patient, surgical and implant factors other than the type of fixation (as identified in section 4.1.2.4) to affect the revision rate, a priori matching of the cemented and cementless groups was performed for multiple known confounders using propensity scores. (Surgical factors included surgeon caseload, defined as the average number of UKRs done per year and stratified into low (<10 cases/year), medium (10 to <30 cases/year) and high volume (≥ 30 cases/year) as described previously. After matching there were 14,814 UKRs (7,407 cemented and 7,407 cementless UKRs) included for analysis.

Confounders were selected for inclusion in the propensity score based on those known to affect the outcomes of interest (Table 4.1) and not on the basis of being associated with the fixation exposure variable as per published recommendations for variable selection in propensity models²¹⁸.

4.1.2.6 Statistical analysis

Logistic regression generated a propensity score representing the probability of receiving a cementless replacement. These scores were generated from patient, surgical (including surgeon caseload), and implant factors. The specific variables used for matching were age, sex, primary diagnosis, bilateral UKRs, ASA grade, thromboprophylaxis, mechano-prophylaxis, year of surgery, surgeon grade, surgeon caseload, surgical approach, component sizes and the use of bone graft. BMI was not used for matching given it had a significant proportion of missing data. However BMI was not problematic given it was well balanced in both fixation groups both before and after matching and this approach is consistent with several other NJR studies^{203, 204}.

By controlling for these covariates, the use of propensity score matching would allow the true effect of implant fixation on revision surgery to be accurately assessed. This a priori approach was supported by the significant differences in patient, surgical and implant factors between the unmatched cemented and cementless groups presented in the results section.

The algorithm used matched on the logit of the propensity score with a 0.02-SD calliper width. The matching ratio was one-to-one. Greedy matching without replacement was used given its superior performance for estimating treatment effects²¹⁹. Standardised mean differences (SMDs) were examined both before and after matching to assess for any covariate imbalance between the cemented and cementless UKRs, with SMDs of 10% or more considered suggestive of covariate imbalance²¹⁹.

Outcomes of interest were: (1) implant survival, (2) indications for revision surgery and (3) patient survival. Cumulative survival was determined using the Kaplan-Meier method. The endpoint for implant survival was revision surgery (any implant component removed, exchanged or added) and the endpoint for patient survival was mortality. Implant and patient survival rates were compared between the cemented and cementless groups, using univariate cox regression models, with the proportional hazards assumptions assessed and satisfied in all analyses. To account for clustering within the matched cohort a robust variance estimator was used in the regression models. As a sensitivity analysis regression analysis was repeated with adjustments made for covariates with residual imbalance after matching (SMD of 10% or more). Additionally a multi-level frailty model was tested in the regression models to control for patient clustering within surgeons. However both adjusted models and the multilevel models gave the same results as the univariate models and hence only these are presented.

The proportional Chi-squared test with Yate's correction was used to compare the frequency of revisions for specific indications between the cemented and cementless UKR groups.

All statistical analyses were performed using Stata (Version 15.1, Texas, USA) except propensity score matching which was performed using R (Version 3.4.0, R Foundation for Statistical Computing, Vienna, Austria). P-values of <0.05 were considered significant, with 95% CIs presented.

4.1.3 Results

4.1.3.1 Propensity score matching

The unmatched cohort consisted of 40,522 Oxford UKRs (30,814 cemented and 9,708 cementless). Baseline characteristics differed between the cemented and cementless groups (Table 4.2). Specific covariates which differed significantly ($SMD > 0.1$) were sex, thromboprophylaxis, mechano-prophylaxis, year of surgery, surgeon caseload, implant component size (tibial, femoral, bearing and bearing type). These differences were clearly highlighted by the distribution of propensity scores before matching (Figure 4.1).

The matching process improved the balance of covariates between cemented and cementless groups (Table 4.2) and was confirmed on analysis of the distribution of propensity scores after matching (Figure 4.2). After matching there remained some residual imbalance of year of surgery.

	Unmatched cohort (n=40,522)			Matched cohort (n=14,814)		
	Cemented (n=30,814)	Cementless (n=9,708)	SMD	Cemented (n=7407)	Cementless (n=7407)	SMD
<i>Covariate</i>						
Gender						
Female	14,707 (47.7%)	4,068 (41.9%)	0.12	3077 (41.5%)	3078 (41.6%)	<0.001
Male	16,107 (52.3%)	5,640 (58.1%)		4330 (58.5%)	4329 (58.4%)	
Age at surgery (year)						
Mean (SD)	64.7 (SD 9.5)	64.8 (SD 9.5)	0.01	64.6 (SD 9.6)	64.7 (SD 9.5)	0.003
BMI (kg/m²)*						
Mean (SD)	30.2 (SD 5) (n=18,669)	30.4 (SD 5.2) (n=8,297)	0.04	30.2 (SD 4.9) (n=5565)	30.4 (SD 5.2) (n=6236)	0.05
Primary diagnosis						
Primary OA	30,474 (98.9%)	9,585 (98.7%)	0.02	7,314 (98.7%)	7,319 (98.8%)	0.006
<i>Other</i>	340 (1.1%)	123 (1.3%)		93 (1.3%)	88 (1.2%)	
Bilateral UKRs	874 (2.8%)	451 (4.6%)	0.1	245 (3.3%)	248 (3.4%)	0.002
ASA grade						
1	6321 (20.5%)	2120 (21.8%)	0.05	1,536 (20.7%)	1,489 (20.1%)	0.02
2	21,983 (71.3%)	6704 (69.1%)		5,227 (70.6%)	5,272 (71.2%)	
3 or above	2510 (8.1%)	884 (9.1%)		644 (8.7%)	646 (8.7%)	

VTE – chemical						
LMWH (+/-other)	17,561 (57.0%)	6,228 (64.2%)	0.40	4,624 (62.4%)	4,687 (63.3%)	0.02
Aspirin only	4,152 (13.5%)	1006 (10.4%)		727 (9.8%)	719 (9.7%)	
Other	5,496 (17.8%)	2,251 (23.2%)		1,851 (25.0%)	1,790 (24.2%)	
None	3,605 (11.7%)	223 (2.3%)		205 (2.8%)	211 (2.8%)	
VTE – mechanical						
Any	29,316 (95.1%)	9,631 (99.2%)	0.25	7,332 (99.0%)	7,330 (99.0%)	0.003
None	1,498 (4.9%)	77 (0.8%)		75 (1.0%)	77 (1.0%)	
Year of surgery						
2005	1100 (3.6%)	8 (0.1%)	1.32	9 (0.1%)	8 (0.1%)	0.18
2006	1889 (6.1%)	40 (0.4%)		38 (0.5%)	40 (0.5%)	
2007	2702 (8.8%)	28 (0.3%)		61 (0.8%)	28 (0.4%)	
2008	3344 (10.9%)	82 (0.8%)		147 (2.0%)	82 (1.1%)	
2009	3460 (11.2%)	261 (2.7%)		238 (3.2%)	261 (3.5%)	
2010	3256 (10.6%)	404 (4.2%)		349 (4.7%)	403 (5.4%)	
2011	3013 (9.8%)	639 (6.6%)		417 (5.6%)	637 (8.6%)	
2012	2962 (9.6%)	718 (7.4%)		695 (9.4%)	705 (9.5%)	
2013	2622 (8.5%)	960 (9.9%)		996 (13.4%)	864 (11.7%)	

2014	2637 (8.6%)	1545 (15.9%)		1500 (20.3%)	1,262 (17.0%)	
2015	2112 (6.9%)	2191 (22.6%)		1528 (20.6%)	1,555 (21.0%)	
2016	1717 (5.6%)	2832 (29.2%)		1429 (19.3%)	1,562 (21.1%)	
Surgeon grade						
Consultant	27,775 (90.1%)	8,571 (88.3%)	0.06	6,688 (90.3%)	6,622 (89.4%)	0.03
<i>Other</i>	3,039 (9.9%)	1,137 (11.7%)		719 (9.7%)	785 (10.6%)	
Surgeon caseload						
<10 cases/year	13,474 (43.7%)	2,656 (27.4%)	0.43	2327 (31.4%)	2364 (31.9%)	0.01
10 to <30 cases/year	12,685 (41.2%)	4,100 (42.2%)		3336 (45.0%)	3328 (44.9%)	
≥30 cases/year	4,655 (15.1%)	2,952 (30.4%)		1744 (23.5%)	1715 (23.2%)	
Surgical approach						
Medial parapatellar	28,154 (91.4%)	8,898 (91.7%)	0.01	6,827 (92.2%)	6,822 (92.1%)	0.003
Other	2,660 (8.6%)	810 (8.3%)		580 (7.8%)	585 (7.9%)	
Minimally invasive surgery						
No	16,287 (52.9%)	4,789 (49.3%)	0.07	3,796 (51.3%)	3,804 (51.4%)	0.002
Yes	14,527 (47.1%)	4,919 (50.7%)		3,611 (48.8%)	3,603 (48.6%)	

Femoral component size						
Ex small	47 (0.2%)	42 (0.4%)	0.14	26 (0.4%)	21 (0.3%)	0.02
Small	6904 (22.4%)	2504 (25.8%)		1,752 (23.7%)	1,727 (23.3%)	
Medium	16,608 (53.9%)	4,606 (47.4%)		3,617 (48.8%)	3,663 (49.5%)	
Large	7,171 (23.3%)	2,529 (26.1%)		1,990 (26.9%)	1,980 (26.7%)	
Ex-Large	84 (0.3%)	27 (0.3%)		22 (0.3%)	16 (0.2%)	
Tibial component size						
AA	93 (0.3%)	37 (0.4%)	0.37	29 (0.4%)	29 (0.4%)	0.01
A	3453 (11.2%)	352 (3.6%)		336 (4.5%)	343 (4.6%)	
B	7288 (23.7%)	1870 (19.3%)		1,513 (20.4%)	1,481 (20.0%)	
C	8769 (28.5%)	2807 (28.9%)		2,137 (28.9%)	2,147 (29.0%)	
D	7098 (23.0%)	2570 (26.5%)		1,974 (26.7%)	1,991 (26.9%)	
E	3216 (10.4%)	1537 (15.8%)		1095 (14.8%)	1084 (14.6%)	
F	897 (2.9%)	535 (5.5%)		323 (4.4%)	332 (4.5%)	

Bearing type						
Anatomic	23,301 (75.6)	9,407 (96.9%)	0.65	7,092 (95.8%)	7,106 (95.9%)	0.009
Symmetric	7,513 (24.4%)	301 (3.1%)		315 (4.3%)	301 (4.1%)	
Bearing size						
3	6226 (20.3%)	3003 (30.9%)	0.37	2056 (27.8%)	2000 (27.0%)	0.02
4	12,126 (39.4%)	4093 (42.2%)		3128 (42.2%)	3160 (42.7%)	
5	6765 (22.0%)	1787 (18.4%)		1459 (19.7%)	1483 (20.0%)	
6	3268 (10.6%)	578 (6.0%)		519 (7.0%)	523 (7.1%)	
7	1506 (4.9%)	161 (1.7%)		150 (2.0%)	156 (2.1%)	
8	563 (1.8%)	57 (0.6%)		62 (0.8%)	56 (0.8%)	
9	320 (1.0%)	29 (0.3%)		33 (0.4%)	29 (0.4%)	
Bone graft						
None	30,745 (99.8%)	9,629 (99.2%)	0.08	7,377 (99.6%)	7,381 (99.7%)	0.009
Bone graft used	69 (0.2%)	79 (0.8%)		30 (0.4%)	26 (0.4%)	

Table 4.2. Patient and surgical factors before and after propensity score matching.

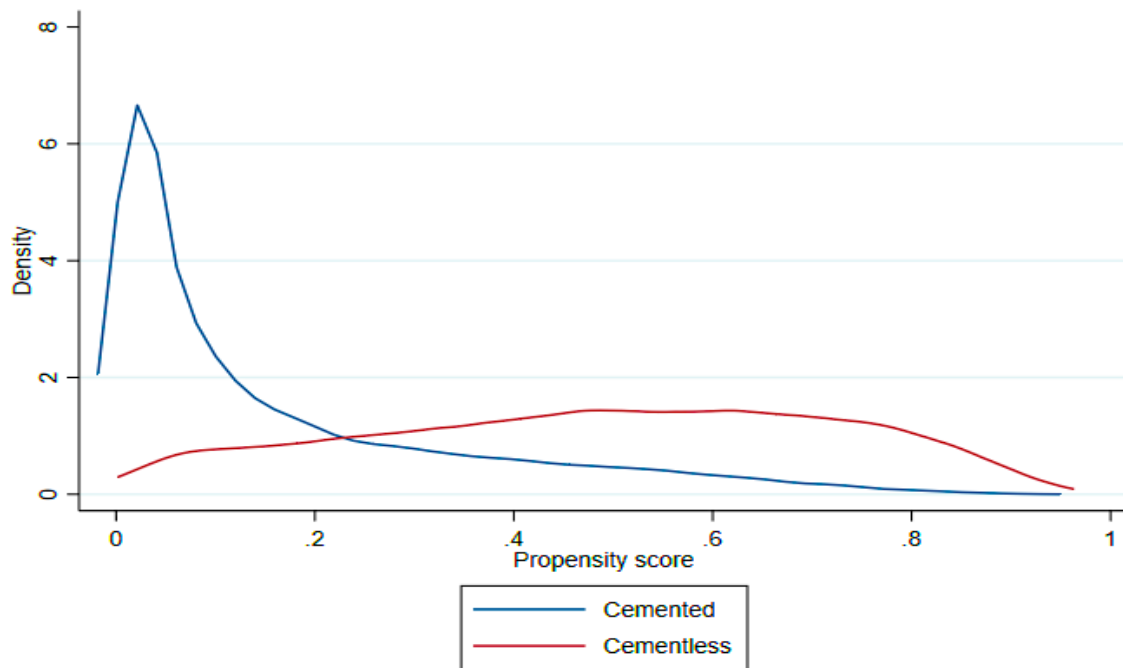


Figure 4.2. Kernel density plot of propensity scores of cemented and cementless UKRs before matching.

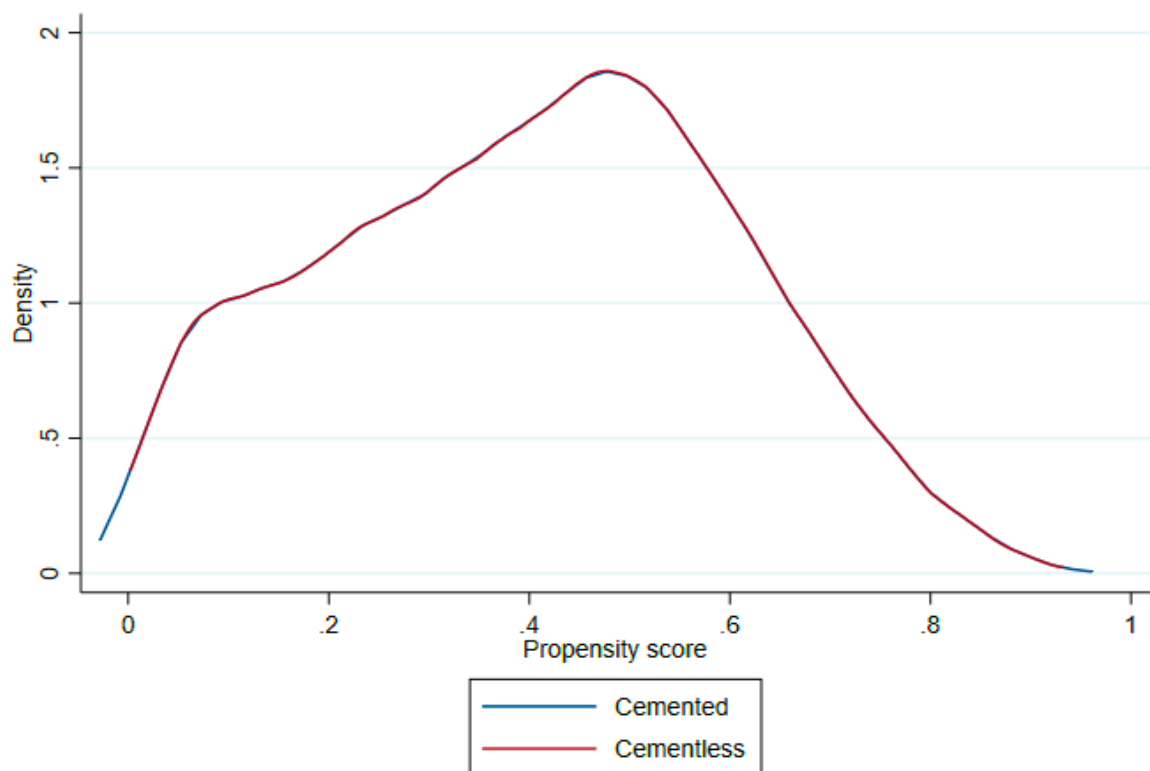


Figure 4.3. Kernel density plot of propensity scores of cemented and cementless UKRs after matching.

4.1.3.2 Revision outcome

For the primary outcome measure both the unmatched and matched results are presented to highlight the importance of matching to allow for fair comparison between fixation types by controlling for confounders which not only influence the direction, but also magnitude of an effect size.

4.1.3.2.1 Unmatched analysis

The unmatched cohort included 40,522 UKR of which 30,814 were cemented and 9,708 were cementless. The mean age at surgery was 64.7 years (SD 9.5), with 18,775 females (46.3%) and 21,747 males (53.7%). The mean BMI was 30.2 kg/m² (SD 5.0) with the primary indication for surgery being osteoarthritis in 40,059 knees (98.9%).

In the unmatched cohort, the mean follow up for both cemented and cementless implants were 6.4 years (SD 3.1) and 3.5 years (SD 2.1) respectively. In total 2,647 knees (258 cementless and 2,389 cemented) underwent revision surgery. The 10-year implant survival rates for unmatched cementless and cemented UKRs were 93.3% (CI 89.8 – 95.7) and 89.1% (CI 88.6 - 89.6) respectively (Figure 4.4). Cementless UKRs had a significantly better implant survival compared with cemented UKRs (hazard ratio (HR) = 0.59, CI 0.52 - 0.68); $p < 0.001$). However the baseline characteristics for unmatched cemented and cementless implants differed significantly (Table 4.2). Therefore in order to understand whether there is any true difference a matched comparison is required and will be presented in the next section.

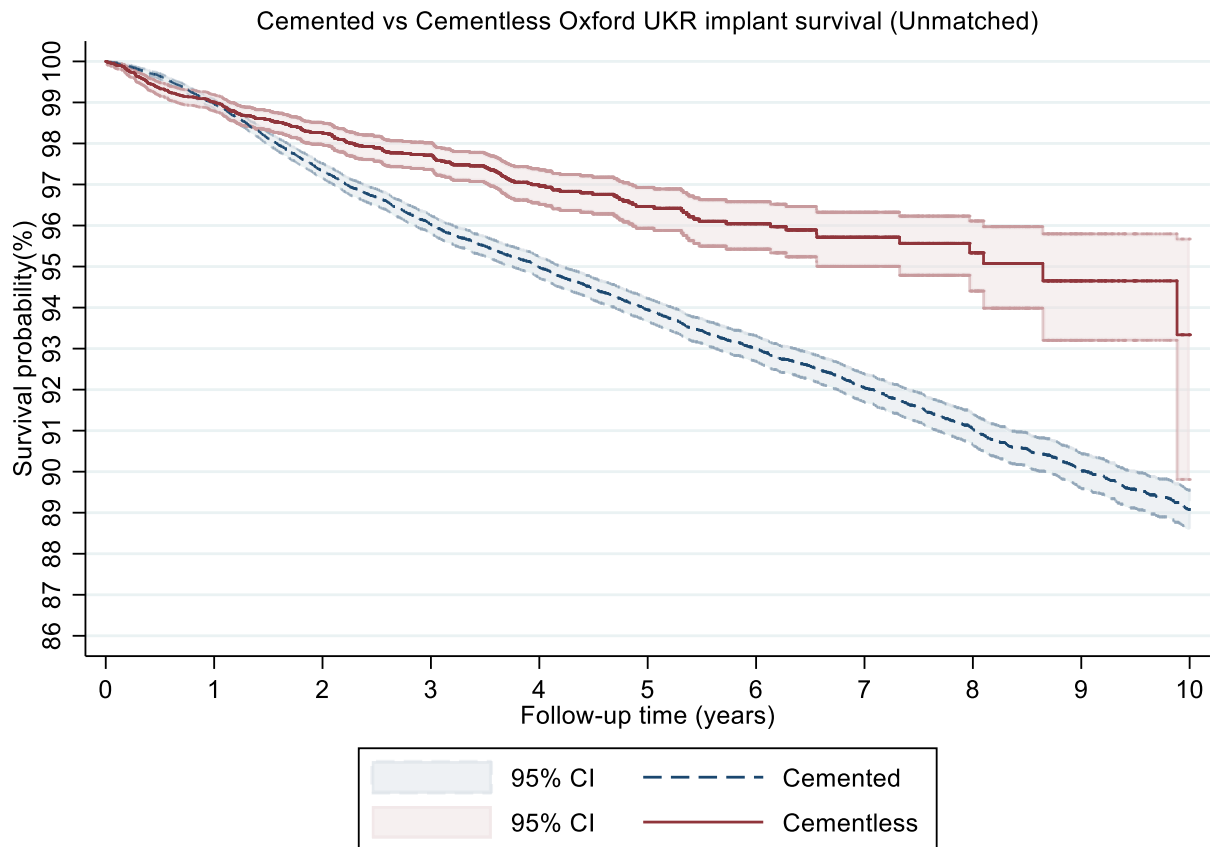


Figure 4.4. Unmatched Kaplan Meier graph of cemented and cementless Oxford UKR implant survival.

4.1.3.2.2 Matched analysis

The matched cohort included 14,814 UKR with 7,407 cemented UKRs and 7,407 cementless UKRs. The mean age at surgery was 65 years (SD 9.5), with 6,155 females (42%) and 8659 males (58%). The mean BMI was 30 kg/m² (SD 5.0) with the primary indication for surgery being osteoarthritis in 14,633 knees (99%). Patient, surgical (including caseload) and implant characteristics became well balanced between the cemented and cementless groups after propensity score matching (Table 4.2). The only covariate with residual imbalance was year of primary surgery, which when adjusted for in the regression models did not change the results presented. Additionally the use of a multilevel frailty model controlling for patient clustering

within operating surgeons did not change the regression findings presented below.

In the matched cohort, the mean follow up for both cemented and cementless implants was 4 years (SD 2). 507 knees, 218 (2.9%) cementless and 289 (3.9%) cemented underwent revision surgery. The 10 year cumulative implant survival rates were 93.2% (CI 89.7 - 95.6) and 90.2% (CI 87.5 - 92.3) for cementless and cemented respectively (Figure 4.5). The corresponding cumulative revision rates were 6.8% (CI 4.4 – 10.3) and 9.8% (CI 7.7 – 12.5) at 10 years respectively. Cementless UKRs had a significantly reduced revision rate compared with cemented UKRs (HR=0.76, CI 0.64 - 0.91; p=0.002). The cumulative revision rates at 10 years have overlapping CIs given the limited numbers of UKRs available at this specific time point. This is well illustrated by the widening CIs in Figure 4.5 at 10 years. The HR on the other hand compares the risk of revision across the whole survival curve and is statistically significant.

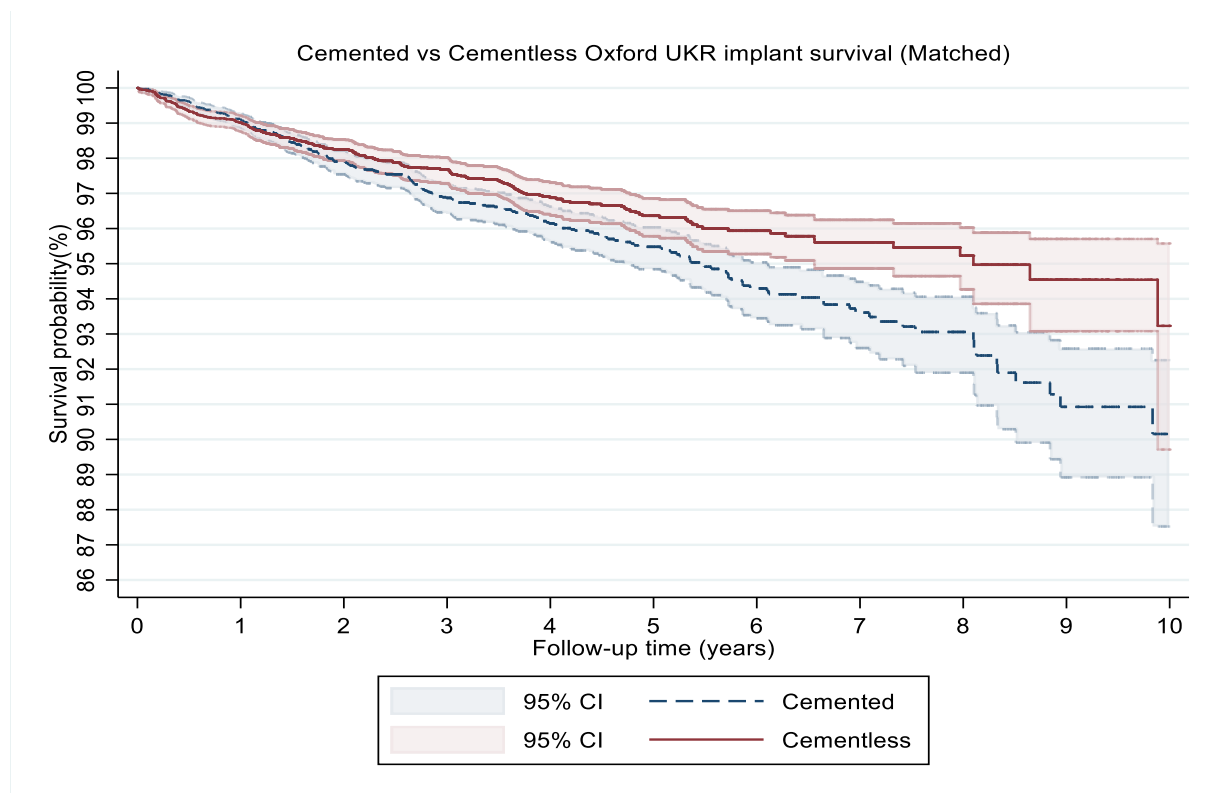


Figure 4.5. Matched Kaplan Meier graph of cemented and cementless Oxford UKR implant survival.

4.1.3.3 Indications for revision surgery

The most common reasons for revision in the cemented group (n= 7,407) were aseptic loosening (n=74, 1.00%), pain (n=55, 0.74%) and osteoarthritis progression (n=72, 0.97%) (Table 4.3).

In the cementless group (n=7,407) the most common reasons for revision were osteoarthritis progression (n=55, 0.74%), pain (n=34, 0.46%) and aseptic loosening (n=31, 0.42%) (Table 4.3).

Four specific revision indications were significantly different between cemented and cementless groups (Figure 4.6): Aseptic loosening, which decreased from 1.0% to 0.42% ($p<0.001$), pain, which decreased from 0.74% to 0.46% ($p=0.03$) and lysis, which decreased from 0.15% to 0.04% ($p=0.03$). The risk of revision for periprosthetic fracture was significantly higher ($p=0.01$) in the cementless group (n=19, 0.26%) compared with the cemented (n=7, 0.09%).

Revision indication	Cemented UKRs (n=7,407)	Mean time to revision indication for cemented UKRs (years)	Cementless UKRs (n=7,407)	Mean time to revision indication for cementless UKRs (years)	Comparison between cemented and cementless revision indication frequencies (P value)
Aseptic loosening*	74 (1.00%)	1.5 (SD 2.1)	31 (0.42%)	2 (SD 2.0)	P <0.001
OA progression	72 (0.97%)	3.5 (SD 2.5)	55 (0.74%)	3.7 (SD 2.0)	P=0.13
Pain*	55 (0.74%)	2.8 (SD 2.1)	34 (0.46%)	2.0 (SD 1.5)	P=0.03
Other	41 (0.55%)	2.5 (SD 2.0)	29 (0.39%)	2.0 (SD 1.3)	P=0.15
Dislocation subluxation revision	28 (0.38%)	1.6 (SD 1.6)	21 (0.28%)	1.2 (SD 1.2)	P=0.40
Instability	13 (0.18%)	2.9 (SD 1.3)	20 (0.27%)	1.9 (SD 1.9)	P=0.25
Component dissociation	13 (0.18%)	1.4 (SD 1.1)	16 (0.22%)	2.2 (SD 2.1)	P=0.59
Malalignment	13 (0.18%)	1.2 (SD 0.9)	24 (0.32%)	1.8 (SD 1.4)	P=0.09
Infection	15 (0.20%)	1.9 (SD 2.1)	13 (0.18%)	1.8 (SD 1.8)	P=0.78
Periprosthetic fracture*	7 (0.09%)	1.0 (SD 0.9)	19 (0.26%)	1.0 (SD 2.4)	P=0.01
Lysis*	11 (0.15%)	2.5 (SD 1.4)	3 (0.04%)	1.6 (SD 1.0)	P=0.03
Wear	7 (0.09%)	4.0 (SD 2.8)	7 (0.09%)	3.5 (SD 2.9)	P=1.0

Stiffness	5 (0.07%)	1.6 (SD 0.6)	7 (0.09%)	1.4 (SD 1.0)	P=0.67
Implant fracture	1 (0.01%)	2.0	0 (0%)	N/A	No revisions
Patellar wear	0 (0%)	N/A	0 (0%)	N/A	No revisions
Tibial wear	0 (0%)	N/A	0 (0%)	N/A	No revisions
Incorrect sizing	0 (0%)	N/A	0 (0%)	N/A	No revisions
Patella mal tracking	0 (0%)	N/A	0 (0%)	N/A	No revisions

Table 4.3. Comparison of revision indications between the matched cemented and cementless Oxford UKRs. The proportional Chi-squared test was used to compare the frequency of revisions for specific indications between groups. Significant differences between groups are marked *.

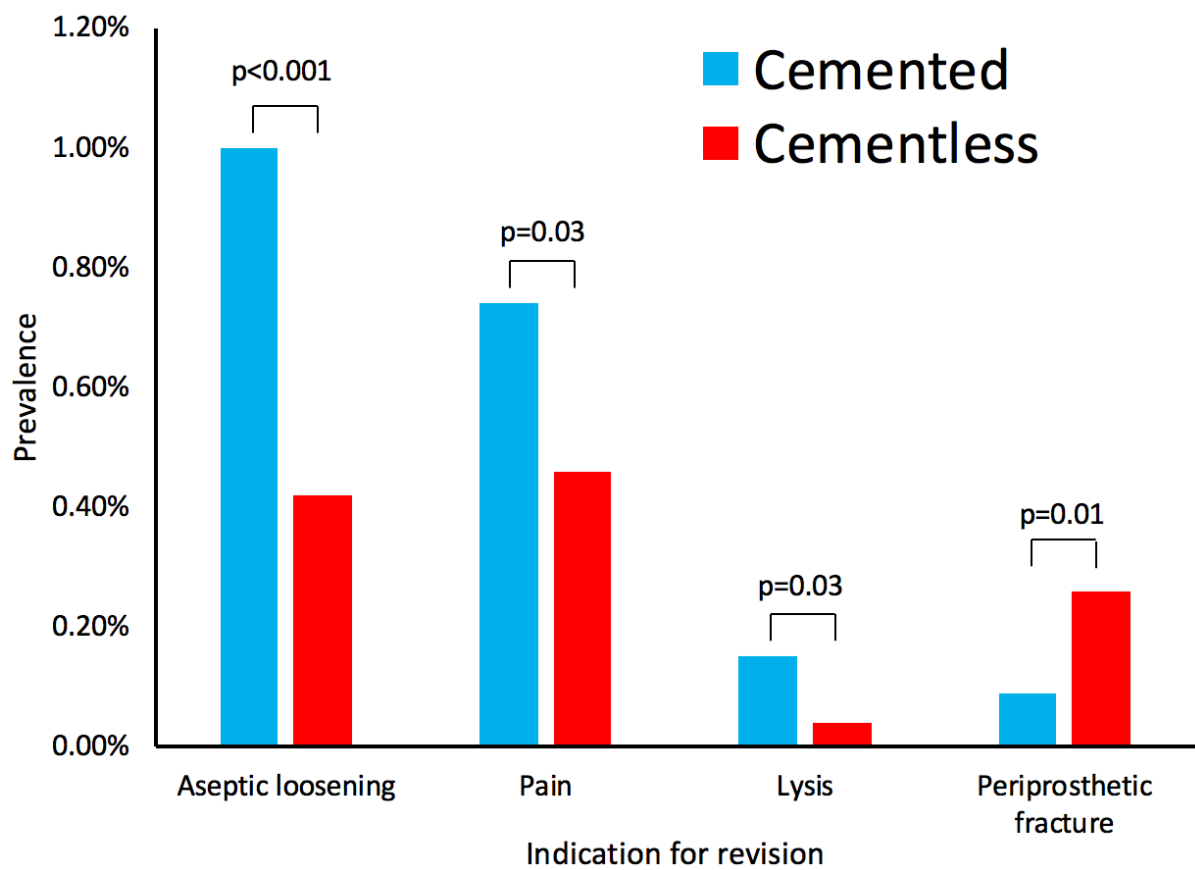


Figure 4.6. Bar chart showing significant differences in revision indications between cemented and cementless Oxford UKRs.

4.1.3.4 Patient survival

In the matched cohort there were 517 (276 cementless and 241 cemented) patient deaths. 11 deaths occurred within 90 days of surgery (seven cementless and four cemented). The cumulative 10 year patient survival rates for cementless UKR were 85.3% (CI 80.8 - 88.9) and 87.6% (CI 84.5 - 90.0) for cemented UKR (Figure 4.7). This difference was not statistically significant (HR=1.16, CI 0.98 - 1.38; p=0.1).

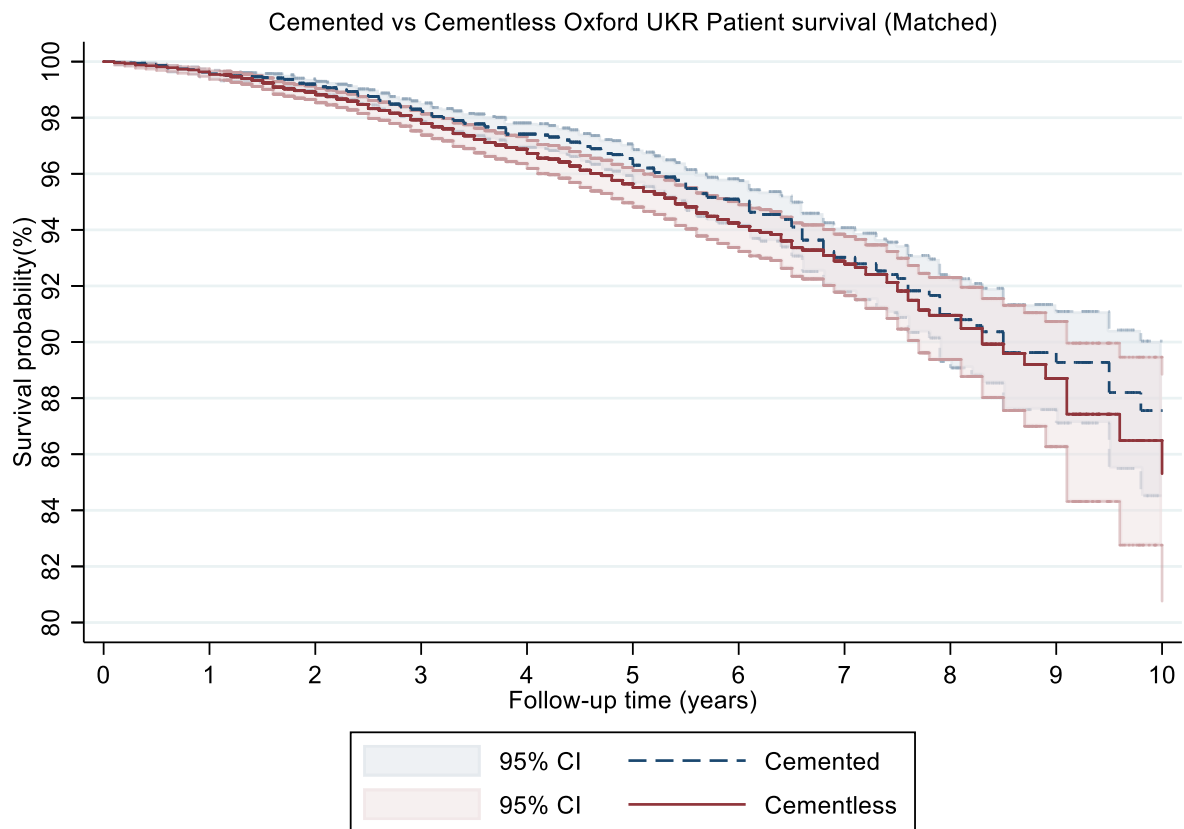


Figure 4.7. Kaplan Meier graph of patient survival of matched cemented and cementless Oxford UKRs.

4.1.4 Discussion

Early cementless UKRs had poor outcomes²²⁰⁻²²³, but over time the results have improved¹⁵³ given advancements in implant design including hydroxyapatite coatings, porous and trabecular metal^{224, 225}. Unmatched data from the NZJR¹⁷, and now unmatched NJR data has shown that the revision rate of the cementless Oxford UKR is lower than the cemented. Given, this is raw unmatched data, one cannot be certain why, given many factors including more experienced surgeons using the cementless implant, may contribute to this effect. The analysis presented in this chapter of approximately 15,000 UKRs propensity matched to exclude other potential patient, surgical and implant factors, has shown the long term revision rate of the cementless Oxford UKR is 24% less (HR 0.76, $p=0.002$) than the cemented. These results suggest that the cementless Oxford UKR is a better performing implant. Therefore the introduction of the cementless Oxford UKR has achieved its objective in lowering UKR revision rates in the joint registries although the 10 year implant survival still lags behind that achieved from TKR (Table 1.1). Nonetheless this reduction in UKR revision rates should in time encourage more surgeons to use UKRs where clinically appropriate.

The number of revisions for aseptic loosening, pain and lysis were all significantly lower in the cementless group. Indeed the combined revision rate from these causes was about half with cementless compared to cemented fixation. Previous randomised studies^{187, 202} have shown the incidence of tibial radiolucent lines are much lower with cementless rather than cemented fixation, suggesting improved fixation. This would explain why the revision rate for aseptic loosening and lysis has decreased. It is not clear why the revision rate for pain has decreased but may be related to the exothermic reaction of cement setting which may irritate surrounding soft tissues and nerves²²⁶. Alternatively in the presence of pain surgeons are more

likely to revise a component with radiolucent lines, which are more common in cemented UKRs, despite evidence that these radiolucent lines are poor predictors of loosening¹⁸⁵.

The only revision indication that occurred more with the cementless UKR than cemented was peri-prosthetic fracture, with the revision rates being 0.26% and 0.09% ($p=0.01$) respectively. This difference in 0.17% is however relatively small compared to the overall decrease in revision rate. The mean time to revision for peri-prosthetic fracture was one year, which is earlier than for most other revisions, so with time the proportion of revisions due to peri-prosthetic fractures should reduce further. Information about the peri-prosthetic fracture site is not recorded by the NJR, but it is likely that the majority were tibial plateau fractures. A cadaver study has shown that the load to fracture is lower with a cementless than a cemented tibial component¹⁹⁹, suggesting this may relate to the interference fit required by cementless components. Given tibial plateau fractures are devastating complications, often requiring complex revisions to TKR with stems and wedges, surgeons should take care to avoid them when implanting cementless components. Specifically surgeons should avoid deep cuts, ensure the vertical cut is just medial to the tibial spine, protect the posterior cortex, insert the tibial trial with finger pressure alone and impact the tibial component with care.

This is the first big data study of a knee replacement that has demonstrated the cementless version has lower revision rates than the cemented in the long term, and that the difference is likely from improved fixation. This may however relate to the design of the Oxford UKR. Given all ligamentous structures are preserved and there is an unconstrained mobile bearing, the loads transmitted to the bone implant interface are predominantly compressive with minimal shear or tension which is ideal for cementless fixation. These results may therefore not apply to all types of UKR or to TKR. Therefore in the next chapter a systematic review

comparing all types of cemented and cementless UKRs is presented to see whether these findings apply to other UKR types.

The main limitation of this chapter is that it is all based on registry data and is therefore a study of revision and not re-operation or other clinical outcomes. However, many of these other outcomes have already been studied in RCTs. Additionally, the reasons for revision in the NJR, are those recorded at the time of surgery even if this subsequently changed due to histopathology and microbiology data. Registries can also underreport revisions^{109, 227} although there is no reason to believe this would differ between the comparative groups, and it is not possible to confirm causality in registry based studies. Another limitation is that, despite matching there is potential for residual confounding and matching can reduce the generalisability of the findings. The groups were not perfectly matched given there was imbalance in the year of primary surgery, as the cementless components were introduced after the cemented. This was mitigated as many of the early cemented cases were excluded as they had different shaped tibial components (numerical sizes). Although operating techniques improve with time, there were no differences in the findings when adjusted regression models for year of surgery were tested. A substantial proportion of BMI data was missing and therefore this was not used for matching although was well balanced between groups. The only way to achieve balance with respect to both known and unknown confounders is with a RCT. However to compare revision rates would require huge numbers and long follow up which would be impractical for an RCT.

In conclusion, this chapter observed the risk of revision of the cementless Oxford UKR was 24% less than that of the cemented version out to 10 years. This was primarily because the risk of revision for aseptic loosening, pain and lysis all decreased in the cementless, suggesting improved fixation.

However it is important to compare the findings of this chapter with non-registry data from studies across the world given the known limitations of registry data. Furthermore by looking at all UKR implants across the world, all types of cemented and cementless UKRs can be compared helping to validate the findings presented in the chapter globally.

4.2 Systematic review comparing cemented and cementless UKRs

4.2.1 Introduction

In Chapter 3 and Chapter 4.1 the concept of the two main fixation methods (cemented and cementless techniques) used to insert UKR components were introduced. Cemented components rely on the use of bone cement to fix the components to surrounding trabecular bone²²⁶ whereas cementless components rely on the principle of press fit fixation and osseointegration^{67, 228}. The current gold standard for knee replacements is cemented fixation given the poor results of the first cementless knee replacements^{8, 228}.

However in recent years there has been increased interest in cementless fixation given new advances in cementless component design⁶⁷, including hydroxyapatite coatings²²⁴ and trabecular metal²²⁵. Additionally given rising life expectancies, there is a need for a more natural biological fixation to last a patient's lifetime²²⁹. Furthermore cementless fixation offers known merits from avoidance of cementation errors and a reduction in radiolucent lines from existing published work^{171, 187, 202}. Indeed the registry propensity matched comparison²⁰⁰ presented in the previous chapter has demonstrated reduced revision risk, rates of aseptic loosening and pain in the cementless Oxford UKRs compared to the cemented version.

However it is important to compare the findings from the previous section with a review of non-registry data from studies all across the world. This offers the opportunity to compare all cemented and cementless UKR brands published in the literature. This chapter presents the first systematic review to compare the long term outcomes of all cemented and cementless UKRs by comparing published revision rates, revision indications and PROMs.

4.2.2 Methods

This systematic review was prospectively registered on PROSPERO, CRD42019134315 and follows the PRISMA guidelines for systematic reviews¹⁵¹.

4.2.2.1 Inclusion and exclusion criteria

The inclusion criteria were any studies in the English language that reported the ≥ 10 year outcomes of any primary medial UKR in patients over the age of 18 years. Studies included were from 2009 onwards to assess the outcomes of implants published within the last 10 years. This is given that the most commonly used cementless UKRs were introduced after cemented versions and first broadly used from 2009 onwards²⁰⁰.

Exclusion criteria included any registry studies given they tend not to distinguish and subdivide implants according to fixation and whether the implant is medial/lateral and to prevent duplication of patients with existing studies in the literature. Additionally registries can under report revisions^{109, 227}. Additional exclusion criteria were case reports, abstracts, hybrid UKRs and any studies in which lateral UKRs formed more than 10% of the whole cohort given the study was focusing on medial UKR outcomes. Studies of all polyethylene tibial components, bicompartamental replacements and those looking at only certain subgroups of the population were excluded given these contribute potential unnecessary confounders. Details of the number of articles actually excluded from the study based on the inclusion and exclusion criteria specified are summarised in Figure 4.8 in the results section.

4.2.2.2 Search strategy

With an expert librarian the databases Medline, Embase and CENTRAL were searched from their inceptions to 23rd April 2019 for all studies reporting knee replacement outcomes.

Key words used in the search strategy included “knee arthroplasty” and “fixation” with all synonyms, abbreviations and variations of these terms. The complete search strategies are summarised in Appendix 5. In addition reference lists of the included publications were also screened to identify any additional reports.

First all study duplicates were removed followed by a title and abstract screening based on the eligibility criteria. All shortlisted papers had full texts extracted and were assessed for eligibility. In cases where the same cohort was published more than once, the most recent publication reporting the overall outcomes of the full cohort was included. There was complete agreement between both independent authors (Hasan Raza Mohammad and Garrett Bullock) who independently screened the studies.

4.2.2.3 Outcomes of interest

The primary outcome of interest was revision. This was measured from ; (1) revision rate and (2) 10 year survivals reported. Revision was defined as any removal/addition of any component to the knee joint as per the registries^{8, 16, 17}. Secondary outcomes were PROMs. The a priori analysis was to first compare fixation groups (cementless vs cemented), and then compare bearing type (mobile vs fixed bearing) results within each fixation category.

4.2.2.4 Data collection and risk of bias

Two authors (Hasan Raza Mohammad and Garrett Bullock) independently extracted data from all included studies. Contact attempts were made for all authors to obtain any missing information as needed. In cases where a study reported results for both cemented and cementless fixation types, only UKR arms reporting long term outcomes were included in our review as per the specified inclusion criteria.

All studies were assessed for risk of bias using the MINORs tool¹⁵² as a percentage and an additional system based on the reporting of the primary outcome (A=clearly reported, B=not reported/unclear) and the number of cases (A > 100 cases, B 51-99 and C <50)^{147, 153}. Studies with a MINORS score over 80% were deemed at low risk of bias and those below 70% at high risk except those with three or more As in the primary outcomes.

4.2.2.5 Data synthesis and analysis

The unit of analysis in this chapter was the number of UKRs. The primary outcome, the revision rate was calculated per 100 component years which is equivalent to the annual rate (% pa) as per the Australian Joint Registry¹⁶ and previous reports. This involved dividing the total number of revisions by the total observed component years multiplied by 100. 95% CIs were generated using the Clopper Pearson method. To calculate the predicted 10 year survival this value was multiplied by 10 and then subtracted from 100. Each revision indication was also calculated per 100 component years using the same methodology. Revisions and their indications per 100 component years were compared between cemented and cementless implants and for fixed and mobile bearings using the chi squared proportional test.

From the included studies Campi et al. (2018A)¹⁴⁸ reported the results for 1,000 UKRs, but of these, 318 UKRs were also used in Mohammad et al.'s¹⁷¹ more recent study. We were able to obtain the results of Campi et al.'s (2018A)¹⁴⁸ unique 682 UKRs to prevent duplication of UKRs in our analysis. Therefore in our systematic review the number of UKRs reported for Campi et al. (2018A)¹⁴⁸ is 682. This prevented overpowering the study and used the most up to date information for the cohort.

All statistical analysis was performed using Stata (Version 15.1, Texas, USA). A p value of <0.05 was deemed statistically significant.

4.2.3 Results

The search identified 5,839 studies which after duplicate removal, title and abstract screening were reduced to 39 articles. Full texts analysis deemed 25 were deemed eligible for inclusion (Figure 4.8). The details of all full text articles excluded and the reasons for exclusion are summarised in Table 4.4.

In total there were 21 studies^{82, 157, 158, 161, 163, 165, 167, 168, 170, 172, 230-240} reporting the long term outcomes of cemented UKRs and five^{148, 171, 234, 241, 242} reporting the outcomes of cementless UKRs (Table 4.5). All the identified studies were observational cohort studies with no long term comparative studies. All studies scored low risk of bias except Aly et al.¹⁵⁷ (Table 4.6). The total number of UKRs in the cemented and cementless groups were 8,790 and 1,946.

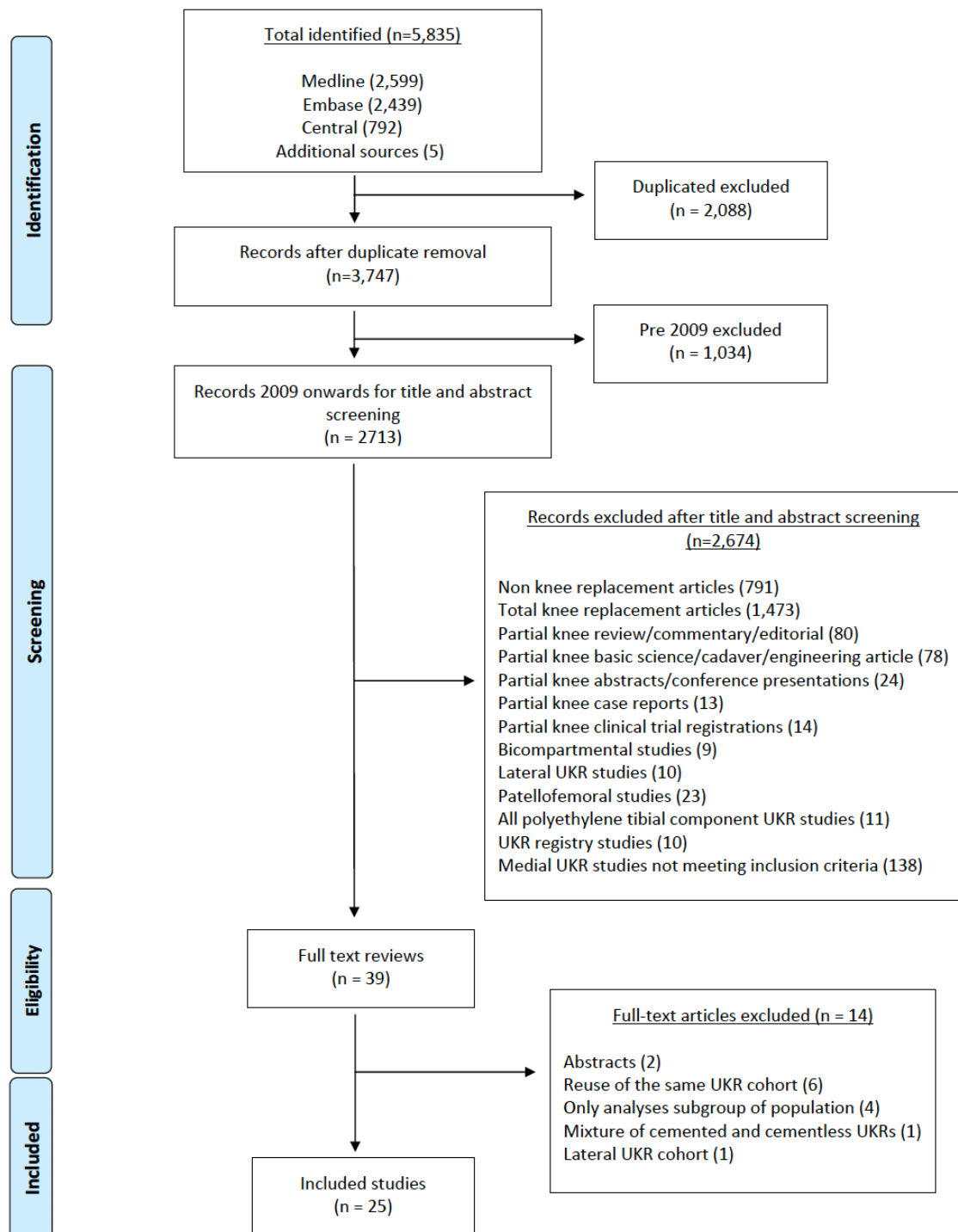


Figure 4.8. PRISMA flowchart.

Study	Reason for exclusion
Abdulkarim et al. (2013) ²⁴³	Abstract only
Ali et al. (2016) ²⁴⁴	Same cohort as Pandit et al. ⁸² but earlier results
Bottomley et al. (2016) ¹⁵⁹	Does not report results of cemented or cementless UKRs separately
Bray et al. (2017) ²⁴⁵	Abstract only
Campi et al. (2018B) ¹⁷² (cementless arm)	Cementless arm only reports short to midterm follow up. Cemented arm included in our review as reports long term outcomes.
Hamilton et al. (2016) ²⁴⁶	Same cohort as Pandit et al. ⁸² and only analyses subgroup of the cohort.
Hamilton et al. (2017) ²⁴⁷	Same cohort as Pandit et al. ⁸² and only analyses subgroup of the cohort.
Hamilton et al. (2017) ²⁴⁸	Same cohort as Pandit et al. ⁸² and only analyses subgroup of the cohort.
Hamilton et al. (2017) ²⁴⁹	Same cohort as Pandit et al. ⁸² and only analyses subgroup of the cohort.
Heyse et al. (2012) ²⁵⁰	Only analyses patients under 60 years of age
Kennedy et al. (2018) ⁸⁵	Same cohort as Pandit et al. ⁸² and does not report overall results of the cohort.
Kim et al. (2017) ²⁵¹	Only analyses patients under 60 years of age
Noaur et al. (2016) ²⁵²	Not available in English language and also only analyses patients under 60 years of age
Parratte et al. (2009) ²⁵³	Only analyses patients under 50 years of age
Saragaglia et al. (2018) ²⁵⁴	Exclude as over 10% of cohort are lateral UKRs

Table 4.4. List of full texts excluded with reasons from the systematic review.

	UKR prosthesis	Number of UKRs	Number of surgical centres
Cementless UKR studies			
Campi et al. (2018A) ¹⁴⁸	Oxford	682	2
Hall et al. (2013) ²⁴¹	Uniflex	85	1
Lecuire et al. (2014) ²⁴²	Alpina	101	1
Mohammad et al. (2019) ¹⁷¹	Oxford	1,000	1
Schlueter-Brust et al. (2014) ²³⁴ (cementless arm)	Uniglides	78	1
		Total: 1,946	Total: 6
Cemented UKR studies			
Alnachoukati et al. (2018) ²³⁵	Oxford	825	4
Aly et al. (2010) ¹⁵⁷	Oxford	45	1
Argenson et al. (2013) ²³¹	Miller-Galante	70	1
Campi et al. (2018B) ¹⁷² (cemented arm)	Oxford	522	1
Chattelard et al. (2013) ²³²	Alegretto, Presevation, Genesis, Hermes, HLS, Lotus, Miller-Galante, Oxford	559	13
Edmonson et al. (2015) ¹⁶¹	Oxford	364	1
Emerson et al. (2016) ¹⁵⁸	Oxford	213	1
Faour Martin et al. (2013) ¹⁶³	Oxford	511	1
Foran et al. (2013) ²³³	Miller-Galante	19	1
Kim et al. (2015) ¹⁶⁵	Oxford	180	1
Kristensen et al. (2013) ¹⁶⁷	Oxford	695	1
Lim et al. (2018) ²³⁷	Miller Galante/Preservation	279	1
Lisowski et al. (2016) ¹⁶⁸	Oxford	138	1
Pandit et al. (2015) ⁸²	Oxford	1,000	1
Price et al. (2011) ²³⁰	Oxford	682	1
Schlueter-Brust et al. (2014) ²³⁴ (cemented arm)	Uniglides	152	1
Song et al. (2016) ²⁴⁰	Miller-Galante	68	1
Venkatesh et al. (2016) ²³⁹	Miller-Galante	175	1
White et al. (2018) ²³⁶	Oxford	554	2
Winnock de Grave et al. (2018) ²³⁸	Zimmer Unicodylar Knee	460	1
Yoshida et al. (2013) ¹⁷⁰	Oxford	1,279	2
		Total: 8,790	Total: 38

Table 4.5. Details of included studies and UKR implants used.

Study	MINORS (%)	Size	Revisions reported	Implant survival reported	Mechanisms of failure reported	Bias risk
Cementless UKR studies						
Campi et al. (2018A) ¹⁴⁸	75	A	A	A	A	Low
Hall et al. (2013) ²⁴¹	75	B	A	A	A	Low
Lecuire et al. (2014) ²⁴²	75	A	A	A	A	Low
Mohammad et al. (2019) ¹⁷¹	87.5	A	A	A	A	Low
Schlueter-Brust et al. (2014) ²³⁴	87.5	A	A	A	A	Low
Cemented UKR studies						
Alnachoukati et al. (2018) ²³⁵	87.5	A	A	A	A	Low
Aly et al. (2010) ¹⁵⁷	56.3	C	A	B	A	High
Argenson et al. (2013) ²³¹	87.5	A	A	A	A	Low
Campi et al. (2018B) ¹⁷²	87.5	A	A	A	A	Low
Chattelard et al. (2013) ²³²	62.5	A	A	B	A	Low
Edmonson et al. (2015) ¹⁶¹	68.8	A	A	A	A	Low
Emerson et al. (2016) ¹⁵⁸	75	A	A	A	A	Low
Faour Martin et al. (2013) ¹⁶³	87.5	A	A	A	A	Low
Foran et al. (2013) ²³³	75	B	A	A	A	Low
Kim et al. (2015) ¹⁶⁵	75	A	A	A	A	Low
Kristensen et al. (2013) ¹⁶⁷	81.3	A	A	A	A	Low
Lim et al. (2018) ²³⁷	87.5	A	A	A	A	Low
Lisowski et al. (2016) ¹⁶⁸	81.3	A	A	A	A	Low
Pandit et al. (2015) ⁸²	81.3	A	A	A	A	Low
Price et al. (2011) ²³⁰	87.5	A	A	A	A	Low
Schlueter-Brust et al. (2014) ²³⁴	87.5	A	A	A	A	Low
Song et al. (2016) ²⁴⁰	87.5	B	A	A	A	Low
Venkatesh et al. (2016) ²³⁹	81.3	A	A	A	A	Low
White et al. (2018) ²³⁶	87.5	A	A	A	A	Low
Winnock de Grave et al. (2018) ²³⁸	81.3	A	A	A	A	Low
Yoshida et al. (2013) ¹⁷⁰	81.3	A	A	A	A	Low

Table 4.6. Risk of bias assessment of included studies.

4.2.3.1 Revision outcome by fixation type

Twenty four out of 25 studies (n=10,054) reported the number of revisions during the study period and the mean follow up which allowed for quantitative analysis (Figure 4.9). The only exception to this was Price et al²³⁰ (n=682) which reported the median follow up. Table 4.7 summarises this in detail for each study.

The overall revision rate for the cemented and cementless groups were calculated separately. In the cemented group (n=8,108) there were 456 revisions out of 62,637 component years resulting in a revision rate of 0.73% pa (CI 0.66-0.80) revisions per 100 component years (Table 4.7). This equates to a 10 year survival of 92.7%. In the cementless group (n=1,946) there were 57 revisions out of 12,740 component years resulting in a revision rate of 0.45% pa (CI 0.34-0.58) revisions per 100 component years (Table 4.7). This equates to a 10 year implant survival of 95.5%. The differences between cementless and cemented revision rates were significant (p<0.001). The revision rates are plotted in Figure 4.9.

There were 13 studies of the cemented Oxford UKR (n=6,326) and two studies of the cementless Oxford UKR (n=1,682). For the cemented Oxford, there were 381 revisions out of 49,384 component years giving a revision rate of 0.77% pa (CI 0.70-0.85). The cementless Oxford studies reported 37 revisions out of 9,874 component years giving a revision rate of 0.37% pa (CI 0.26-0.52). The difference between the revision rates was significant (p<0.001).

There were 10 studies of non-Oxford UKRs, of which eight had cemented UKRs (n=1,782) and three had cementless UKRs (n=264). For the cemented UKRs, there were 75 revisions out of 13,253 component years giving a revision rate of 0.57% pa (CI 0.45-0.71). For the cementless UKRs, there were 20 revisions from 2,866 component years giving a revision rate

of 0.69% pa (CI 0.43-1.10). There were no significant differences in the cemented and cementless non Oxford UKR study's revision rates ($p=0.41$).

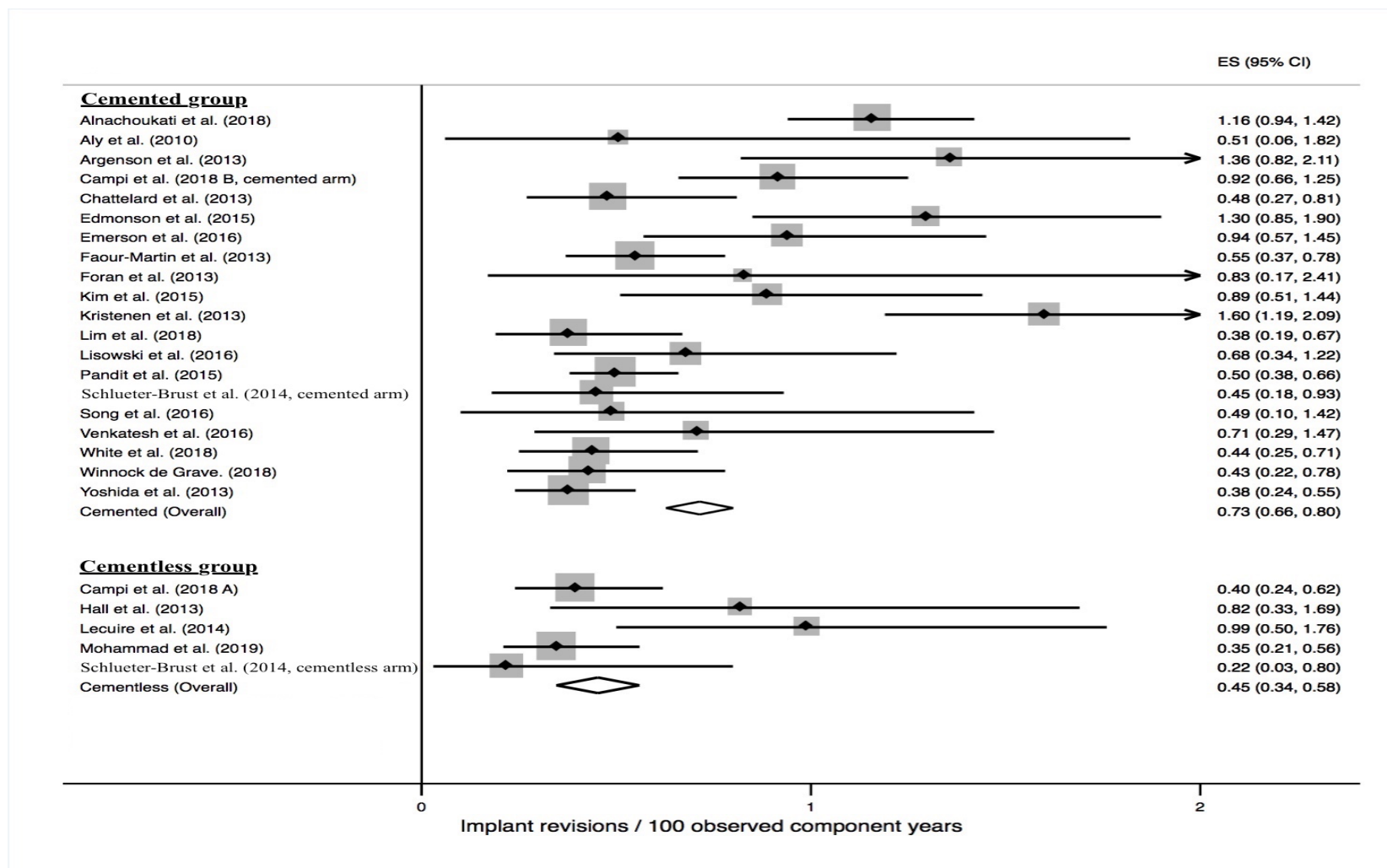


Figure 4.9. Forest plot of revision rate per 100 component years of included cemented and cementless UKRs

Study	No of knees	Mean follow up (years)	Observed component years	No of revisions	Revision rate per 100 component years (CI)
Cementless UKRs					
Campi et al. (2018A) ¹⁴⁸	682	7	4774	19	0.40 (CI 0.24-0.62)
Mohammad et al. (2019) ¹⁷¹	1,000	5.1	5100	18	0.35 (CI 0.21-0.56)
Schlueter-Brust et al. (2014) ²³⁴ (cementless arm)	78	11.6	904.8	2	0.22 (CI 0.03-0.80)
Mobile bearing Cementless			10,779	39	0.36 (CI 0.26-0.50)
Hall et al. (2013) ²⁴¹	85	10	850	7	0.82 (CI 0.33-1.69)
Lecuire et al. (2014) ²⁴²	101	11	1111	11	0.99 (CI 0.50-1.76)
Fixed bearing Cementless			1961	18	0.92 (CI 0.54-1.45)
CEMENTLESS OVERALL			12,740	57	0.45 (CI 0.34-0.58)
Cemented UKRs					
Alnachoukati et al. (2018) ²³⁵	825	9.7	8002.5	93	1.16 (CI 0.94-1.42)
Aly et al. (2010) ¹⁵⁷	45	8.75	393.8	2	0.51 (CI 0.06-1.82)
Campi et al. (2018B) ¹⁷² (cemented arm)	522	8.3	4332.6	40	0.92 (CI 0.66-1.25)
Edmonson et al. (2015) ¹⁶¹	364	5.5	2002	26	1.30 (CI 0.85-1.90)
Emerson et al. (2016) ¹⁵⁸	213	10	2130	20	0.94 (CI 0.57-1.45)
Faour Martin et al. (2013) ¹⁶³	511	10.38	5304.2	29	0.55 (CI 0.37-0.78)
Kim et al. (2015) ¹⁶⁵	180	10	1800	16	0.89 (CI 0.51-1.44)
Kristensen et al. (2013) ¹⁶⁷	695	4.6	3197	51	1.60 (CI 1.20-2.10)
Lisowski et al. (2016) ¹⁶⁸	138	11.7	1614.6	11	0.68 (CI 0.34-1.22)
Pandit et al. (2015) ⁸²	1,000	10.3	10300	52	0.50 (CI 0.38-0.66)
Schlueter-Brust et al. (2014) ²³⁴ (cemented arm)	152	10.2	1550.4	7	0.45 (CI 0.18-0.93)
White et al. (2018) ²³⁶	554	6.6	3656.4	16	0.44 (CI 0.25-0.71)
Yoshida et al. (2013) ¹⁷⁰	1,279	5.2	6650.8	25	0.38 (CI 0.24-0.55)
Mobile bearing cemented			50,934	388	0.76 (CI 0.69-0.84)
Argenson et al. (2013) ²³¹	70	20	1400	19	1.36 (CI 0.82-2.11)
Foran et al. (2013) ²³³	19	19	361	3	0.83 (CI 0.17-2.41)

Lim et al. (2018) ²³⁷	279	10.5	2929.5	11	0.38 (CI 0.19-0.67)
Song et al. (2016) ²⁴⁰	68	9	612	3	0.49 (CI 0.10-1.42)
Venkatesh et al. (2016) ²³⁹	175	5.6	980	7	0.71 (CI 0.29-1.47)
Winnock de Grave et al. (2018) ²³⁸	460	5.5	2530	11	0.43 (CI 0.22-0.78)
Fixed bearing cemented			8,813	54	0.61 (CI 0.46-0.80)
Chattelard et al. (2013) ²³² Mixture of mobile and fixed	559	5.17	2890	14	0.48 (CI 0.27-0.81)
CEMENTED OVERALL	8,108		62,637	456	0.73 (CI 0.66-0.80)

Table 4.7. The calculated revision rates per 100 component years for each for the included studies.

4.2.3.2 Revisions by bearing type

In the cemented group (n=8,108) there were 6,478 mobile bearing UKRs^{82, 157, 161, 163, 165, 167, 168, 170, 172, 234-236} and 1,071 fixed bearing UKRs^{231, 233, 237-240} clearly indicated. Chatellard et al²³² (n=559) had a mixture of mobile and fixed bearing UKRs and hence was not included in this analysis. There were 388 revisions out of 50,934 component years and 54 revisions out of 8,813 component years for mobile and fixed bearing cemented UKRs respectively. This resulted in revision rates of 0.76% pa (CI 0.69-0.84) and 0.61% pa (CI 0.46-0.80) respectively (Figure 4.10, Table 4.7). The corresponding 10 year implant survival for mobile and fixed cemented UKRs were 92.4% and 93.9%. The differences in revision rates between mobile and fixed bearing cemented UKRs were not significant (p=0.13).

In the cementless group (n=1,946) there were 1,760 mobile bearing UKRs^{148, 171, 234} and 186 fixed bearing UKRs^{241, 242}. There were 39 revisions out of 10,779 component years and 18 revisions out of 1,961 component years. This resulted in revision rates of 0.36% pa (CI 0.26-0.50) and 0.92% pa (CI 0.54-1.45) respectively (Figure 4.10, Table 4.7). The 10 year survival for mobile and fixed bearing cementless UKRs were 96.4% and 90.8% with this difference being significant (p=0.001).

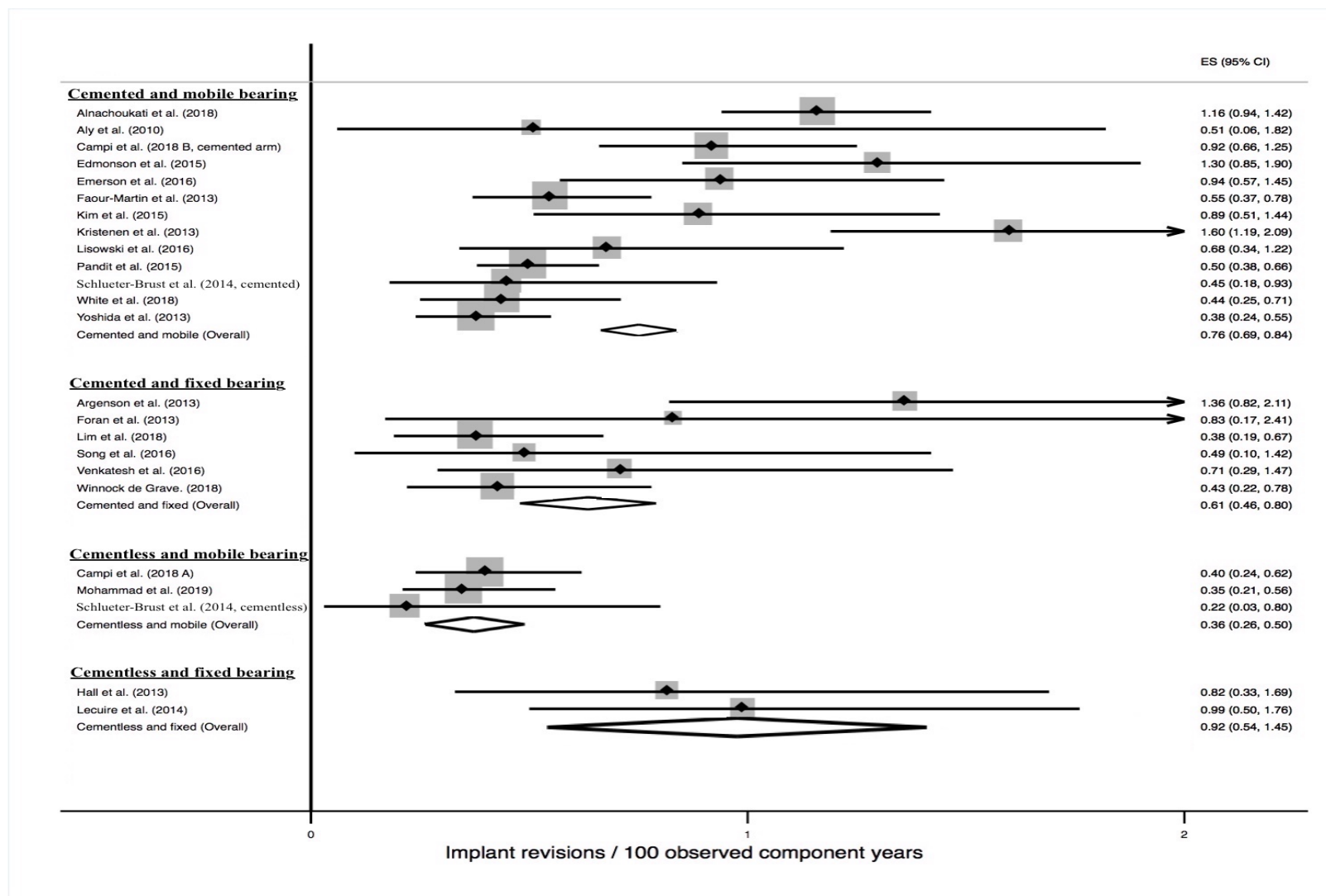


Figure 4.10. Forest plot of revision rate per 100 component years of mobile and fixed bearing UKRs by fixation

4.3.2.3 Survival

Of the 21 cemented studies, 19 studies reported the long term survival. 15 studies reported the implant survivals at 10 years and ranged between 83.7 to 96.3% (Table 4.8). All five cementless studies reported long term implant survivals. Three studies reported the 10 year implant survival ranging between 96.6 to 97.5% (Table 4.8).

Study	Implant survival reported	Time point
Cementless UKR		
Campi et al. (2018A) ¹⁴⁸	96.6%	10 years
Hall et al. (2013) ²⁴¹	76% (CI 60-97)	12 years
Lecuire et al. (2014) ²⁴²	88% (CI 81-95)	13 years
Mohammad et al. (2019) ¹⁷¹	97.5% (CI 95.7-98.5)	10 years
Schlueter-Brust et al. (2014) ²³⁴ (cementless arm)	97.4%	10 years
Cemented UKR		
Alnachoukati et al. (2018) ²³⁵	85.0% (CI 81.2-88.8)	10 years
Aly et al. (2010) ¹⁵⁷	n.r	10 years
Argenson et al. (2013) ²³¹	94.0% (CI 91.0-97.0)	10 years
Campi et al. (2018B) ¹⁷² (cemented arm)	n.r	10 years
Chattelard et al. (2013) ²³²	83.7% (CI 80.2-87.2)	10 years
Edmonson et al. (2015) ¹⁶¹	87.9% (CI 82.5-93.3)	11 years
Emerson et al. (2016) ¹⁵⁸	88.0% (CI 82.4-93.6)	10 years
Faour Martin et al. (2013) ¹⁶³	96.3%	10 years
Foran et al. (2013) ²³³	93.0% (CI 83-98)	15 years
Kim et al. (2015) ¹⁶⁵	90.5% (CI 85.9-95)	10 years
Kristensen et al. (2013) ¹⁶⁷	85.3% (CI 78.7-90)	10.7 years
Lim et al. (2018) ²³⁷	95.1% (CI 92.2-97.7)	10 years
Lisowski et al. (2016) ¹⁶⁸	90.6% (CI 85.2-96)	15 years
Pandit et al. (2015) ⁸²	96.0% (CI 92.5-99.5)	10 years
Price et al. (2011) ²³⁰	93.6% (CI 90.6-96.6)	10 years
Schlueter-Brust et al. (2014) ²³⁴ (cemented arm)	95.4%	10 years
Song et al. (2016) ²⁴⁰	95.6%	10 years
White et al. (2018) ²³⁶	95.2% (CI 92.3-98.4)	12 years
Winnock de Grave et al. (2018) ²³⁸	94.2% (CI 86.8-97.5)	10 years
Venkatesh et al. (2016) ²³⁹	96.0%	10.9 years
Yoshida et al. (2013) ¹⁷⁰	95.4% (CI 91.2-99.7)	10 years

Table 4.8. Long term implant survivals reported by each of the included studies.

4.3.2.4 Mechanisms of failure

All studies (23 studies, n=9,532; 7,586 cemented and 1,946 cementless) except Campi et al. (2018B)¹⁷² and Price et al.²³⁰, reported the mechanisms of failure by fixation type and mean follow up time. Appendix 6 shows the full breakdown of the reasons for revision for each individual study included in this analysis.

In the cemented group leading causes for revision were disease progression (1.8%), aseptic loosening (1.1%), bearing dislocation (0.6%) and pain (0.6%) (Table 4.9). In the cementless group leading causes of revision were bearing dislocation (0.8%), disease progression (0.7%), aseptic loosening (0.4%) and polyethylene wear/fracture (0.4%) (Table 4.9).

The revision rates per 100 component years for aseptic loosening and disease progression were significantly lower ($p=0.02$ and $p=0.009$ respectively) in the cementless group compared to the cemented group (0.06 vs 0.13% pa and 0.10 vs 0.21% pa respectively). The revision rate for polyethylene wear/impingement was significantly higher ($p=0.03$) in the cementless group (0.05 vs 0.02% pa). No other revision indication was significantly different between cementless and cemented UKRs (Table 4.9).

Indication for revision	No of cemented cases (n=7,586)	Percentage of cemented cases	Revisions per 100 component years for each indication (% pa)	No of cementless cases (n=1,946)	Percentage of cementless cases	Revisions per 100 component years for each indication (%pa)	Comparison between groups P value
Disease progression*	125	1.6%	0.21	13	0.7%	0.10	P=0.009
Aseptic loosening*	76	1.0%	0.13	7	0.4%	0.06	P=0.02
Bearing dislocation	41	0.5%	0.07	15	0.8%	0.12	P=0.08
Pain	50	0.7%	0.09	5	0.3%	0.04	P=0.09
Infection	34	0.4%	0.06	3	0.2%	0.02	P=0.14
Other	15	0.2%	0.03	3	0.2%	0.02	P=1.0
Unknown	16	0.2%	0.03	0	0%	0	P=0.09
Instability	17	0.2%	0.03	0	0%	0	P=0.06
Polyethylene wear/fracture*	12	0.2%	0.02	7	0.4%	0.05	P=0.03
Periprosthetic fracture	10	0.1%	0.02	3	0.2%	0.02	P=0.72
Hemarthrosis	6	0.1%	0.01	0	0%	0	P=0.60
Malposition	16	0.2%	0.03	1	0.1%	0.008	P=0.34

Table 4.9. Indications for revision surgery in the cemented and cementless cohorts. The Chi squared proportional test was utilised to compare each revision indication per 100 component years except when the expected frequency <5 where the fisher exact test was utilised.

4.2.3.5 Patient reported outcome measures

Thirteen out of 21 cemented studies and four out of five cementless studies reported the long term PROMS for the overall cohort studied. Studies reporting preoperative PROMs all showed an improvement at the ≥ 10 year scores. For the cemented UKRs the 10 year OKS reported ranged between 37 to 41.9 and for the cementless it ranged from 38 to 41.7 (Table 4.10).

Study	Patient reported outcome measure	Time point
Cementless UKR		
Campi et al. (2018A) ¹⁴⁸	OKS 41.7 (SD 6.8)	10 years
Hall et al. (2013) ²⁴¹	OKS 38 (range 13-48), WOMAC 20 (range 0-72)	10 years
Lecuire et al. (2014) ²⁴²	AKSS 171.4 (SD 25.3)	10 years
Mohammad et al. (2019) ¹⁷¹	OKS 41.2 (SD 9.8), Tegner 2.8 (SD 1.3), AKSS-O 89.1 (SD 13.0), AKSS-F 80.4 (SD 14.6)	10 years
Schlueter-Brust et al. (2014) ²³⁴ (cementless arm)	n.r	n.r
Cemented UKR		
Alnachoukati et al. (2018) ²³⁵	AKSS-F 77 (SD 28), AKSS-O 90 (SD 18)	10 years
Aly et al. (2010) ¹⁵⁷	HSS 177.6 (range 78-198)	10 years
Argenson et al. (2013) ²³¹	KSS Clinical 91 (range 50-100) KSS Functional 88 (range 45-100)	20 years
Campi et al. (2018B) ¹⁷² (cemented arm)	n.r	n.r
Chattelard et al. (2013) ²³²	n.r	n.r
Edmonson et al. (2015) ¹⁶¹	AKSS-O 87, AKSS-F 73, OKS 37, HSS 84	10 years
Emerson et al. (2016) ¹⁵⁸	AKSS-O 93, AKSS-F 78	8 years
Faour Martin et al. (2013) ¹⁶³	AKSS-O 90.2 (SD 7.82), AKSS-F 88.6 (SD 17.8)	10 years
Foran et al. (2013) ²³³	39 knees HSS 85-100, 6 knees HSS 70-84 and 4 knees had HSS 60-69	10 years
Kim et al. (2015) ¹⁶⁵	AKSS-O 85.4 (range 58-100), AKSS-F 80.5(range 50-100)	10 years
Kristensen et al. (2013) ¹⁶⁷	n.r	n.r
Lim et al. (2018) ²³⁷	n.r for overall cohort	n.r
Lisowski et al. (2016) ¹⁶⁸	OKS 41.9(SD 6.4), KSS 81(SD 20.7)	11.7 years
Pandit et al. (2015) ⁸²	OKS 40 (SD 9), AKSS-O 80 (SD 15), AKSS-F 76 (SD 22), Tegner 2.7 (SD 1.3)	10 years
Price et al. (2011) ²³⁰	n.r	n.r
Schlueter-Brust et al. (2014) ²³⁴ (cemented arm)	n.r	n.r
Song et al. (2016) ²⁴⁰	n.r for overall cohort	n.r
Venkatesh et al. (2016) ²³⁹	KSS Clinical 91.8 (range 51-100) KSS Functional 92 (range 55-100)	Most recent follow up
White et al. (2018) ²³⁶	n.r	n.r
Winnock de Grave et al. (2018) ²³⁸	OKS 43.3 (range 7-48)	Most recent follow up
Yoshida et al. (2013) ¹⁷⁰	OKS 38.1 (SD 6.8)	10 years

Table 4.10. Patient reported outcomes reported at approximately 10 years.

4.2.4 Discussion

This is the first systematic review comparing the long term outcomes of cemented and cementless UKRs in the literature and has shown the cementless UKR has a revision rate about one third less than that of the cemented. This difference primarily appears to be given the rates of revision for aseptic loosening more than halved. Interestingly the findings of this review are in agreement with those found for the registry based propensity matched comparison²⁰⁰ of cemented and cementless Oxford UKRs presented in Chapter 4.1 which found the revision rate of cementless was about one third of cemented given rates of aseptic loosening more than halved. Therefore although old cementless UKRs historically had a reputation for poor outcomes, the results from this chapter suggest that modern designs achieve better results than the current cemented implants.

The fact that cementless UKRs had significantly lower revision rates only for the Oxford UKRs could be because of the limited numbers in the non-Oxford implant group making it more prone to type two error. However despite this, the revision rates of the non-Oxford UKR fixation groups were essentially equivalent. The other possibility is the design of the Oxford UKR, which is ligament preserving with a mobile bearing resulting in predominantly compressive loads with minimal shear, is ideal for cementless fixation.

Randomised studies^{187, 202} comparing cemented and cementless UKRs showed a dramatic decrease in the incidence of radiolucent lines at the implant bone interface, which is indicative of improved fixation. This probably explains why the rates of revision for loosening reduced. The decrease in revision rate for arthritis progression with cementless fixation is more difficult to explain. Possible explanations include cement fragments causing direct damage to the lateral compartment or cementing errors causing medial overstuffing resulting in lateral

overload. The cementless Oxford UKR femoral component, compared to the cemented, has an additional anterior peg to improve fixation⁶⁷. To accommodate this more bone has to be removed anterior to the femoral component which may decrease the risk of the bone impinging on the bearing, which is known to increase the risk of disease progression²⁵⁵. Additionally the overall mean follow up, weighted on each studies sample size differed between fixation groups (Cemented group = 7.7 years, Cementless group = 6.5 years). Arthritis progression tends to occur late, so the longer follow-up in the cemented group will disproportionately increase its revision rate specifically for this indication.

No obvious differences in long term PROMs were found between the cementless and cemented groups. However both groups had better PROMs than those commonly reported for TKR¹⁴⁶.

There are two fundamentally different design concepts for UKR; mobile and fixed bearings. The debate of which is better has been a contentious issue²⁵⁶. Theoretical advantages of a mobile bearing UKR include lower linear polyethylene wear, better long term knee kinematics, and a more even load distribution at the implant-bone interface²⁵⁷. However fixed bearings have the advantage of not dislocating. This study showed that mobile bearing UKRs had significantly lower revision rates than fixed bearing UKRs in the cementless but not cemented groups. Other reviews and clinical studies, which were predominantly based on cemented components also found no differences in their outcomes²⁵⁷⁻²⁵⁹.

The main limitation of this review is that all included studies were observational cohorts with no comparative control arm. Although there has been a formal comparison of the overall revision rates of cemented and cementless UKRs from these studies using the proportional chi

squared test, the findings must be interpreted with caution. This comparison is made overall between studies, not from a pooled comparison within studies and does not account for confounding factors, nor selection bias related to the selection of patients included with different lengths of follow up. There is considerable heterogeneity between studies (Figure 4.9) where the revision rate per 100 component years can be seen to vary between studies, particularly for the cemented studies. Additionally given the cementless studies are understandably from fewer centres this may introduce a possible expertise bias. However it is encouraging that the results mirror those from the propensity matched registry comparison²⁰⁰ presented in Chapter 4.1, which addresses many of the above limitations. Larger UKR numbers would cause the revision rate to fall, but this would not explain the lower revision rates in the cementless group as they had far fewer UKRs than the cemented group. Although all the studies in both groups reported the ≥ 10 year outcomes, the mean follow up weighted on each studies sample size differed between fixation groups (Cemented = 7.7 years, Cementless = 6.5 years). This can influence comparisons between indications for revision if the revisions tend to occur either early or late in the follow-up, such as lateral disease progression and bearing wear/fracture.

In summary in Chapters 4.1 and 4.2 it has been highlighted that, compared to cemented, cementless UKRs appear to have lower revision rates and therefore superior long term implant survival with similar functional outcomes. One of the main reasons for this is that the rate of revision for aseptic loosening decreased, suggesting that cementless UKR provides better fixation.

5. THE EFFECT OF OTHER FACTORS ON UKR REVISION RATES

In this chapter we assess the effect of surgeon caseload and two surgical interventions (new Microplasty instrumentation and the Twin Peg femoral component) on the Oxford UKR's revision rates using NJR data. The chapter is divided into three sections reflecting three main questions; 1) Does surgeon caseload effect revision rates of cemented and cementless UKRs, 2) Does new Microplasty instrumentation effect revision rate and 3) Does a Twin Peg femoral component effect the revision rate. Each will be discussed in turn.

* This chapter has been published as three publications²⁶⁰⁻²⁶².

1) Mohammad HR, Matharu GS, Judge A, Murray DW. The Effect of Surgeon Caseload on the Relative Revision Rate of Cemented and Cementless Unicompartamental Knee Replacements: An Analysis from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man. *J Bone Joint Surg Am* 2020;102(8):644-53. (Appendix 1).

2) Mohammad HR, Matharu GS, Judge A, Murray DW. New surgical instrumentation reduces the revision rate of unicompartamental knee replacement: A propensity score matched comparison of 15,906 knees from the National Joint Registry. *Knee* 2020; S0968-0160(20)30046-6. (Appendix 1).

3) Mohammad HR, Matharu GS, Judge A, Murray DW. A matched comparison of revision rates of cemented Oxford Unicompartamental Knee Replacements with Single and Twin Peg femoral components, based on data from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man. *Acta Orthop* 2020;1-6. (Appendix 1).

5.1 The effect of surgeon caseload on the revision rate of cemented and cementless Oxford UKRs

5.1.1 Introduction

Surgeon caseload or volume is defined as the number of operations that a surgeon performs per year. It has been previously demonstrated to effect implant revision rates, with low-volume surgeons having much higher revision rates than high-volume surgeons. This relationship is particularly marked for UKR and is likely an important reason why UKR revision rates are so high in the joint registries (Figure 5.1). In the UK, the most common surgeon caseload for UKR is 1 case/year and the average is 5 cases/year, compared with an average of 34 cases/year for TKR²¹.

There are concerns that cementless implants are less forgiving than cemented implants with regard to obtaining stable fixation. Therefore, low-volume surgeons actually might have worse results following UKR if they change to cementless fixation. It is not known whether the relative performance of cemented and cementless UKR implants is influenced by surgeon caseload.

The NJR does not report UKR results by surgeon caseload and fixation type⁸. We analysed NJR data to assess the effect of surgeon caseload on all Oxford UKRs and then on the relative revision rates of cemented and cementless Oxford UKR implants.

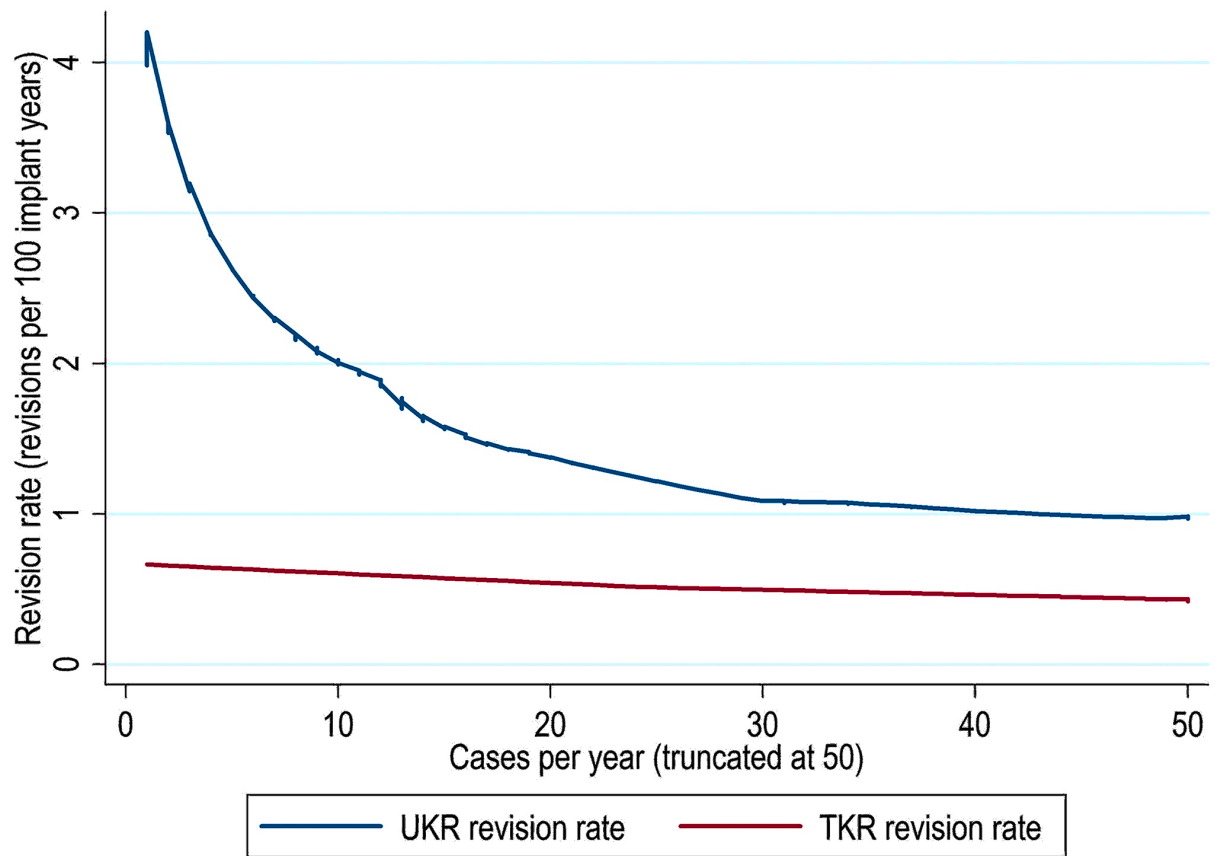


Figure 5.1. Lowess curve showing the effect of surgeon caseload on implant revision rates.

Taken with permission from Liddle et al.²¹.

5.1.2 Methods

The same unmatched and matched NJR Oxford UKR cohort from section 4.1 was utilised for this analysis. For further details on the NJR data collection procedure, identification of potential confounders, NJR data extract used, data cleaning and propensity matching technique employed please refer to section 4.1.

5.1.2.1 Outcome of interest

The study outcome of interest was implant survival. The end point for implant survival was all-cause revision surgery (any component inserted, exchanged, or removed since primary surgery) for all indications.

5.1.2.2 Statistical analysis

The exposure of interest was surgeon caseload, defined as the mean number of UKR procedures performed per year. This was calculated as described in section 4.1.2.3. Each patient was allocated a value representing the caseload of the operating surgeon. Surgeon caseloads were grouped into 3 categories: low-volume (<10 cases/year), medium-volume (10 to <30 cases/year), and high-volume (≥ 30 cases/year). These thresholds were described by Liddle et al.²¹ and are evidence-based, unlike other thresholds. Liddle et al.²¹ found that revision rates fell steeply with increasing caseload up 10 cases/year. Thereafter, revision rates decreased at a slower rate until they plateaued at ≥ 30 cases/year (Figure 5.1).

Cumulative implant survival was calculated with use of Kaplan-Meier analysis. Cumulative implant survival rates of all UKRs (both cemented and cementless UKRs combined) across

different surgeon caseloads using the unmatched cohort outlined in section 4.1. Then using the matched cohort (from section 4.1) to allow fair comparison and prevent confounding, the cemented and cementless UKR implant survivals across different surgeon caseloads were compared using cox regression models. For clustering within the matched cohort, a robust variance estimator was utilised. Additionally as a sensitivity analysis a multi-level frailty model was tested to control for patient clustering within operating surgeons, but this did not alter the results presented. All analyses were performed with use of Stata software (version 15.1, StataCorp, Texas, USA).

5.1.3 Results

5.1.3.1 Unmatched cohort analysis

The unmatched cohort included 40,522 UKR implants (30,814 cemented and 9,708 cementless). The number of cementless implants used per year has been increasing, with 2,832 cementless and 1,717 cemented Oxford UKRs implanted in 2016. The mean patient age at the time of implantation was 64.7 years (SD 9.5), with 21,747 (53.7%) of the patients being male. The mean BMI was 30.2 kg/m² (SD 5.0), and osteoarthritis was the surgical indication for 40,059 knees (98.9%).

The mean durations of follow-up for the cemented and cementless implants in the unmatched cohort were 6.4 (SD 3.1) and 3.5 (SD 2.1) years, respectively. In total, 2,647 implants (258 cementless, 2,389 cemented) were revised. The 10-year survival rates for the unmatched cementless and cemented UKR implants were 93.3% (CI = 89.8 - 95.7) and 89.1% (CI = 88.6 - 89.6), respectively. Cementless UKR implants had significantly better survival (HR = 0.59, CI = 0.52 - 0.68; $p < 0.001$).

However, the baseline characteristics for unmatched cemented and cementless implants differed significantly (Section 4.1). The proportion of low-volume surgeons was significantly greater for cemented implants than for cementless implants (43.7% compared with 27.4%; $p < 0.001$), whereas the proportion of high-volume surgeons was significantly greater for cementless implants than for cemented implants (30.4% compared with 15.1%; $p < 0.001$).

Analysis of the effect of caseload on the whole unmatched cohort showed 10-year implant survival rates of 86.6% (CI = 85.8 - 87.3), 90.8% (CI = 90.1 - 91.5), and 94.1% (CI = 93.2 -

94.8) for low, medium, and high-volume surgeons (Figure 5.2). The revision rates for medium and high-volume surgeons were significantly lower than those for low-volume surgeons, with hazard ratios of 0.67 (CI = 0.62 - 0.73; $p < 0.001$) and 0.42 (CI = 0.37 - 0.48; $p < 0.001$), respectively.

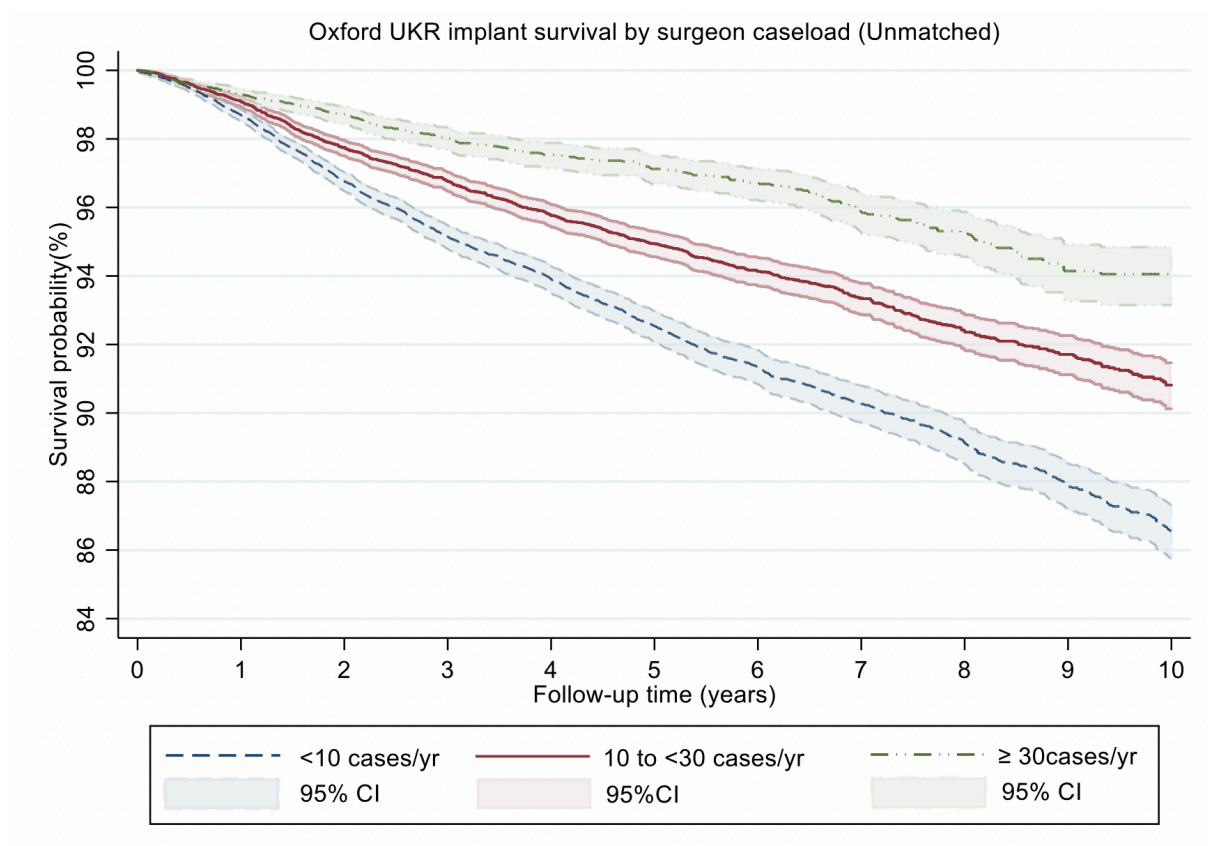


Figure 5.2. Oxford UKR implant survival by surgeon caseload in the unmatched cohort.

5.1.3.2 Matched cohort analysis

The matched cohort included 14,814 UKR implants (7,407 cemented and 7,407 cementless). The mean patient age was 64.7 years (SD 9.5), and 8,659 implants (58.5%) were implanted in males. The mean BMI was 30.3 kg/m² (SD 5.0), and osteoarthritis was the surgical indication for 14,633 knees (98.8%).

Patient, surgical, and implant factors were balanced between fixation groups after propensity matching (Section 4.1). The mean duration of follow-up for both cemented and cementless implants was 4 years (SD 2.0). In total, 507 implants (218 cementless, 289 cemented) were revised. The 10-year survival rates were 93.2% (CI = 89.7 - 95.6) and 90.2% (CI = 87.5 - 92.3) for the cementless and cemented implants, respectively. Cementless implants had a significantly lower revision rate (HR = 0.76, CI = 0.64 - 0.91; $p = 0.002$).

In the matched cohort, the 10-year implant survival rates for the cementless and cemented implants were 86.8% (CI = 73.6 - 93.7) and 81.8% (CI = 73.0 - 88.0) for low-volume surgeons, 94.3% (CI = 92.2 - 95.9) and 92.5% (CI = 89.9 - 94.5) for medium-volume surgeons, and 97.5% (CI = 96.5 - 98.2) and 94.2% (CI = 90.8 - 96.4) for high-volume surgeons. The 10-year cumulative revision rates are presented in Figure 5.3.

For all caseloads, cementless implants had a lower revision rate than cemented implants. The rate of revision of cementless implants was 26% lower than that of cemented implants among low-volume surgeons (HR = 0.74 [CI = 0.56 - 0.98]; $p = 0.03$), 21% lower among medium-volume surgeons (HR = 0.79 [CI = 0.60 - 1.02]; $p = 0.08$), and 20% lower among high-volume surgeons (HR = 0.80 [CI = 0.52 - 1.24]; $p = 0.32$). There was no significant interaction between fixation and caseload ($p = 0.92$).

The numbers of revisions per 100 component-years for the cementless and cemented implants were 1.12 (CI = 0.89 - 1.37) and 1.49 (CI = 1.24 - 1.78) for low-volume surgeons, 0.73 (CI = 0.59 - 0.89) and 0.93 (CI = 0.77 - 1.11) for medium-volume surgeons, and 0.45 (CI = 0.31 - 0.62) and 0.57 (CI = 0.42 - 0.76) for high-volume surgeons.

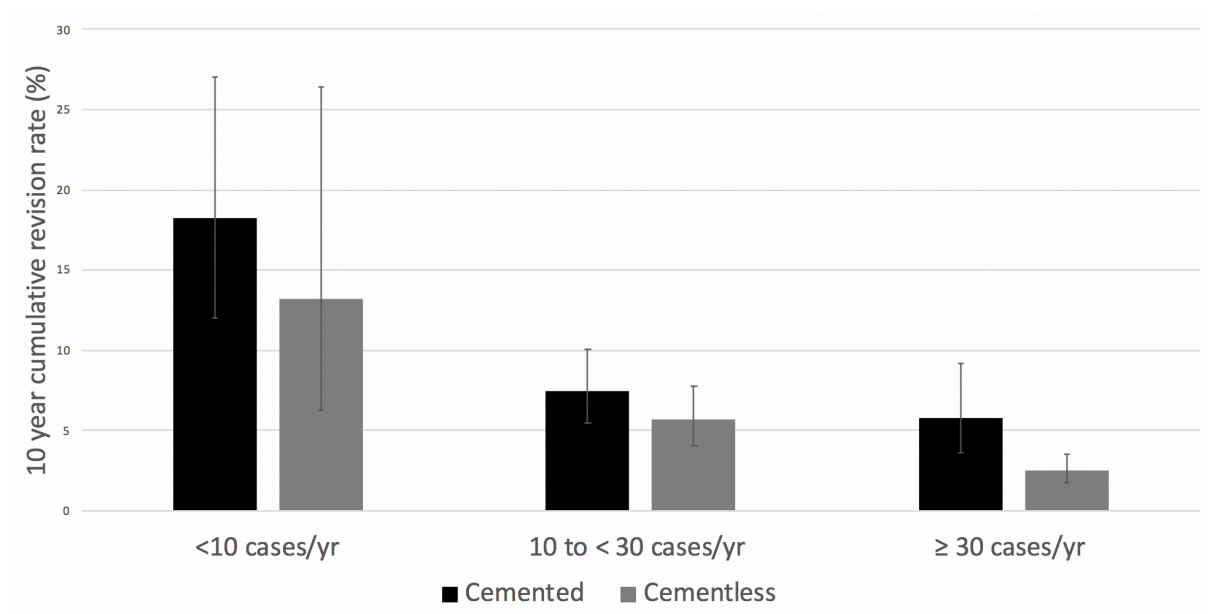


Figure 5.3. 10 year cumulative revision rates for matched cemented and cementless Oxford UKRs across different caseload groups.

5.1.4 Discussion

This chapter has shown that the numbers of cementless Oxford UKRs implanted has been rapidly increasing in the UK, with nearly twice as many cementless than cemented implants used in 2016²⁰⁰. Despite this the NJR has not published the results of the Oxford UKR by fixation type. The unmatched analysis showed a 10-year survival 93.3% for the cementless Oxford UKR and was 41% lower (HR=0.59, $p<0.001$) than the cemented version. These results are the same as those in the NZJR¹⁷, which reported a 10-year survival rate of 93% for the cementless Oxford. The 10-year survival rate for the cementless Oxford implant was better than or similar to other UKR implants reported in the NJR⁸. However, these comparisons are of little value given other surgeon or patient-related factors are likely to have had a greater influence on the revision than the implant design itself.

Having matched for confounding variables, the revision rate for the cementless implant was, as previously demonstrated in Chapter 4.1, 24% less than that for the cemented implant. Therefore, the remaining difference, from 24% to 41%, is explained by other variables such as caseload. Increasing surgeon caseload was associated with a decrease in the revision rate. Additionally, more high-volume surgeons and less low-volume surgeons were using cementless implants than cemented implants, confirming that an unmatched comparison could provide misleading results. Importantly, there was no interaction between caseload and fixation, with cementless fixation being associated with a decrease in the revision rate by about a quarter for low, medium, and high-volume surgeons. This is the first time that a cementless knee replacement has been demonstrated to have lower revision rates than its cemented for both low and high-volume surgeons.

Cementless fixation is generally accepted as less forgiving, requiring better bone quality, implant designs, and surgical techniques^{263, 264}. In particular, bone resections must be performed accurately, with care being taken to avoid any gaps between the host bone and the components in order to ensure primary stability⁶⁷. It is surprising that low-volume UKR surgeons, who tend to be less experienced, had better results with cementless fixation than with cemented fixation. Additionally in Chapter 3, cementless UKRs did not have a high revision rate in patients with reduced bone mineral density¹⁸³. This may be because the bone around the medial compartment has had increased loading, given the varus arthritis, and can adequately support the implant, even though the bone quality is generally poor. Furthermore given the design of the Oxford UKR, loads are predominantly compressive with minimal shear, which is ideal for cementless fixation⁶⁷.

The rates of revision of both cemented and cementless UKR implants reduced with increasing surgeon volume. Although this finding probably is partly related to improved surgical technique with increased volume, it also may be related to the indications for UKR. The primary indications are AMOA, full-thickness cartilage present laterally and functionally normal ligaments²⁰⁸. These criteria are assessed radiographically and confirmed intraoperatively, however this data is not collected by the NJR, which only reports the primary surgical indication. However research suggests that these indications are met in up to 50% of presenting cases⁸³. An insight into the indications can be determined from the usage of UKR, which is defined as the percentage of primary knee replacements that are UKR. Previous work²⁶⁵ has shown that surgeons with high usage ($\geq 30\%$) tend to use the correct indications and achieve better results, whereas surgeons with low usage ($< 10\%$) often use UKR for early arthritis and achieve worse results.

Low-volume UKR surgeons had high revision rates regardless of whether they used cementless or cemented UKR implants. These surgeons should consider focusing on their UKR practice rather than fixation type. Given their high revision rates, they should consider either stopping performing UKR or seeing if, by adhering to the recommended indications, they might increase their caseload to >10 cases/year^{13, 21, 265}. In this chapter, between 80 to 90% of surgeons were considered low volume, but it is likely that if they adhered to the recommended indications⁸³ they could perform >10 UKR procedures per year. Medium and high-volume UKR surgeons using cemented components should consider changing to cementless fixation as doing so may improve their outcomes. High-volume surgeons using cementless components were found to achieve very good results, with a 10-year implant survival rate of 97.5%, which is similar to the best performing TKRs^{8, 16, 17}.

The main limitation of this chapter is that given registry data was used the only outcome which could be assessed was revision. Although registries can underreport revisions, this should not differ between comparative groups. Furthermore, propensity matching has limitations of potential residual confounding and can reduce the result generalisability. The only way to achieve perfect matching is with a randomised trial but this is impractical as large sample sizes across all surgeon volumes would be required. Therefore, propensity matching is most appropriate.

In conclusion, surgeon caseload had a profound effect on the survival of both cemented and cementless UKR implants, with low caseload being associated with higher revision rates for both implant types. Surgeon caseload, however, did not affect the relative performance of cemented and cementless replacements. Cementless replacements had revisions rates approximately 25% less across all surgeon caseloads, suggesting superior implant

performance. Given low-volume UKR surgeons had high revision rates they should consider stopping or performing more UKRs. Medium and high-volume surgeons using cemented Oxford UKR components should consider changing to cementless fixation. High-volume surgeons using cementless UKR implants achieved particularly good results, with a 10-year survival of 97.5%, similar to the best performing TKRs.

5.2 The effect of new Microplasty instrumentation on UKR revision rates

5.2.1 Introduction

The high revision rate of UKR may, in part, be a result of poor positioning of the implant or other technical problems with the operation, which is made particularly difficult with minimally invasive approaches where intra-operative visualisation is restricted^{266, 267}. This is relevant for the Oxford UKR, which is implanted using a minimally invasive approach⁶⁷. Phase 3 instrumentation, which was introduced over 20 years ago, is difficult to use. The surgeon has to judge by eye the height of the tibial cut and the orientation of the femoral component, which is susceptible to errors.

New instrumentation known as Microplasty (Zimmer Biomet, Swindon, UK) was introduced to make the operation simpler, more reproducible and reliable²⁶⁸. The use of Microplasty instrumentation has been steadily increasing. It consists of a stylus system for selecting tibial resection level, a femoral drill guide linked to an intramedullary rod to help femoral component positioning, slotted saw guides and instruments to protect the medial collateral ligament and avoid impingement (Figure 5.4). Although the Microplasty instrumentation can improve implant positioning²⁶⁹ it is currently unknown whether it makes any difference to the revision rate. Additionally, as Microplasty instrumentation is more complex than the Phase 3 instrumentation (Non-Microplasty), there is a concern that the outcome might be worse when it is first used due to learning curve issues.

NJR data was utilised to compare the revision rates following Microplasty and Non-Microplasty Oxford UKRs. To ensure that any difference in implant performance was due to the instrumentation rather than other factors, Microplasty and Non-Microplasty cases were matched on patient, surgeon and implant factors.

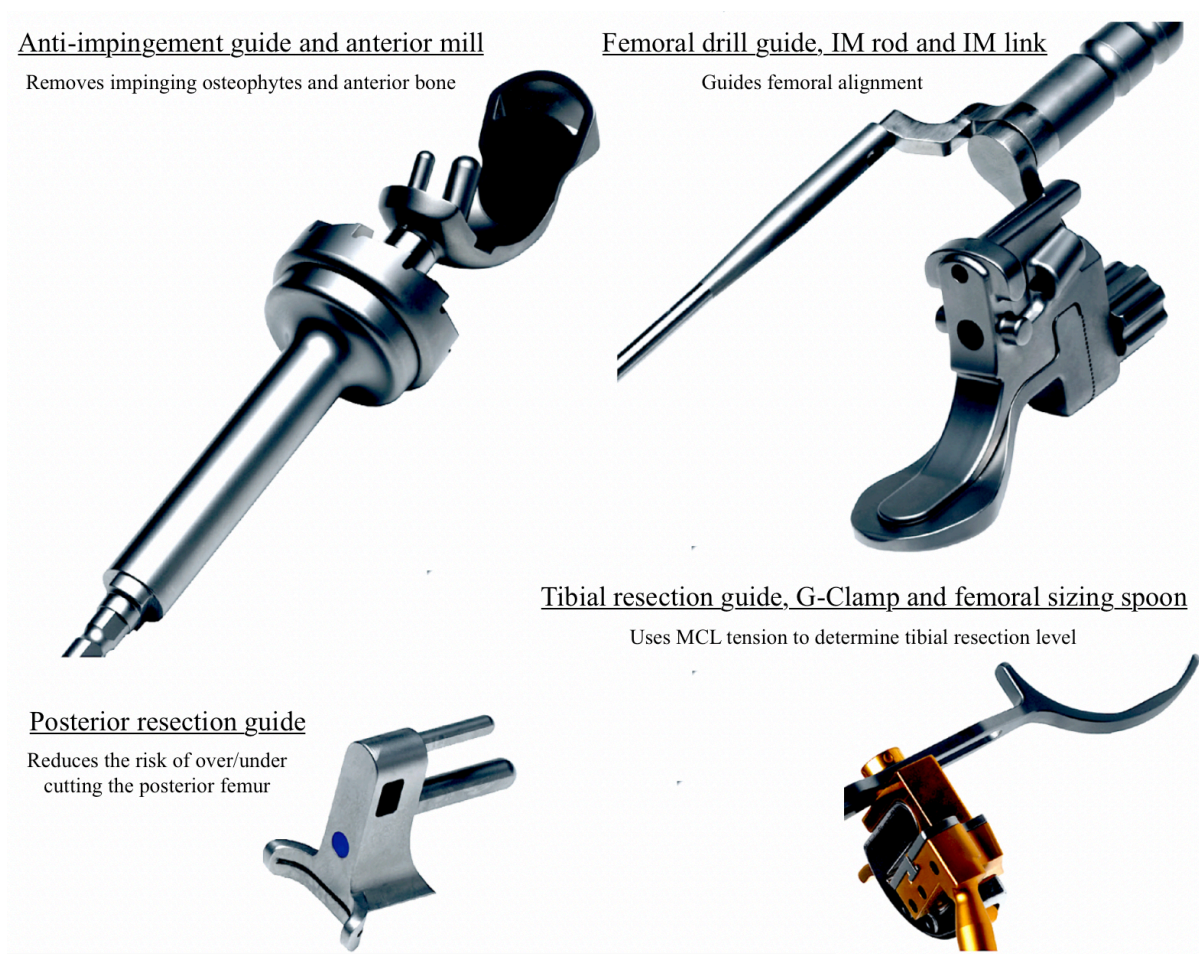


Figure 5.4. Schematic of Microplasty instrumentation. Recreated from²⁶⁸.

5.2.2 Methods

A retrospective observational study was performed using NJR records for all patients who had an Oxford UKR implanted. A formal application was submitted to the NJR Research Sub-Committee to access the relevant data and perform the work described in this chapter at the Musculoskeletal Research Unit at the University of Bristol. This application was approved on 5th July 2018 (Appendix 4). For further details on the NJR data collection procedure and identification of potential confounders please refer to section 4.1.

5.2.2.1 NJR data extract

The dates at which Microplasty Instrumentation (Zimmer Biomet, Swindon, UK) was introduced to each UK hospital (changeover date) were obtained from Zimmer Biomet and this information supplied to the NJR who link to their database. Prior to this date, or if there was no date, the hospital was assumed to be using the Non-Microplasty instrumentation. After this date, it was assumed that they were using Microplasty Instrumentation. During the first year after the changeover date, it was assumed that there was a transition period, which included the surgeons' learning curve and the changeover between systems. In Oxford, prototype Microplasty instruments have been used for many years and there was no exact date of their changeover to Microplasty, so all UKRs conducted in Oxford were excluded.

Anonymised patient data were extracted from the NJR database which included all primary Oxford UKRs implanted between 1st January 2012 and 31st December 2017 ($n = 28,273$). The starting date was chosen given Microplasty was first used outside Oxford in 2012 and the former the latest data available from the NJR. Prior to obtaining the dataset the entire NJR

database was linked to the ONS database using unique patient identifiers for all cause patient mortality data.

5.2.2.2 Data cleaning

The data extract contained 28,273 Oxford UKRs and was loaded into Stata (Version 15.1, Texas, USA) and subsequently cleaned. Each continuous, categorical and string variable was systematically assessed for inconsistencies and implausible/missing data.

Data cleaning involved the removal of all UKRs performed in Oxford centres, lateral UKRs, hybrids, complex primaries, old tibial sizes, symmetric bearings and missing component data. After data cleaning, there were 23,234 medial UKRs (11,024 Microplasty and 12,210 Non-Microplasty UKRs) eligible for study inclusion (Figure 5.5).

After data cleaning the only variable with any missing data was BMI. However this did not vary significantly between groups and was well balanced between comparative groups both before and after matching.

Following data cleaning all numerical variables distributions were assessed graphically for normality, with the data subsequently summarised based on the respective distribution. Binary categorical variables, such as sex, were maintained in their format. Multi-level categorical variables were made binary where possible to aid data processing and analysis. The remaining multilevel categorical variables were groups retained to a minimum number of levels required to clinically differentiate them from each other. This method is described in additional detail in section 4.1.

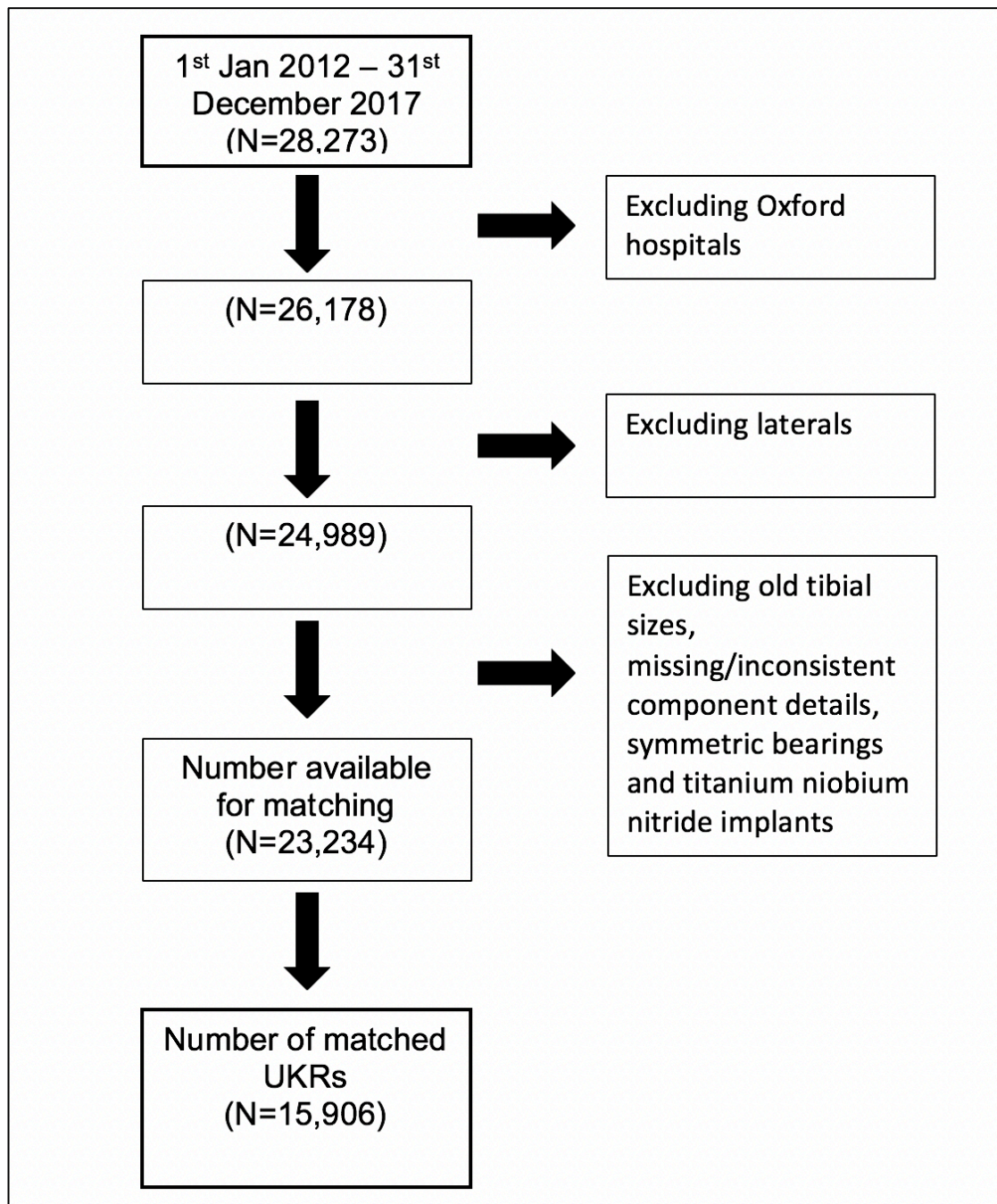


Figure 5.5. Data cleaning of Microplasty NJR dataset.

5.2.2.3 Outcome of interest

The primary outcome of interest for this comparative study was the five year implant survival of Microplasty and Non Microplasty UKRs. Additionally, an a priori decision was to perform a subgroup analysis of Microplasty UKRs, into those inserted within one year of centre introduction and those after one year of introduction to a centre. Secondary outcomes of interest were the indications for revision surgery.

5.2.2.4 Propensity score matching

The unmatched cohort consisted of 23,234 UKRs (12,210 Non microplasty UKRs and 11,024 Microplasty UKRs). Given the potential for patient, surgical and implant factors other than Microplasty instrumentation (identified in section 4.1.2.4) to affect the revision rate Microplasty and Non Microplasty groups were matched for multiple known confounders using propensity scores. After matching there were 15,906 UKRs (7,953 Non Microplasty and 7,953 Microplasty UKRs) included for analysis.

Confounders were selected for the propensity score were known to affect the outcome of interest (Table 4.1) and not on the basis of being associated with the Microplasty exposure variable as per published recommendations for variable selection in propensity models.

5.2.2.5 Statistical analysis

A multilevel logistic regression model was used to generate a propensity score representing the probability that a patient received a Microplasty-assisted UKR. This approach controlled for clustering at the hospital level. The specific variables patients were matched on were age, gender, primary diagnosis, unilateral/bilateral UKRs, ASA grade, chemical thromboprophylaxis, mechanical thromboprophylaxis, operating surgeon grade, surgeon caseload, surgical approach, operating technique and implant fixation. Component size was not used for matching, given Microplasty instrumentation is designed to improve component size selection. BMI was not used for matching given it had a large proportion of missing data but was well balanced between groups both before and after matching.

By controlling these covariates using propensity score matching the true effect of Microplasty instrumentation on revision surgery could be accurately assessed. This a priori approach was supported by the significant differences in patient, surgical and implant factors between the unmatched Microplasty and Non Microplasty groups (Table 5.1).

One-to-one matching on the logit of the propensity score with a 0.02-SD calliper width was utilised. Greedy matching without replacement was used given its superior performance for estimating treatment effects. Standardised mean differences (SMDs) were examined both before and after matching to assess for any covariate imbalance between the Microplasty and Non-Microplasty UKRs, with SMDs of 10% or more considered suggestive of covariate imbalance. After matching, 15,906 UKRs (7,953 Microplasty and 7,953 Non-Microplasty UKRs) were included for analysis. Microplasty UKRs for subgroup analyses were further divided into procedures conducted within the first year after Microplasty's introduction

(n=5,529) and after the first year (n=2,424) to explore for any adverse elevation in revision rates as part of the learning curve process of the operating surgeons.

Cumulative implant survival was determined using the Kaplan–Meier method. The endpoint for implant survival was revision surgery (any component removed, exchanged or added).

Cumulative implant revision rates were compared between groups, using Cox regression models. To account for clustering within the matched cohort, a robust variance estimator was used in regression models. Adjusted models were also assessed which included covariates with residual imbalance after matching (SMD of 10% or more). However these did not modify the results and are therefore not presented.

A secondary analysis was undertaken based on the revision rate per 100 component years. This was calculated for both groups by dividing the number of revisions by the total number of observed component years (mean follow-up multiplied by number of knees). The 95% CI were calculated using the Clopper Pearson exact method. Revision rates between groups were compared using the chi-squared proportional test.

To compare the indications for revision surgery, the revision rates per 100 component years for each revision indication were calculated. The proportional chi-squared test was used to test for differences between Microplasty and Non-Microplasty except when the expected frequencies were below five in which case the Fisher's Exact Test was utilised. All statistical analyses were performed using Stata (Version 15.1, Texas, USA) except propensity score matching that was performed using R (Version 3.4.0, R Foundation for Statistical Computing, Vienna, Austria). P-values of < 0.05 were considered significant, with 95% CIs presented.

5.2.3 Results

5.2.3.1 Propensity score matching

The unmatched cohort consisted of 23,234 UKRs (12,210 Non microplasty UKRs and 11,024 Microplasty UKRs). Baseline characteristics differed between the Microplasty and Non microplasty UKR groups (Table 5.1). Specific covariates which differed significantly ($SMD > 0.1$) were thromboprophylaxis, surgeon grade, surgeon caseload, minimally invasive approach and fixation type used. These differences were clearly highlighted by the distribution of propensity scores before matching (Figure 5.6).

The matching process improved the balance of covariates between Microplasty and Non Microplasty UKR groups (Table 5.1) and was confirmed on analysis of the distribution of propensity scores after matching (Figure 5.7). After matching there remained some residual imbalance of surgeon caseload and grade.

	Unmatched cohort (n=28,273)			Matched cohort (n=15,906)		
	Non Microplasty UKRs (n=12,210)	Microplasty assisted UKRs (n=11,024)	SMD	Non Microplasty UKRs (n=7,953)	Microplasty assisted UKRs (n=7,953)	SMD
Covariate						
Gender						
Female	5,484 (44.9%)	4,969 (45.1%)	0.003	3623 (45.6%)	3612 (45.4%)	0.003
Male	6,726 (55.1%)	6,055 (54.9%)		4330 (54.4%)	4341 (54.6%)	
Age at surgery (year)						
Mean (SD)	64.3 (SD 9.4)	64.8 (SD 9.3)	0.06	64.6 (SD 9.5)	64.5 (SD 9.4)	0.007
BMI (kg/m²)*						
Mean (SD)	30.1 (SD 4.9) (n=9,245)	30.5 (SD 5.1) (n=9,557)	0.08	30.1 (SD 4.9) (n=6134)	30.6 (SD 5.1) (n=6831)	0.08
Primary diagnosis						
Primary OA	12,092 (99%)	10,922 (99.1%)	0.004	7,864 (98.9%)	6,888 (99.2%)	0.03
<i>Other</i>	118 (1%)	102 (0.9%)		89 (1.1%)	65 (0.8%)	
Bilateral UKRs	435 (3.6%)	304 (2.8%)	0.05	287 (3.6%)	197 (2.5%)	0.066
ASA grade						
1	2395 (19.6%)	1985 (18.0%)	0.06	1,575 (19.8%)	1,404 (17.7%)	0.05
2	8,833 (72.3%)	8024 (72.8%)		5,684 (71.5%)	5840 (73.6%)	
3 or above	982 (8.0%)	1015 (9.2%)		694 (8.7%)	699 (8.8%)	

VTE chemical –						
LMWH (+/-other)	7,910 (64.8%)	6,002 (54.4%)	0.26	5,081 (63.9%)	5,224 (65.7%)	0.05
Aspirin only	676 (5.6%)	664 (6%)		556 (7.0%)	466 (5.9%)	
Other	3,259 (26.7%)	4,196 (38.1%)		2,160 (27.2%)	2,126 (26.7%)	
None	362 (3.0%)	162 (1.5%)		156 (2.0%)	137 (1.7%)	
VTE mechanical –						
Any	12,065 (98.8%)	10,908 (99.0%)	0.01	7,883 (99.1%)	7,838 (98.6%)	0.05
None	145 (1.2%)	116 (1.0%)		70 (0.9%)	115 (1.5%)	
Surgeon grade						
Consultant	11,768 (96.4%)	10,072 (91.4%)	0.21	7,676 (96.5%)	7,312 (91.9%)	0.19
<i>Other</i>	442 (3.6%)	952 (8.6%)		277 (3.5%)	641 (8.1%)	
Surgeon caseload						
<10 cases/year	4780 (39.1%)	2666 (24.2%)	0.33	2919 (36.7%)	2154 (27.1%)	0.21
10 to <30 cases/year	4776 (39.1%)	5336 (48.4%)		3267 (41.1%)	3819 (48.0%)	
≥30 cases/year	2654 (21.7%)	3022 (27.4%)		1767 (22.2%)	1980 (24.9%)	

Surgical approach						
Medial parapatellar	11,219 (91.9%)	9,902 (89.8%)	0.07	7,385 (92.9%)	7,246 (91.1%)	0.06
Other	991 (8.1%)	1,122 (10.2%)		568 (7.1%)	707 (8.9%)	
Minimally invasive surgery						
No	6,141 (50.3%)	6,184 (56.1%)	0.12	4,063 (51.1%)	4,444 (55.9%)	0.09
Yes	6,069 (49.7%)	4,840 (43.9%)		3,890 (48.9%)	3,509 (44.1%)	
Fixation						
Cemented	8,570 (70.2%)	4,369 (39.6%)	0.65	4,350 (54.7%)	4,346 (54.7%)	0.001
Cementless	3,640 (29.8%)	6,655 (60.4%)		3,603 (45.3%)	3,607 (45.4%)	
Bone graft						
None	12,157 (99.6%)	10,989 (99.6%)	0.02	7,912 (99.5%)	7,930 (99.7%)	0.04
Bone graft used	53 (0.4%)	35 (0.3%)		41 (0.5%)	23 (0.3%)	

Table 5.1. Patient and surgical factors before and after propensity score matching.

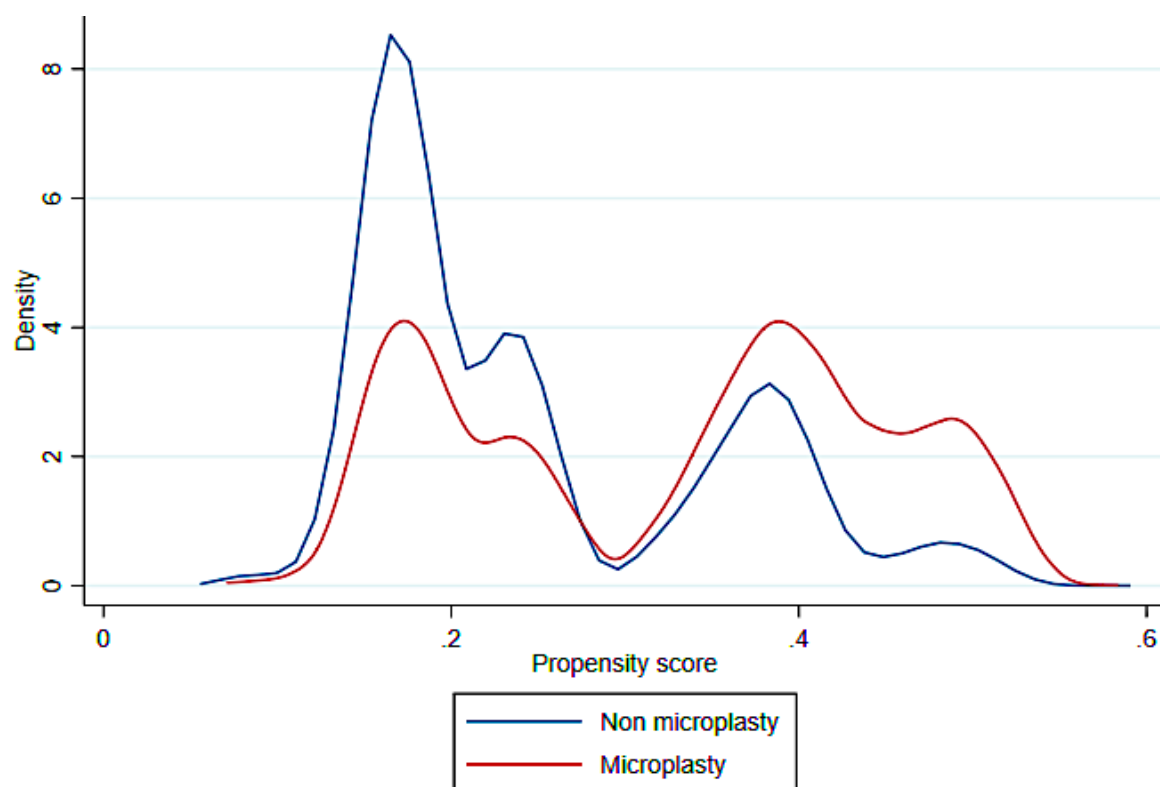


Figure 5.6. Kernel density plot of propensity scores before matching.

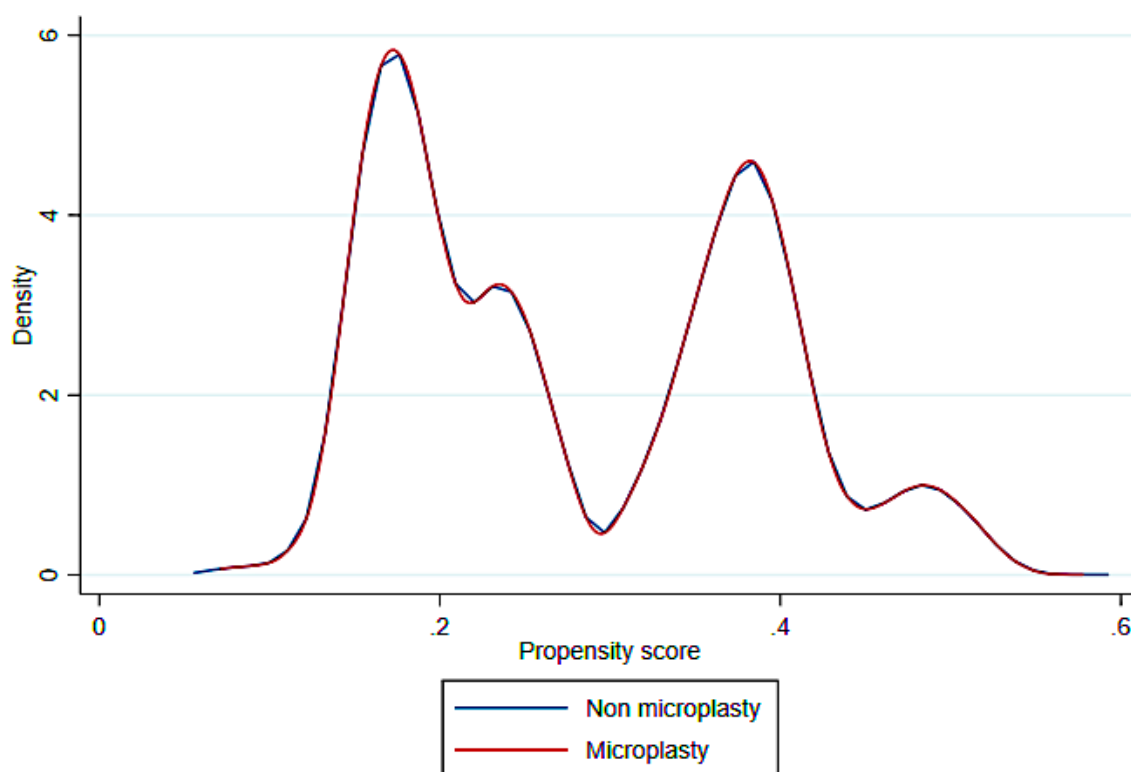


Figure 5.7. Kernel density plot of propensity scores after matching.

5.2.3.2 Revision rates

The matched cohort included 15,906 UKRs with 7,953 Microplasty UKRs and 7,953 Non-Microplasty UKRs. The mean age at surgery was 64.5 years (SD 9.5), with 7,235 females (45.5%) and 8,671 males (54.5%). The mean BMI was 30.4 kg/m² (SD 5.0) with the primary indication for surgery being osteoarthritis in 15,752 knees (99.0%).

Patient, surgical and implant characteristics were well balanced between the Microplasty and Non Microplasty groups after propensity score matching (Table 5.1). The only covariates with some residual imbalance were surgeon grade and surgeon caseload, which, when adjusted for in the regression models, did not change the findings presented.

In the matched cohort, the mean follow up for Microplasty and Non Microplasty UKRs were 2.3 years (SD 1.3) and 3.3 years (SD 1.8) respectively. In total 451 knees underwent revision surgery. There were 160 (2.0%) revisions in the Microplasty group and 291 (3.7%) revisions in the Non Microplasty UKR group.

The five year cumulative implant survival rates were 96.7% (CI 96.0 - 97.2) for Microplasty and 94.5% (CI 93.8 - 95.1) for Non-Microplasty UKRs (Figure 5.8). Microplasty UKRs had a significantly reduced revision rate compared with Non-Microplasty UKRs (HR=0.77, CI 0.64 - 0.94; p=0.008).

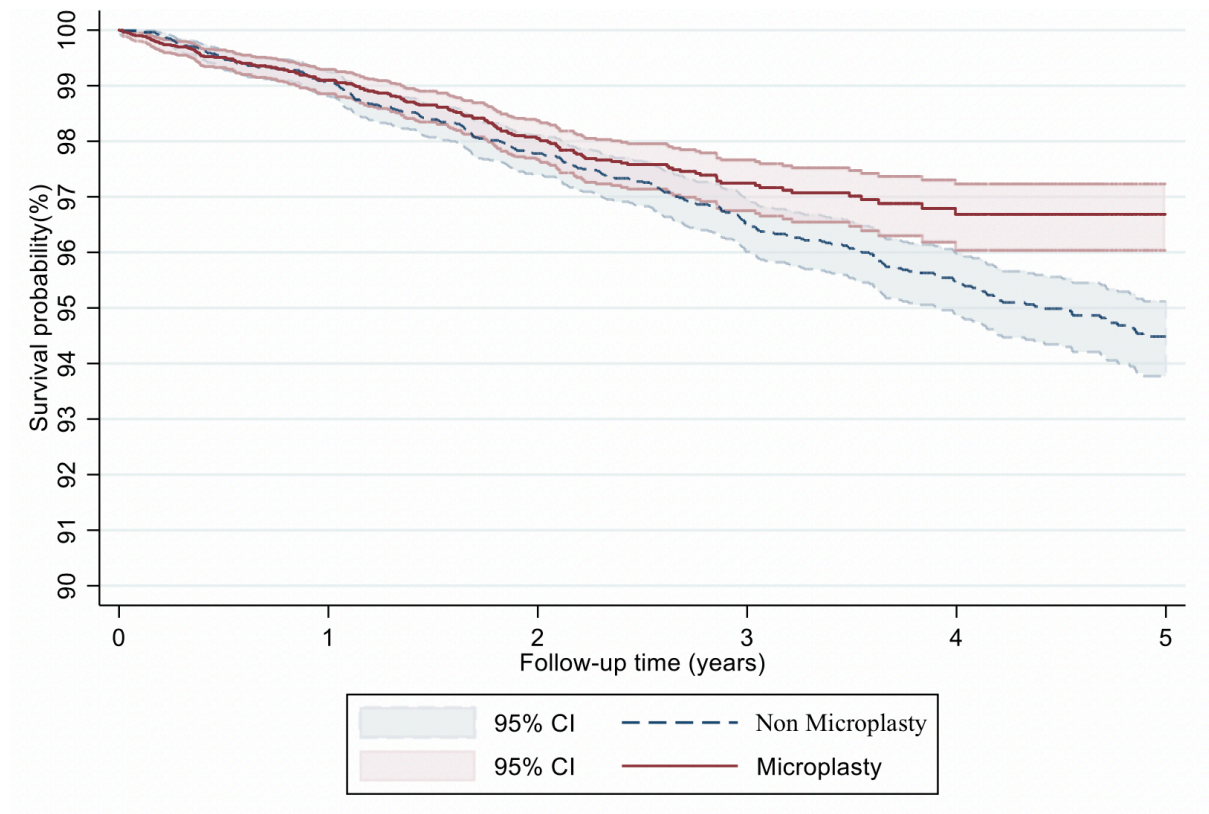


Figure 5.8. Kaplan Meier graph of matched Microplasty assisted UKRs and Non Microplasty UKR implant survival.

Subgroup analysis of Microplasty UKR inserted within a year of its introduction (n=2,424) and those inserted more than a year after its introduction (n=5,529) had four year implant survival rates of 96.2% (CI 95.3 - 97.0) and 96.8% (CI 95.6 - 97.8) respectively (Figure 5.9). Microplasty UKRs inserted within one year of its introduction had non-significantly reduced revision rates when compared to Non-Microplasty UKRs (HR 0.86, CI 0.67 - 1.10, p=0.23). Microplasty UKRs inserted more than a year after its introduction had significantly reduced revision rates compared to Non-Microplasty (HR 0.69, CI 0.54 - 0.89, p=0.004).

The revisions per 100 component years for Microplasty UKR (0.87, CI 0.75 - 1.02) were significantly lower ($p=0.02$) than for Non Microplasty (1.11, CI 0.99 - 1.24). Microplasty UKRs inserted within a year of its introduction ($n = 2,424$) and those inserted more than a year and after its introduction ($n = 5,529$) had revision rates per 100 component years of 0.98 (CI 0.78 - 1.22) and 0.79 (CI 0.63 - 0.99) respectively. When compared to the Non-Microplasty group, the decrease in revision rates of Microplasty UKRs inserted within a year of its introduction was not significant (0.98 vs 1.11, $p=0.34$). Microplasty UKRs inserted more than a year after its introduction had significantly lower (0.79 vs 1.11, $p=0.008$) revision rates than Non-Microplasty.

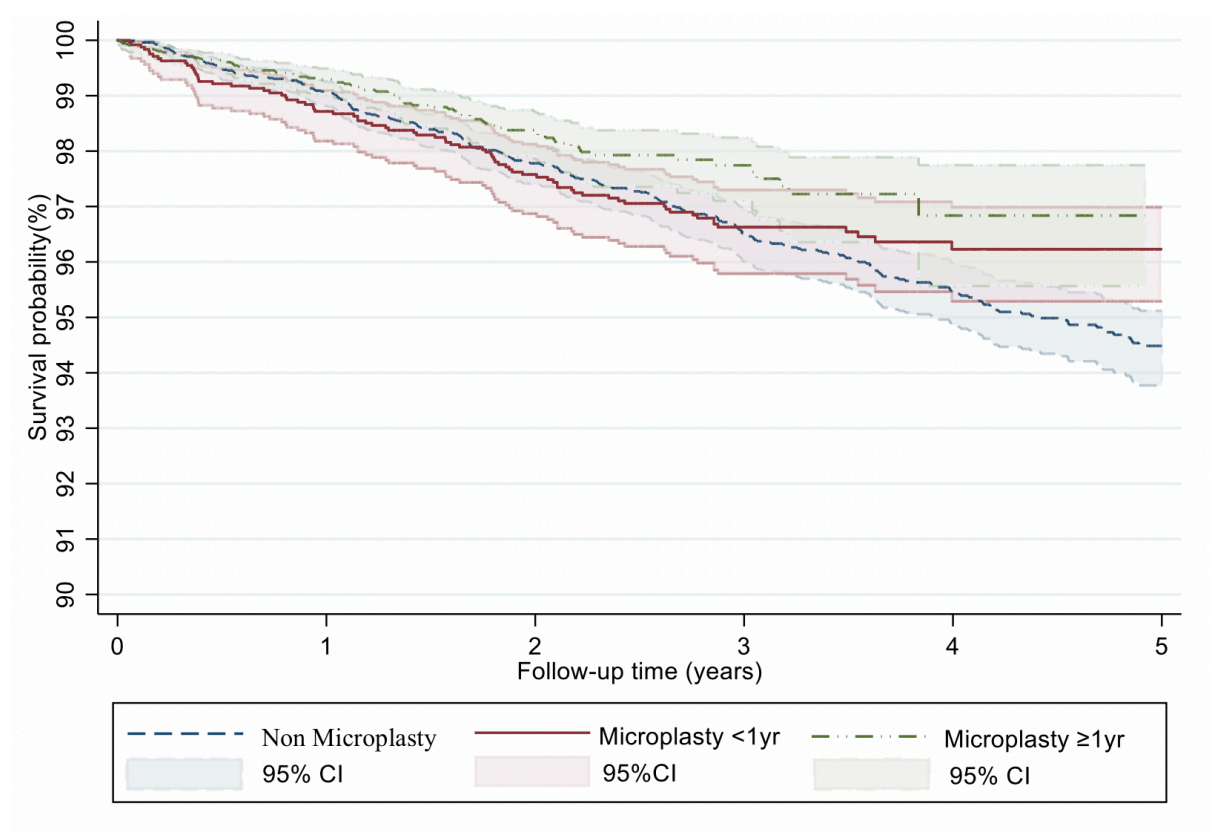


Figure 5.9. Kaplan Meier graph of matched Microplasty assisted UKRs inserted under one year, over one year and Non Microplasty UKR implant survival.

5.2.3.3 Indications for revision

The indications for revision with the highest revision rates per 100 component years in Non-Microplasty UKRs were osteoarthritis progression (0.31), aseptic loosening (0.26) and pain (0.19) (Table 5.2). In Microplasty UKRs the highest revision rates per 100 component years were osteoarthritis progression (0.21), aseptic loosening (0.19) and pain (0.12) (Table 5.2). Microplasty UKRs had a significantly reduced revision risk per 100 component years compared to Non-Microplasty UKRs for indications; osteoarthritis progression ($p < 0.05$, 0.21 vs 0.31) and other reasons ($p = 0.003$, 0.08 vs 0.18). Microplasty assisted UKRs had a significantly increased risk of periprosthetic fracture ($p = 0.03$, 0.09 vs 0.04). No other revision indications differed significantly between groups.

Reasons for revision	Matched cohort						
	Non Microplasty absolute number of revisions	Mean time to revision (Years)	Non Microplasty revisions per 100 component years	Microplasty absolute number of revisions	Mean time to revision (Years)	Microplasty revisions per 100 component years	Comparison of revisions per 100 component years (P value)
Aseptic loosening	69 (0.87%)	2.3 (SD 1.3)	0.26	35 (0.44%)	1.5 (SD 0.9)	0.19	P=0.13
OA progression*	82 (1.03%)	2.8 (SD 1.4)	0.31	39 (0.49%)	1.9 (SD 1.0)	0.21	P=0.048
Pain	49 (0.62%)	2.3 (SD 1.1)	0.19	22 (0.28%)	1.5 (SD 0.7)	0.12	P=0.08
Other*	48 (0.60%)	2.0 (SD 1.4)	0.18	14 (0.18%)	1.2 (SD 0.8)	0.08	P=0.003
Dislocation subluxation revision	17 (0.21%)	1.5 (SD 1.5)	0.06	22 (0.28%)	1.1 (SD 0.8)	0.12	P=0.052
Instability	26 (0.33%)	2.3 (SD 1.1)	0.10	10 (0.13%)	1.4 (SD 0.8)	0.05	P=0.11
Component dissociation	18 (0.23%)	1.4 (SD 1.1)	0.07	12 (0.15%)	1.0 (SD 0.9)	0.07	P=0.91
Malalignment	23 (0.29%)	2.0 (SD 1.4)	0.09	11 (0.14%)	1.2 (SD 1.5)	0.06	P=0.30

Infection	12 (0.15%)	0.9 (SD 1.0)	0.05	13 (0.16%)	0.9 (SD 0.7)	0.07	P=0.27
Periprosthetic fracture*	10 (0.13%)	0.5 (SD 0.3)	0.04	16 (0.20%)	0.5 (SD 0.6)	0.09	P=0.03
Lysis	8 (0.1%)	2.7 (SD 0.9)	0.03	4 (0.05%)	2.2 (SD 1.3)	0.02	P=0.77
Wear	7 (0.09%)	2.9 (SD 1.4)	0.03	5 (0.06%)	1.7 (SD 1.7)	0.03	P=0.97
Stiffness	5 (0.06%)	2.4 (SD 1.3)	0.02	6 (0.08%)	1.8 (SD 1.8)	0.03	P=0.36
Implant fracture	0 (0%)		N/A	0 (0%)		N/A	N/A
Patellar wear	0 (0%)		N/A	0 (0%)		N/A	N/A
Tibial wear	0 (0%)		N/A	0 (0%)		N/A	N/A
Incorrect sizing	0 (0%)		N/A	0 (0%)		N/A	N/A
Patella mal tracking	0 (0%)		N/A	0 (0%)		N/A	N/A

Table 5.2 Reasons for revision in matched Microplasty and Non Microplasty UKR cohort. Comparisons between were Microplasty and Non-Microplasty revisions per 100 component years were conducted using the Chi squared test. Significant differences are marked with *.

5.2.4 Discussion

This chapter demonstrates that Microplasty instrumentation improved the five year implant survival of the Oxford UKR compared to traditional instrumentation (Non Microplasty) and decreased the overall revision rate by 23%. Although previous studies have demonstrated that Microplasty usage results in improved implant positioning²⁷⁰⁻²⁷² and requirement for tibial recuts/bone preservation^{269, 272}, this is the first study using big data which has investigated its effect on revision rates.

There were different effects on revision rate with time from Microplasty's introduction. Microplasty UKRs inserted less than a year after its introduction to a hospital decreased the revision rate compared to Non Microplasty UKRs by 14%. However the difference was not statistically significant, partly given the limited number of UKRs. Additionally there was a likely delay in surgeons within a hospital changing to use Microplasty after the instruments became available. Another factor could be from the learning curve, but it is encouraging that even early on, Microplasty did not increase the risk of revision relative to Non Microplasty suggesting no adverse effect. Microplasty UKRs inserted more than a year after its introduction reduced revision rates by a third compared to the Non-Microplasty group, which was significant and likely to represent the true advantage of the new instrumentation.

It is difficult to interpret the results for the indications for revision given the mean follow-up of the Microplasty and Non-Microplasty UKR were different. A direct comparison of revision indication rates would be inappropriate because the numbers of revisions are related to the length of follow-up. Given the number of revisions under each revision indication is so low, Kaplan Meier and cox regression analysis are not appropriate for each indication. Another

approach is to use the revision rate per 100 component years¹⁵⁵ but is based on the assumption that the annual revision rate is constant. This is a reasonable assumption for the overall revision rate and its results were the same as the Kaplan Meier and cox regression analysis in this chapter. However, although it is a reasonable assumption for many individual modes of failure it may not be for all. For example peri-prosthetic fractures tend to occur early²⁶² so the group with a shorter follow up would be expected to have a higher revision rate. This may explain why Microplasty has a peri-prosthetic fracture rate that is just significantly higher than that of Non-Microplasty. Conversely arthritis progression tends to occur late⁸² so the group with a longer follow up would be expected to have a higher revision rate for this indication. This may explain why Non-Microplasty has an arthritis progression rate that is just significantly higher than that of Microplasty. The only other significant difference relates to “other reasons” for revision, which is unclear what these are. Therefore it is not clear exactly why Microplasty has a lower revision rate, but it is likely to be multifactorial.

With the Non-Microplasty instrumentation, surgeons judged the position of the tibial component and the orientation of the femoral component by eye⁶⁷. Microplasty includes a stylus system for selecting tibial resection level and a guide to control femoral component orientation. It has other advantages including slotted saw guides and instruments to protect the MCL and to avoid impingement. In addition, as the instrumentation guides component positioning the surgeon can focus on restoration of normal ligament balance, tension and function. Previous studies²⁷⁰⁻²⁷² have shown that the use of Microplasty does result in better component positioning, bone preservation, thinner bearings, avoidance of tibial recuts and better PROMs²⁶⁹. Improved component position and avoiding impingement should decrease rates of loosening, pain and dislocation. Additionally protecting the MCL should prevent

overcorrection and lateral arthritis. Finally Microplasty has made the operation more simple, logical, reliable and repeatable^{270, 271}.

The main study strength of this chapter is that over 15,000 UKRs were analysed and is completely unbiased given the use of NJR data excluding data from the designer surgeons in Oxford. The study is long enough to report the five year revision rate and showed that it was significantly lower with Microplasty than Non-Microplasty instrumentation. Perhaps more importantly the 97% five-year survival of Microplasty UKR was not substantially worse than that achieved by TKR in the joint registries^{8, 16, 17}. Therefore Microplasty instrumentation has helped to address the higher revision rates of UKRs, although this requires further investigation in the long term.

The main limitation is that the exact date when individual surgeons changed from Non-Microplasty to Microplasty instrumentation is not available and the duration of the learning curve is unknown. Therefore it was assumed that surgeons started using Microplasty as soon as it was introduced to their centre and that the transition period, which included the learning curve, lasted one year. Furthermore it is possible that some cases were done using other instrumentation, such as patient specific instrumentation. However if other instrumentation were used the numbers would have been too small to influence results. As mentioned previously in sections 4.1.4 and 5.1.4, the limitations of NJR analyses are that the only outcome assessed is revision, these can be underreported^{109, 227} and the indications can change postoperatively. Despite propensity matching there is potential for residual confounding. The groups were not perfectly matched given there was imbalance in the operating surgeon grade and surgeon caseload. However there were no differences in findings when these were

adjusted for in the regression models. A substantial proportion of BMI data was missing so this was not used for matching but was well balanced between comparative groups.

In summary, this chapter observed that the five year survival of Microplasty assisted Oxford UKRs was 97% and was significantly better than that of Non-Microplasty UKRs with no adverse learning curve effect observed. The advantages of Microplasty became greater after the one-year transition period, where its revision rate was about one third less than Non Microplasty UKRs. This is likely to represent its true benefit.

5.3 The effect of a Twin Peg cemented femoral component on revision rates

5.3.1 Introduction

The initial Phase 3 Oxford UKR femoral component, like its predecessors, was spherical and cemented. It had a single peg that was thought to be helpful as it allowed the component to seat optimally (Figure 5.10). However given between 25-50% of aseptic loosening were from the femoral component^{17, 147}, it was felt that the introduction of a Twin Peg component might improve fixation (Figure 5.10). During surgery a small hole is made in the femur anterior to the main peg hole to stabilise the femoral saw guide. A second peg, which would fit in the small hole, was therefore added, allowing the new component to be used with standard instrumentation. In order to support the peg, the spherical part of the component was extended about 15 degrees further anteriorly⁶⁷. To accommodate this anterior extension more bone is removed in front, which reduces the risk of the bearing impinging on bone. Given these modifications the femoral component could be implanted in increased knee flexion.

The Twin Peg cemented femoral component was introduced in 2003 but has only been widely used since 2009²⁷³. A cementless version of the Twin Peg component was also introduced at a similar time. The Twin Peg cemented component is used with the same cemented tibial component and polyethylene bearing as the Single Peg component⁶⁷. There have not been any direct comparative clinical studies of Single Peg and Twin Peg cemented femoral components to date.

In this chapter NJR data was used to compare the revision rate and mechanisms of implant failure, in particular femoral component aseptic loosening, following cemented medial Oxford UKRs using Single and Twin Peg femoral components.



Figure 5.10. Single and Twin Peg femoral components used for the Oxford UKR.

5.3.2 Methods

A retrospective observational study was performed using NJR records for all patients who had an Oxford UKR implanted. A formal application was submitted to the NJR Research Sub-Committee to access the relevant data and perform the work described in this chapter at the Musculoskeletal Research Unit at the University of Bristol. This application was approved on 5th July 2018 (Appendix 4). For further details on the NJR data collection procedure and identification of potential confounders please refer to section 4.1.

5.3.2.1 NJR data extract

An extract of data was received from the NJR containing details of all primary Oxford UKRs recorded in the NJR for any indication between 1st January 2009 to 31st December 2017 (n=41,593). The former date was the first year the Twin Peg became widely available in the UK and the later date was the most recent data the NJR could supply. Prior to obtaining the dataset the entire NJR database was linked to the ONS database using unique patient identifiers for all cause patient mortality data.

5.3.2.2 Data cleaning

The data extract which contained 41,593 Oxford UKRs was loaded into Stata (Version 15.1, Texas, USA) and subsequently coded and cleaned. Each continuous, categorical and string variable was systematically assessed for inconsistencies and implausible/missing data.

Data cleaning involved the removal of the lateral UKRs, hybrids, complex primaries, old tibial sizes, symmetric bearings, missing component data and cementless UKRs. After data cleaning there were 20,692 medial cemented Oxford UKRs (17,855 Single Peg and 2,837 Twin Peg) eligible for study inclusion (Figure 5.11).

After data cleaning the only variable with any missing data was BMI. However this did not vary significantly between groups and was well balanced between comparative groups both before and after matching. Data cleaning is as described earlier in this chapter and in detail in section 4.1.

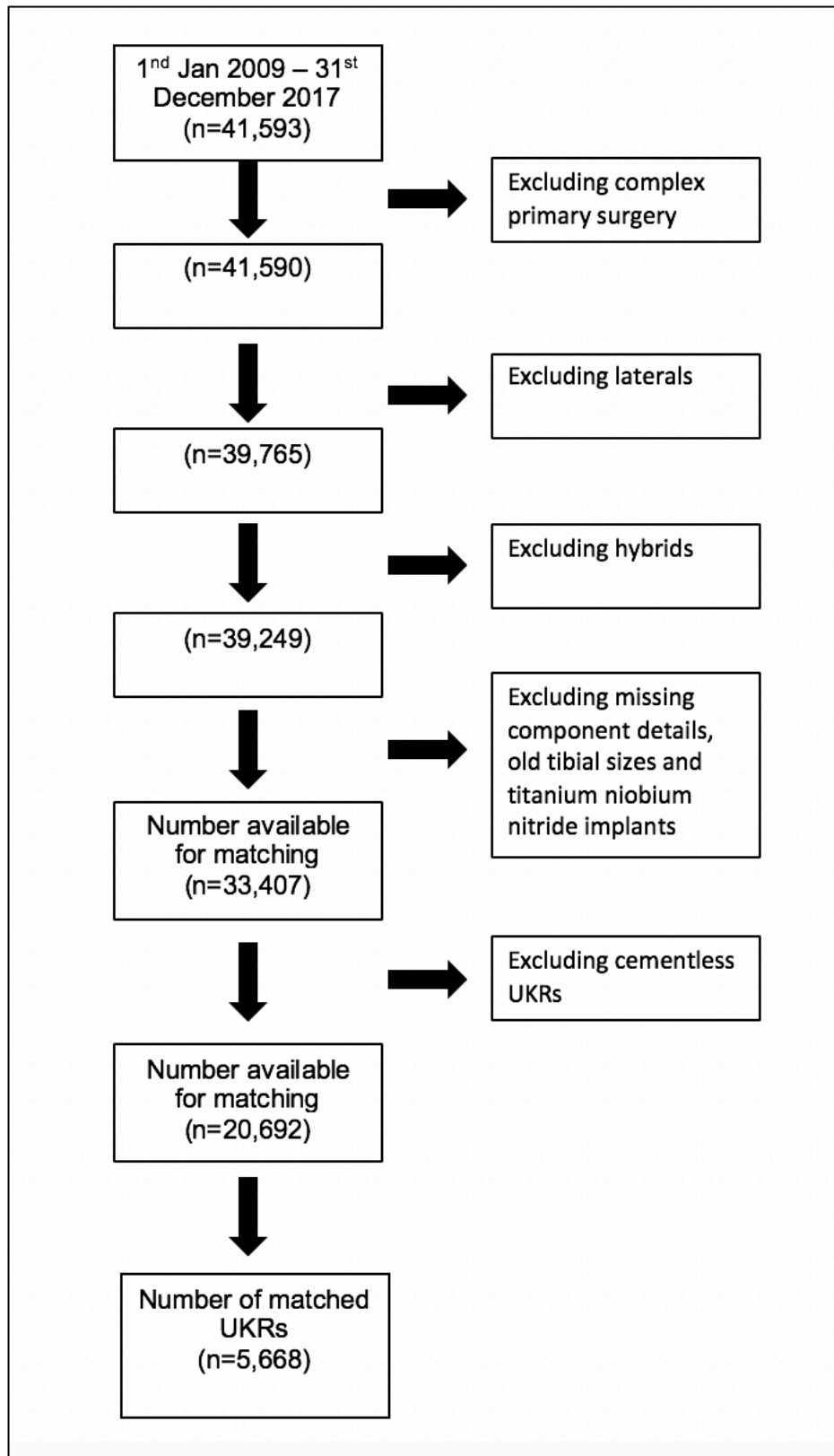


Figure 5.11. Data cleaning process for Peg study NJR dataset.

5.3.2.3 Outcome of interest

The primary outcome of interest for this comparative study was the five year implant survival of Single and Twin Peg cemented UKRs. The secondary outcomes for this study were the indications for revision surgery.

5.3.2.4 Propensity score matching

The unmatched cohort consisted of 20,692 medial cemented Oxford UKRs (17,855 Single Peg and 2,837 Twin Peg). Given the potential for patient, surgical and implant factors other than femoral component peg number (identified in section 4.1) to affect the revision rate, a priori propensity score matching of comparative groups for multiple known confounders was conducted. After matching there were 5,668 UKRs (2,834 Single Peg and Twin Peg cemented UKRs) included for analysis.

Confounders were selected for inclusion in the propensity score based on those known to affect the outcomes of interest (Table 4.1) and not on the basis of being associated with the femoral peg number exposure variable as per published recommendations for variable selection in propensity models.

5.3.2.5 Statistical analysis

Logistic regression generated a propensity score representing the probability of receiving a Twin Peg UKR. These scores were generated from patient, surgical and implant factors. Specifically, factors used for matching were; age, sex, primary diagnosis, unilateral/bilateral UKRs, ASA grade, chemical thromboprophylaxis, mechanical thromboprophylaxis, year of surgery, operating surgeon grade, surgeon caseload, surgical approach, operating technique and implant component sizes. BMI was not used for matching given it had a significant proportion of missing data. However BMI was not problematic given it was well balanced in both the Single and Twin Peg groups both before and after matching.

By controlling for these covariates the use of propensity score matching would allow the true effect of femoral peg number on revision surgery to be accurately assessed. This a priori approach was supported by the significant differences in patient, surgical and implant factors between the unmatched Single and Twin Peg groups (Table 5.3).

The algorithm used matched on the logit of the propensity score with a 0.02-SD calliper width. Greedy matching without replacement was used with a one to one matching ratio. SMDs were examined both before and after matching to assess for any covariate imbalance between comparative groups, with SMDs of 10% or more considered suggestive of covariate imbalance.

Outcomes of interest were: (1) implant survival, (2) indications for revision surgery. Cumulative survival was determined using the Kaplan-Meier method. The endpoint for implant survival was revision surgery (any implant component removed, exchanged or added) and the endpoint for patient survival was mortality. Implant and patient survival rates were

compared between the Single and Twin Peg UKR groups, using univariate cox regression models, with the proportional hazards assumptions assessed and satisfied in all analyses. To account for clustering within the matched cohort a robust variance estimator was used in the regression models. Regression analysis was repeated with adjustments made for covariates with residual imbalance after matching (SMD of 10% or more). Additionally a multi-level frailty model was tested in the regression models to control for patient clustering within surgeons. However both adjusted models and the multilevel models gave the same results as the univariate models and are therefore not presented.

The NJR database allows for revisions for UKRs with any aseptic loosening to be analysed and also for aseptic loosening by each component involved (e.g femoral or tibial component). The primary analysis was of revision for aseptic femoral loosening. Aseptic tibial loosening and overall loosening rates were also analysed as there were some cases of combined tibial and femoral loosening.

The proportional Chi-squared test with Yate's correction or Fisher's exact test was used to compare the indications for revision surgery between groups. The latter was only used when either group had an expected frequency of under-five.

All statistical analyses were performed using Stata (Version 15.1, Texas, USA) except propensity score matching which was performed using R (Version 3.4.0; R Foundation for Statistical Computing, Vienna, Austria). P-values of <0.05 were considered significant, with 95% CIs presented.

5.3.3 Results

5.3.3.1 Propensity score matching

The unmatched cohort consisted of 20,692 medial cemented Oxford UKRs (17,855 Single Peg and 2,837 Twin Peg UKRs). Baseline characteristics differed between the Single Peg and Twin Peg groups (Table 5.3). Specific covariates which differed significantly ($SMD > 0.1$) were thromboprophylaxis, year of surgery, surgeon caseload, minimally invasive surgery, femoral component size and bearing size. These differences were clearly highlighted by the distribution of propensity scores before matching (Figure 5.12).

The matching process improved the balance of covariates between Single Peg and Twin Peg groups (Table 5.3) and was confirmed on analysis of the distribution of propensity scores after matching (Figure 5.13). After matching there remained some residual imbalance of year of surgery. To account for this adjusted regression models were also tested but provided the same results.

	Unmatched cohort			Matched cohort		
	Single peg (n=17,855)	Twin peg (n=2,837)	SMD	Single peg (n=2,834)	Twin peg (n=2,834)	SMD
Covariate						
Gender						
Female	8,454 (47%)	1,431 (50%)	0.06	1,441 (51%)	1,428 (50%)	0.009
Male	9,401 (53%)	1,406 (50%)		1,393 (49%)	1,406 (50%)	
Age at surgery (year)						
Mean (SD)	65 (SD 10)	65 (SD 10)	0.02	65 (SD 10)	65 (SD 10)	0.01
BMI (kg/m²)*						
Mean (SD)	30 (SD 5) (n=13,159)	30 (SD 5) (n=1,868)	0.04	30 (SD 5) (n=2,165)	30 (SD 5) (n=1,865)	0.03
Primary diagnosis						
Primary OA	17,676 (99%)	2,797 (99%)	0.04	2,799 (99%)	2,794 (99%)	0.02
Other	179 (1%)	40 (1%)		35 (1%)	40 (1%)	
Bilateral UKRs	469 (3%)	44 (2%)	0.08	55 (2%)	44 (2%)	0.03
ASA grade						
1	3,344 (19%)	488 (17%)	0.05	483 (17%)	488 (17%)	0.05
2	13,024 (73%)	2,082 (73%)		2,119 (75%)	2,079 (73%)	
3 or above	1,487 (8%)	267 (10%)		232 (8%)	267 (10%)	
VTE – chemical						
LMWH (+/-other)	10,447 (59%)	2,020 (71%)	0.4	1,972 (70%)	2,017 (71%)	0.06
Aspirin only	1426 (8%)	208 (7%)		240 (8%)	208 (7%)	
Other	4,731 (26%)	590 (21%)		593 (21%)	590 (21%)	
None	1,251 (7.0%)	19 (1%)		29 (1%)	19 (1%)	

VTE mechanical	–					
Any	17,430 (98%)	2,800 (99%)	0.08	2,798 (99%)	2,797 (99%)	0.003
None	425 (2%)	37 (1%)		36 (1%)	37 (1%)	
Year of surgery						
2009	2416 (14%)	133 (5%)	0.7	74 (3%)	133 (5%)	0.3
2010	2396 (13%)	175 (6%)		85 (3%)	175 (6%)	
2011	2371 (13%)	178 (6%)		167 (6%)	178 (6%)	
2012	2285 (13%)	192 (7%)		246 (9%)	192 (7%)	
2013	2296 (13%)	276 (10%)		366 (13%)	276 (10%)	
2014	2173 (12%)	457 (16%)		486 (17%)	457 (16%)	
2015	1633 (9%)	475 (17%)		520 (18%)	475 (17%)	
2016	1275 (7%)	440 (15%)		492 (17%)	440 (15%)	
2017	1010 (6%)	511 (18%)		398 (14%)	508 (18%)	
Surgeon grade						
Consultant	16,462 (92%)	2,656 (94%)	0.06	2,668 (94%)	2,653 (94%)	0.02
<i>Other</i>	1,393 (8%)	181 (6%)		166 (6%)	181 (6%)	
Surgeon caseload						
<10 cases/year	7,266 (41%)	893 (31%)	0.3	915 (32%)	892 (31%)	0.04
10 to <30 cases/year	7,731 (43%)	1,104 (39%)		1,131 (40%)	1,103 (39%)	
≥30 cases/year	2,858 (16%)	840 (30%)		788 (28%)	839 (30%)	

Surgical approach						
Medial parapatellar	16,283 (91%)	2,513 (89%)	0.09	2,536 (89%)	2,511 (89%)	0.03
Other	1,572 (9%)	324 (11%)		298 (11%)	323 (11%)	
Minimally invasive surgery						
No	9,171 (51%)	1,691 (60%)	0.2	1,675 (59%)	1,689 (60%)	0.01
Yes	8,684 (49%)	1,146 (40%)		1,159 (41%)	1,145 (40%)	
Femoral component size						
Ex small	43 (0.2%)	6 (0.2%)	0.1	4 (0.1%)	6 (0.2%)	0.02
Small	4,076 (22.8%)	796 (28.0%)		788 (27.8%)	793 (28.0%)	
Medium	9,536 (53.4%)	1,451 (51.2%)		1,462 (51.6%)	1,451 (51.2%)	
Large	4,170 (23.4%)	582 (20.5%)		577 (20.4%)	582 (20.5%)	
Ex-Large	30 (0.2%)	2 (0.1%)		3 (0.1%)	2 (0.1%)	
Tibial component size						
AA	83 (0.5%)	11 (0.4%)	0.09	12 (0.4%)	11 (0.4%)	0.02
A	2109 (11.8%)	399 (14.1%)		382 (13.5%)	397 (14.0%)	
B	4151 (23.3%)	607 (21.4%)		614 (21.7%)	607 (21.4%)	
C	5071 (28.4%)	798 (28.1%)		809 (28.5%)	798 (28.2%)	

D	4120 (23.1%)	636 (22.4%)		642 (22.7%)	636 (22.4%)	
E	1871 (10.5%)	294 (10.4%)		286 (10.1%)	293 (10.3%)	
F	450 (2.5%)	92 (3.2%)		89 (3.1%)	92 (3.2%)	
Bearing size						
3	3972 (22.3%)	635 (22.4%)	0.1	652 (23.0%)	635 (22.4%)	0.04
4	7201 (40.3%)	1,163 (41.0%)		1,128 (39.8%)	1,162 (41.0%)	
5	3786 (21.2%)	623 (22.0%)		617 (21.8%)	622 (21.9%)	
6	1705 (9.6%)	282 (9.9%)		286 (10.1%)	281 (9.9%)	
7	760 (4.3%)	105 (3.7%)		120 (4.2%)	105 (3.7%)	
8	282 (1.6%)	16 (0.6%)		15 (0.5%)	16 (0.6%)	
9	149 (0.8%)	13 (0.5%)		16 (0.6%)	13 (0.5%)	
Bone graft						
None	17,810 (99.7%)	2,833 (99.9%)	0.03	2,830 (99.9%)	2,830 (99.9%)	<0.001
Bone graft used	45 (0.3%)	4 (0.1%)		4 (0.1%)	4 (0.1%)	

Table 5.3. Patient and surgical factors before and after propensity score matching.

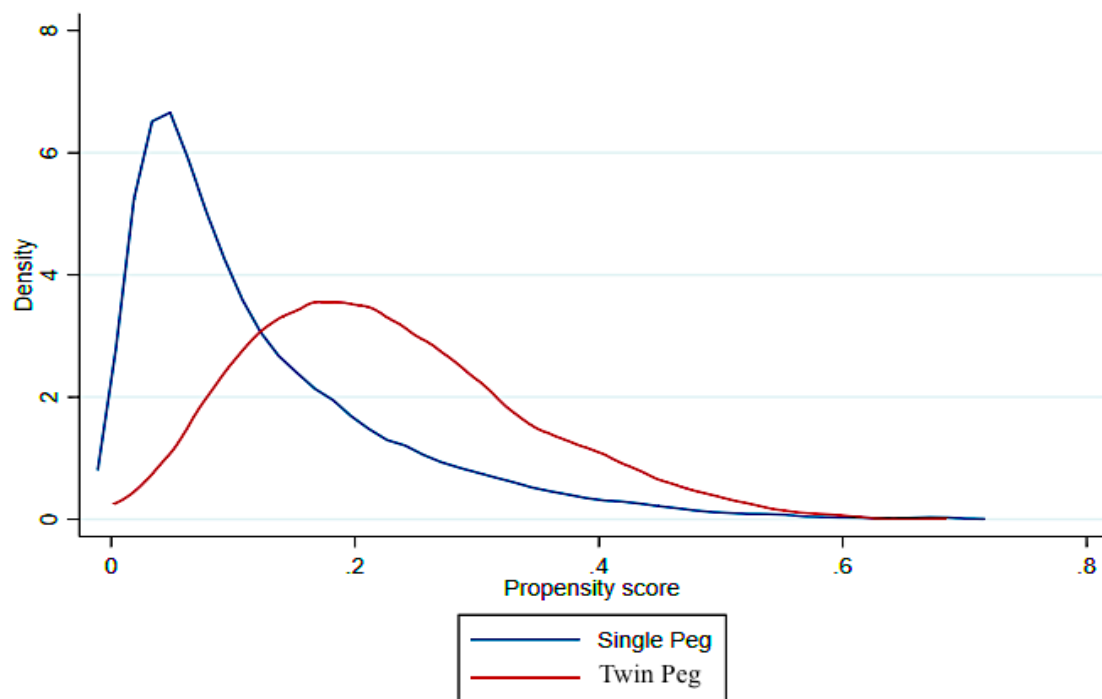


Figure 5.12. Kernel density plot of propensity scores before matching.

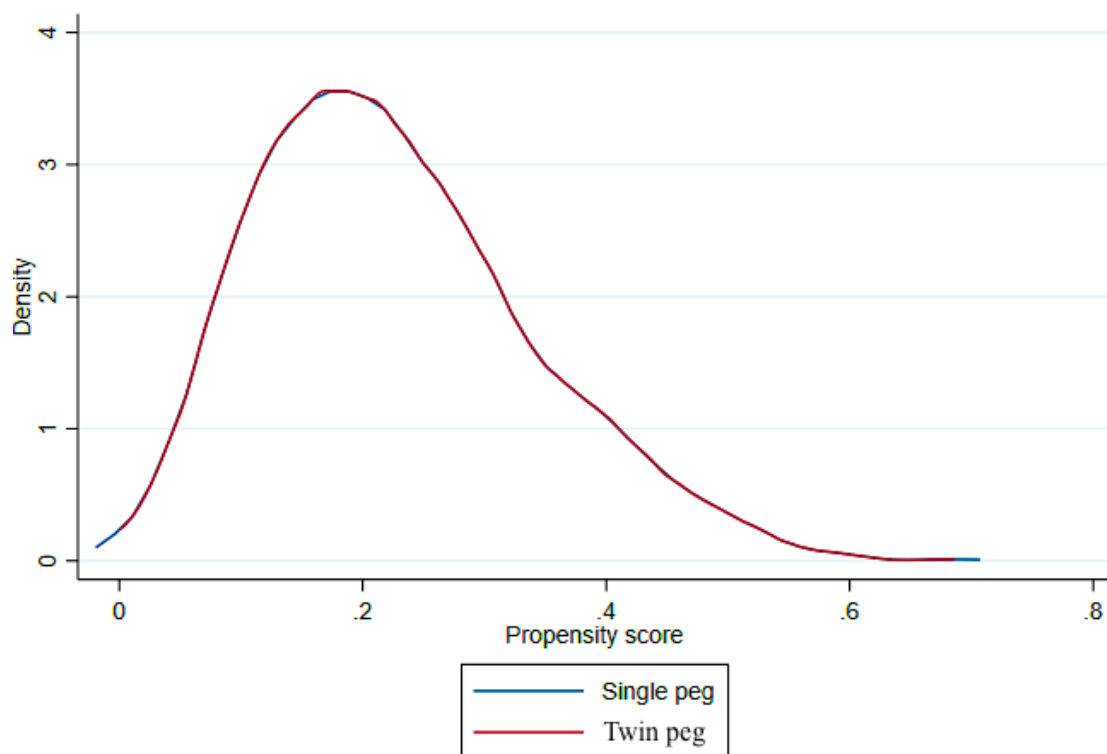


Figure 5.13. Kernel density plot of propensity scores after matching.

5.3.3.2 Revision rate

The matched cohort included 5,668 Oxford UKRs, with 2,834 Single Peg UKRs and 2,834 Twin Peg UKRs. The mean age at surgery was 65 years (SD 10), with 51% of the cohort being female. The mean BMI was 30.0 (SD 5.0) with the primary indication for surgery being osteoarthritis in 99%.

Patient, surgical and implant characteristics became well balanced between the Single Peg and Twin Peg groups after propensity score matching (Table 5.3). The only covariate with residual imbalance was year of primary surgery, which when adjusted for in the regression models, did not change the findings and is presented below.

In the matched cohort, the mean follow up for both Single and Twin Peg UKRs was 3.3 (SD 2.0) and 3.4 years (SD 2.0) respectively. In total 176 knees underwent revision surgery; 102 (3.6%) Single Peg UKRs and 74 (2.6%) Twin Peg UKRs. The five year cumulative all-cause implant survival rates were 94.8% (CI 93.6 - 95.8) for Single Peg UKRs and 96.2% (CI 95.1 - 97.1) for Twin Peg UKRs (Figure 5.14). The difference in cumulative revision rates between Twin Peg and Single Peg UKRs was statistically significant (HR=0.74, CI 0.55 - 0.99, p=0.04).

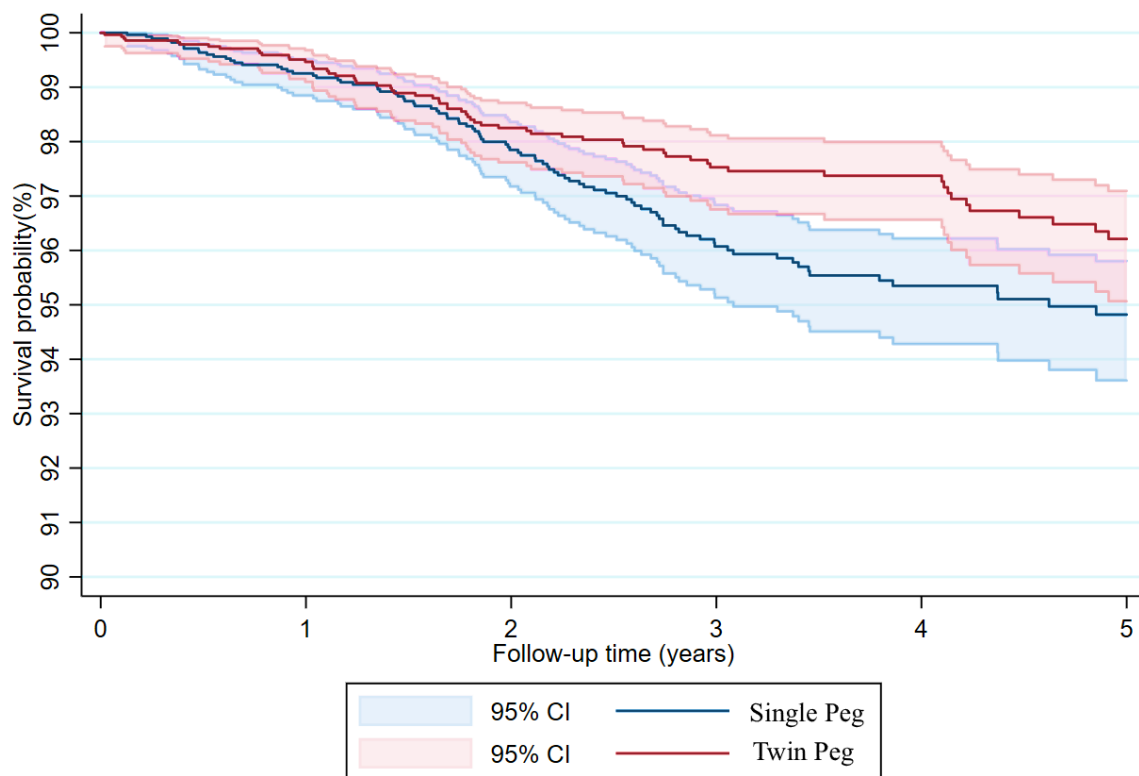


Figure 5.14. Kaplan Meier graph of matched Single Peg and Twin Peg UKR implant survival.

5.3.3.3 Indications for revision

The most common reasons for revision in the Single Peg group were osteoarthritis progression (n=26, 0.9%), pain (n=23, 0.8%) and aseptic loosening (n=18, 0.6%) (Table 5.4). In the Twin Peg UKR group the most common reasons for revision were osteoarthritis progression (n=25, 0.9%), aseptic loosening (n=14, 0.5%) and pain (n=9, 0.3%) (Table 5.4). There was a statistically significant ($p=0.01$) difference in the revision rate for pain between the Single Peg (n=23, 0.8%) and the Twin Peg (n=9, 0.3%). The revision rate for femoral component aseptic loosening was significantly lower ($p=0.03$) in the Twin Peg group (n=3, 0.1%) compared to the Single Peg group (n=11, 0.4%). However there was no statistically significant change in the revision rate for aseptic loosening overall (Twin Peg n=14, 0.5%; Single Peg n=18, 0.6%; $p=0.5$) or tibial component loosening (Twin Peg n=12, 0.4%; Single Peg n=10, 0.4%; $p=0.7$).

Reasons for revision	Single Peg UKRs (n=2,834)	Mean time to revision indication Single Peg (Years)	Twin Peg UKRs (n=2,834)	Mean time to revision indication Dual Peg (Years)	Comparison between Single and Twin peg (P value)
Aseptic loosening (Any component)	18 (0.6%)	2.0 (SD 1.1)	14 (0.5%)	2.9 (SD 2.4)	0.5
Femoral component aseptic loosening*	11 (0.4%)	1.8 (SD 0.8)	3 (0.1%)	3.3 (SD 2.9)	0.03
Tibial component aseptic loosening	10 (0.4%)	2.1 (SD 1.4)	12 (0.4%)	3.1 (SD 2.6)	0.7
Lysis	3 (0.1%)	1.8 (SD 0.6)	4 (0.1%)	3.3 (SD 2.9)	1.0
OA progression	26 (0.9%)	2.6 (SD 1.4)	25 (0.9%)	3.1 (SD 2.0)	0.9
Pain*	23 (0.8%)	2.1 (SD 1.0)	9 (0.3%)	2.6 (SD 2.1)	0.01
Other	19 (0.7%)	2.7 (SD 1.9)	14 (0.5%)	2.7 (SD 1.8)	0.4
Dislocation subluxation revision	8 (0.3%)	1.5 (SD 1.0)	4 (0.1%)	0.9 (SD 0.6)	0.3
Instability	6 (0.2%)	1.9 (SD 1.0)	7 (0.2%)	3.2 (SD 2.9)	0.8
Component dissociation	4 (0.1%)	2.1 (SD 0.4)	3 (0.1%)	2.9 (SD 2.6)	1.0
Malalignment	8 (0.3%)	1.5 (SD 0.7)	2 (0.1%)	2.1 (SD 2.9)	0.1
Infection	7 (0.2%)	1.2 (SD 1.1)	5 (0.2%)	1.1 (SD 0.8)	0.6
Periprosthetic fracture	3 (0.1%)	2.3 (SD 3.0)	3 (0.1%)	1.0 (SD 1.0)	1.0
Wear	3 (0.1%)	3.4 (SD 1.9)	4 (0.1%)	5.7 (SD 2.7)	1.0
Stiffness	2 (0.1%)	2.2 (SD 0.2)	5 (0.2%)	2.1 (SD 1.6)	0.5

Implant fracture	1 (0%)	2.0	0 (0%)	N/A	N/A
Patellar wear	0 (0%)	N/A	0 (0%)	N/A	No revisions
Tibial wear	0 (0%)	N/A	0 (0%)	N/A	No revisions
Incorrect sizing	0 (0%)	N/A	0 (0%)	N/A	No revisions
Patella mal- tracking	0 (0%)	N/A	0 (0%)	N/A	No revisions

Table 5.4. Indications for revisions in the matched Peg NJR cohort. Comparisons between groups were conducted using the Chi squared test or the Fisher's exact test when either group had an expected frequency of under-five. Significant differences between groups are marked *.

5.3.4 Discussion

This is the first comparative study of Single and Twin Peg cemented medial Oxford UKRs. The five year implant survival improved from 94.8% with the Single Peg to 96.2% with the Twin Peg group (HR=0.74, p=0.04). The revision rate for femoral component aseptic loosening (0.4% to 0.1%) and pain (0.8% to 0.3%) more than halved with the Twin Peg compared to the Single Peg design. The Twin Peg was not associated with an increase in any revision indication.

The Twin Peg femoral component was introduced to reduce the rate of femoral loosening and with this chapter showing a reduction from 11 out of 2834 cases with the Single Peg to three out of 2834 cases with the Twin Peg. Although the rates of loosening are very low, limiting information on the size of the reduction, it is definitely not elevated with the Twin Peg UKR.

The Twin Peg component halved the number of revisions for pain which could be for multiple reasons. Surgeons are able to record more than one revision indication, so some cases may have been painful aseptic loosening where surgeons recorded both femoral loosening and pain. As femoral loosening is usually obvious at revision it is possible, that cases of painful early femoral loosening were just recorded as pain. Another explanation is that with the Twin Peg there is a reduction in the incidence of anterior bearing impingement on bone, which is a potential cause of pain. Normally the distal femur is prepared with a mill and this removes just enough bone to accommodate the Single Peg femoral component. However additional bone needs to be removed in front of the milled surface to accommodate the anterior part of the bearing in full extension⁶⁷. The Twin Peg component has some anterior extension to support the additional peg which therefore cannot be inserted if this anterior bone is not removed⁶⁷. Therefore with the Twin Peg component, surgeons cannot forget to remove this bone.

No revision indication increased significantly with the Twin Peg group which suggests that the use of the Twin Peg UKR has no downside, which is perhaps not surprising as the same operative technique, instrumentation, tibial component and bearing are used. Before this study there were no clinical studies comparing Single Peg and Twin Peg UKR designs, with the only direct comparative studies in the literature being cadaveric^{274, 275}. Reiner et al.²⁷⁵ found that the pull out force from cadaveric bone, which was used as a measure of fixation quality, was substantially higher for the Twin Peg. In another study Reiner et al.²⁷⁴ observed a trend towards less subsidence in the Twin Peg design in cadaveric bone although this did not reach significance. White et al.²⁷³ reported the five year implant survival of Twin Peg UKRs as 98%, but this study did not have a Single Peg UKR comparative arm, so the authors compared the findings to other well-known Single Peg cohorts^{195, 276} finding no differences in outcomes. However, the study²⁷³ was limited by a small sample size with only five revisions for analysis.

The main limitation of this study is the short follow up of the Twin Peg component. Additionally as discussed in earlier in this chapter and in 4.1.4, registry data is limited to the outcome of revision and the revision reasons can change postoperatively. However studies of Single^{195, 276} and Twin Peg^{273, 277} cohorts appear to report equivalent functional outcomes. Another limitation is that, despite matching potential residual confounding can affect results. Following matching the only variable with appreciable imbalance was the year of primary surgery, which is important as technique and instrumentation improves with time. However there were no differences in the findings presented when the models were adjusted for year of surgery. There was a substantial proportion of missing BMI data so this was not used for matching although this variable was well balanced between comparative groups. Given virtually all Twin Peg cases were matched greatly improves the generalisability of this study.

In summary, this chapter found the risk of revision of the cemented Oxford UKR was 26% lower with the Twin Peg femoral component compared to the Single Peg. This is likely secondary to the rates for femoral component loosening and pain more than halving. Importantly the Twin Peg was not associated with a significant increase in revision rate for any reason. This suggests that the cemented Twin Peg femoral component should be used instead of the Single Peg design to help reduce revision rates.

6. A RADIOSTEREOMETRIC ANALYSIS TO ASSESS BEARING WEAR IN THREE DIFFERENT POLYETHYLENE TYPES

6.1 Introduction

Polyethylene bearing wear is an important failure mechanism for fixed-bearing UKR given the small contact area and high contact stress from incongruent surfaces²⁷⁸⁻²⁸⁰. To minimise wear and allow normal kinematics, the Oxford UKR has a fully congruent and mobile polyethylene bearing⁶⁷ (Figure 6.1). Despite this, there are anecdotal reports of wear resulting in bearing fracture for the Phase 3 Oxford²⁸¹, with Chapter 2 identifying bearing related revisions as an issue¹⁴⁷. In addition preliminary analysis of five year wear data from a previously published RCT²⁰² showed higher wear rates in the Phase 3 compared to the Phase 2 Oxford. Therefore it is important to investigate wear at 10 years and seek explanations.

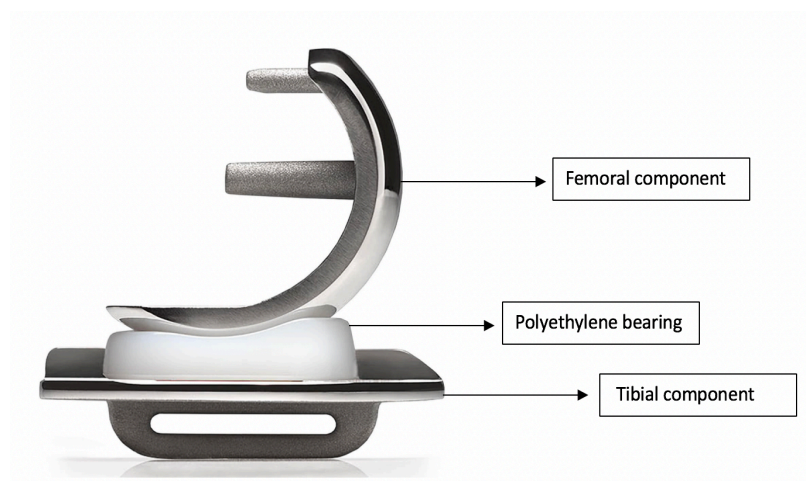


Figure 6.1. Schematic of mobile bearing Oxford UKR. Adapted from²⁸².

* This chapter has been published²⁸³. Mohammad HR, Campi S, Kennedy JA, Judge A, Murray DW, Mellon SJ. Long-term in vivo wear of different bearing types used for the Oxford Unicompartmental Knee Replacement. Bone Joint Res 2019; 8(11): 535. (Appendix 1).

Polyethylene wear can be quantified by either volumetric loss or the linear penetration of the femoral component into the polyethylene relative to the tibial component. Linear wear is more relevant for UKR, given failure from wear is usually from polyethylene failure or fracture from linear wear rather than particulate debris-induced osteolysis from volumetric wear²⁸¹. Linear wear of the Oxford UKR bearings has been assessed using various methodologies including wear simulation⁷⁹, retrieval analysis^{182, 255}, and RSA^{77, 284, 285}. Only RSA quantifies wear in functioning knees.

RSA was first developed by Selvik et al.²⁸⁶ in Sweden and is a powerful imaging technique that provides accurate three dimensional measurements of objects' relative displacements using sequential radiographic images. This makes it the ideal tool to measure component wear or migration²⁸⁷. During the procedure two separate radiographs are taken from two different views whilst the subject stands in a calibration frame. The frame provides a unique coordination system that can be used to calculate movement in three planes²⁸⁷.

As discussed in Chapter 1, there have been three iterations of the Oxford UKR. The Phase 1 was used between 1976 and 1987, Phase 2 between 1987 and 1998, and Phase 3 from 1998 onwards⁶⁷. An RSA study⁷⁷ of the Phase 1 with 20 years' follow-up found a mean linear bearing wear rate of 70 $\mu\text{m}/\text{year}$. Similar studies^{77, 285} of Phase 2 bearings at ten and 20 years found mean linear wear rates of 20 $\mu\text{m}/\text{year}$. Although there are small design differences between Phase 2 and 3 bearings, such as the plan shape of the tibial component (i.e. the shape as seen in the transverse plane), the main difference was that the Phase 2 bearing was implanted using a TKR approach, whereas the Phase 3 bearing is implanted using a minimally invasive technique⁶⁷.

Since the introduction of the Phase 3 bearing in 2005, there was a change in polyethylene resin used to manufacture the bearing from Hi-Fax 1900 (Montell Polyolefins, Wilmington, Delaware) to GUR 1050 (Ticona, Oberhausen, Germany), as the manufacture of the 1900 resin was discontinued²⁸⁸. The main difference between the resins is the molecular weight, which is 4.4×10^6 g/mol - 4.9×10^6 g/mol for the 1900 resin and 5.5×10^6 g/mol - 6.0×10^6 g/mol for the 1050 resin. Although wear simulations²⁸⁹ in TKR have shown no difference between these resins, they have never been tested clinically. In addition, although the Oxford bearings are usually manufactured by a direct compression moulding process (DCM), some bearings were machined from bar stock around the time of the transition from 1900 to 1050 resin, which may have consequences²⁸⁸.

The objective of this chapter was to determine the wear rate of the Phase 3 Oxford UKR bearings using an accurate and validated RSA technique for UKRs^{284, 290, 291}. In addition, subgroup analyses were planned to compare of the wear rates of bearings made from different resin types (1900 vs 1050) and manufacturing techniques (moulding vs machining).

6.2 Methods

6.2.1 Ethical approval

Ethical approval for this study was obtained from the local ethics committee, South Central – Oxford B Research Ethics Committee (REC), REC reference 16/SC/0456. For additional details of ethics and participant information sheets sent please refer to Appendix 7.

6.2.2 Patient recruitment

All patients gave informed consent for participation in the study (Appendix 7). Bearing code numbers from patients with follow-up of ten years or greater were identified from the database of medial Phase 3 Oxford UKRs performed by Professor David Murray and Mr Christopher Dodd^{171, 195}. Three types of polyethylene bearings were identified; (1) 1900 machined, (2) 1050 machined and (3) 1050 moulded. A power calculation revealed that 18 bearings were required in each of the groups for an appropriate comparison to be made. For additional details on the power calculation please refer to section 6.2.4.

An appropriate number of 1900 machined (n=19), 1050 machined (n=21), and 1050 moulded bearings (n=23) were successfully recruited for the study and attended clinic. All patients had their primary Oxford UKR performed between 3rd October 2002 and 14th July 2008. All procedures were within the recommended indications described by Goodfellow et al.⁶⁷.

6.2.3 Measuring polyethylene bearing wear

Patients attended a research clinic where their OKS was recorded by research physiotherapists independent of the clinical teams taking care of the patients. Subsequently patients were assessed by independent research radiographers who took simultaneous stereo pairs of anteroposterior radiographs obliquely at 30° whilst each patient was fully weight-bearing, as has previously been described^{77, 285}. Each patient stood within a calibration frame with 0.8 mm tantalum markers embedded at known locations (Figure 6.2). The fiducial and control markers in front and behind the frame, respectively, allowed for image calibration of the stereo images taken. Previously validated model-based RSA²⁸⁴ software version 3.21 (Medis Specials, Leiden, The Netherlands) was then used to estimate the position of the tibial and femoral component based on each implant's outline using a Canny detection algorithm²⁹². For each component, a virtual silhouette could be created from the photogrammetric relationship from the calibration and the computer-aided design (CAD) models. This allowed virtual representation of the components in three dimensional space (Figure 6.3).

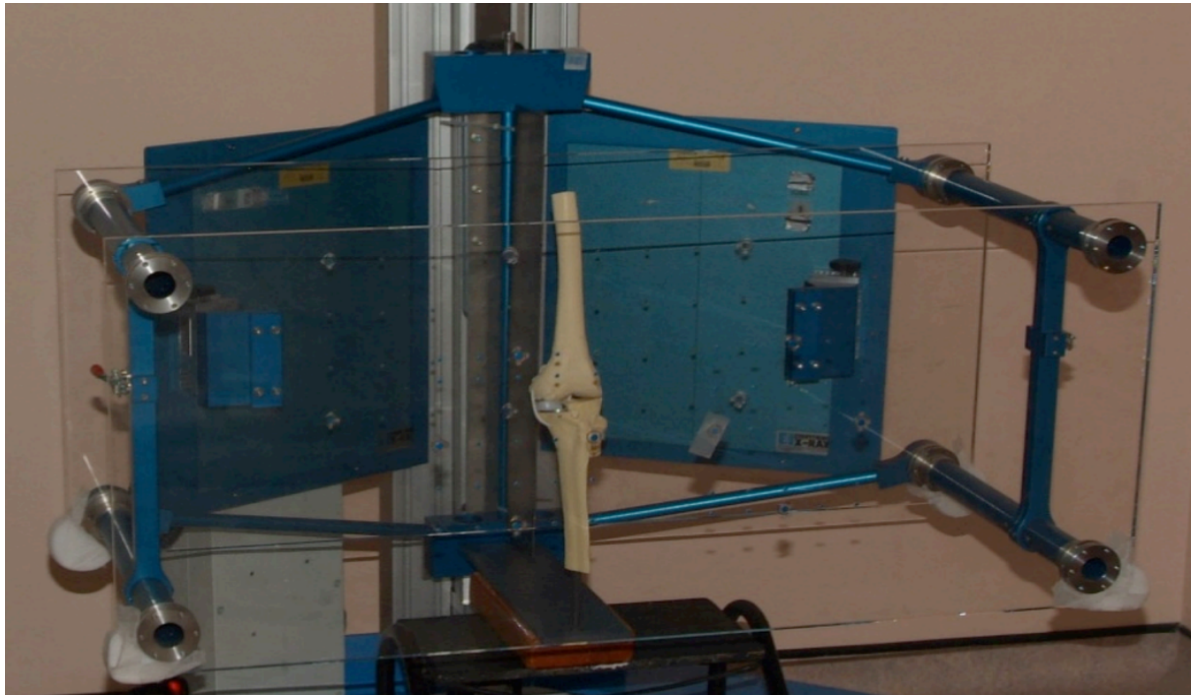


Figure 6.2. Calibration frame in which stereo radiographs were taken. Adapted from²⁹³.

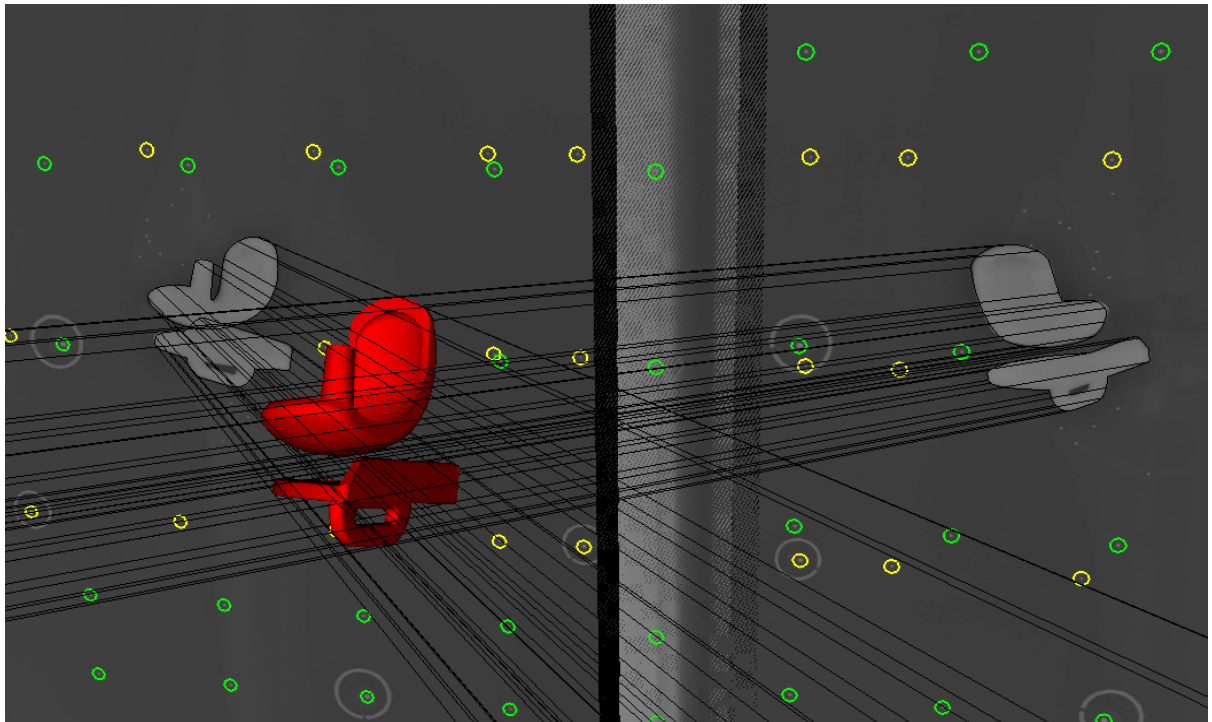


Figure 6.3. CAD models representing the components in three dimensional space.

Once the implants were posed, their coordinates were inputted into Matlab (Version 7.0.4.287; The MathWorks, Natick, Massachusetts, USA), which allowed for the closest linear distance between the femoral component and tibial tray to be calculated and taken as the bearing thickness at follow-up^{77, 284, 285}.

As the bearing has fully congruous contact on both upper and lower surfaces, the overall bearing linear wear was calculated by subtracting the closest linear distance at follow-up between femoral component and tibial tray from the estimated thickness of the bearing at implantation. The estimated bearing thickness was determined by adding 0.5 mm to the nominal bearing thickness and then adding a further 0.05 mm for manufacturer tolerance, as previously described and validated^{77, 285}. This additional thickness had previously been determined from measurement of unused bearings²⁸⁵. The overall bearing wear was then divided by the time between the date of primary surgery and the RSA clinic appointment to determine the annual linear wear rate. The accuracy of the RSA system is approximately 0.1 mm^{77, 284, 285}, meaning that linear wear rate can be accurately assessed using RSA, particularly when follow-up exceeds ten years.

6.2.4 Statistical analysis

A power calculation was conducted using a power of 0.8, significance of 0.05, a SD of 0.02 from data from the Phase 2 Oxford UKR, and an important clinical difference of 0.02 mm/year²⁸⁵. This study required at least 18 bearings per group to allow for a meaningful comparison.

To determine if resin type affected wear rate, we compared the wear rate of 1900 machined and 1050 machined bearings. To determine if the manufacturing process affected wear rate, we compared the wear rate of 1050 machined and 1050 moulded bearings. Given that the annual wear rate data were normally distributed, we used the unpaired t-test to conduct these comparisons.

To compare baseline characteristics between groups, the one-way analysis of variance (anova) was used for age, BMI, and OKS. Sex and femoral and tibial component sizes between groups were compared with the Fisher's exact test. To analyse the relationship of each factor with annual wear rate, each factor was correlated using the Spearman's rank test and plotted graphically. If a linear relationship was evident, a linear regression model was utilised with 95% CIs reported. The effect of bearing type on the linear relationship was evaluated using an interaction term. Subgroup analyses comparing wear rates for different sex, age, BMIs and OKS groups were performed using the unpaired t test.

All statistical tests were conducted using Stata (Version 13.1; Texas, USA). A p value of ≤ 0.05 was deemed as statistically significant.

6.3 Results

6.3.1 Baseline demographics

The number of UKRs recruited were 19, 23, and 21 for the 1900 machined, 1050 moulded, and 1050 machined bearings groups, respectively. The mean BMI at final follow-up was 28.2 kg/m² (SD 4.0) and the mean age at primary surgery was 62.6 years (SD 8.7). The mean OKS recorded at the time of RSA was 42.6 (SD 6.1), corresponding to excellent long-term functional outcomes¹⁸⁹.

There were no significant differences in the baseline demographics and most recent OKS of the three comparative groups (Table 6.1). However the mean age of the 1050 machined group was few years younger than the other two groups. As anticipated, given the different dates in which each bearing type were introduced there were significant differences in mean follow up ($p < 0.001$). Mean follow-up was 14.1 years (SD 0.4), 12.1 years (SD 1.1), and 10.0 years (SD 0.5) for the 1900 machined bearings, 1050 machined bearings, and 1050 moulded bearings, respectively. Long-term OKS (10 years or more) were 42.7 (SD 5) in 1900 machined, 42.6 (SD 6.4) in 1050 machined, and 42.4 (SD 6.7) in 1050 moulded groups with no significant differences between groups ($p = 0.98$).

Baseline parameter	1900 machined bearing (n = 19)	1050 machined bearing (n = 21)	1050 moulded bearing (n = 23)	p-value
Mean age (year)	65.2 (9.1 SD)	58.8 (8.6 SD)	63.9 (7.6 SD)	0.06*
Mean BMI (kg/m ²)	28.4 (3.8 SD)	28.3 (3.5 SD)	27.8 (4.5 SD)	0.88*
Sex (n)				0.54†
Male	9 (47%)	12 (57%)	15 (65%)	
Female	10 (53%)	9 (43%)	8 (35%)	
OKS at most recent follow up at RSA clinic	42.7 (SD 5.0)	42.6 (SD 6.4)	42.4 (SD 6.7)	0.98*
Femoral component sizes (n)				0.28†
Small	7 (37%)	7 (33%)	4 (17%)	
Medium	6 (32%)	4 (19%)	10 (43%)	
Large	5 (26%)	10 (48%)	9 (39%)	
Extra-large	1 (5%)	0 (0%)	0 (0%)	
Tibial component sizes (n)				0.52†
A	1 (5%)	0 (0%)	0 (0%)	
B	2 (11%)	2 (10%)	1 (4%)	
C	7 (37%)	6 (29%)	7 (30%)	
D	3 (16%)	4 (19%)	6 (26%)	
E	5 (26%)	2 (10%)	4 (17%)	
F	1 (5%)	7 (33%)	5 (22%)	
Bearing sizes (n)				0.91†
3	6 (32%)	6 (29%)	5 (22%)	
4	9 (47%)	9 (43%)	12 (52%)	
5	3 (16%)	5 (24%)	6 (26%)	
6	1 (5%)	1 (5%)	0 (0%)	

Table 6.1. The baseline characteristics in the three bearing types. No significant differences were detected between groups * anova †Fisher's exact test.

6.3.2 Comparison of wear between groups

The mean linear penetration rate was 60 $\mu\text{m}/\text{year}$ (SD 42) for the 1900 machined group, 76 $\mu\text{m}/\text{year}$ (SD 32) for the 1050 machined group and 57 $\mu\text{m}/\text{year}$ (SD 30) for the 1050 moulded group (Table 6.2). There was one outlier in the 1050 moulded group, which had an annual wear rate of 151 $\mu\text{m}/\text{year}$. On inspection of this UKRs' radiographs, there was a large posterior osteophyte that would have impinged on the bearing, perhaps explaining this wear rate elevation (Figure 6.4).

When analysing the effect of resin type by comparing the two machined bearings, there was no significant difference in the wear rate of the 1900 resin or the 1050 resin (60 $\mu\text{m}/\text{year}$ and 76 $\mu\text{m}/\text{year}$, respectively; $p = 0.20$). When analysing the effect of manufacturing process by comparing the two 1050 resins, the wear rate for the moulded bearings was significantly lower than for the machined bearings (57 $\mu\text{m}/\text{year}$ and 76 $\mu\text{m}/\text{year}$, respectively; $p = 0.05$).

When data from all bearings ($n = 63$) were combined, the mean wear rate was 64 $\mu\text{m}/\text{year}$ (SD 35) at a mean follow-up of 12 years (SD 1.9).

Group	Mean follow-up, years (SD)	Mean linear penetration, μm (SD)	Mean bearing wear rate, $\mu\text{m}/\text{year}$ (SD)
1900 machined (n = 19)	14.1 (SD 0.4)	847 (SD 589)	60 (SD 42)
1050 machined (n = 21)	12.1 (SD 1.1)	908 (SD 353)	76 (SD 32)
1050 moulded (n = 23)	10.0 (SD 0.5)	563 (SD 290)	57 (SD 30)

Table 6.2. The total wear and bearing wear rates for each bearing type.

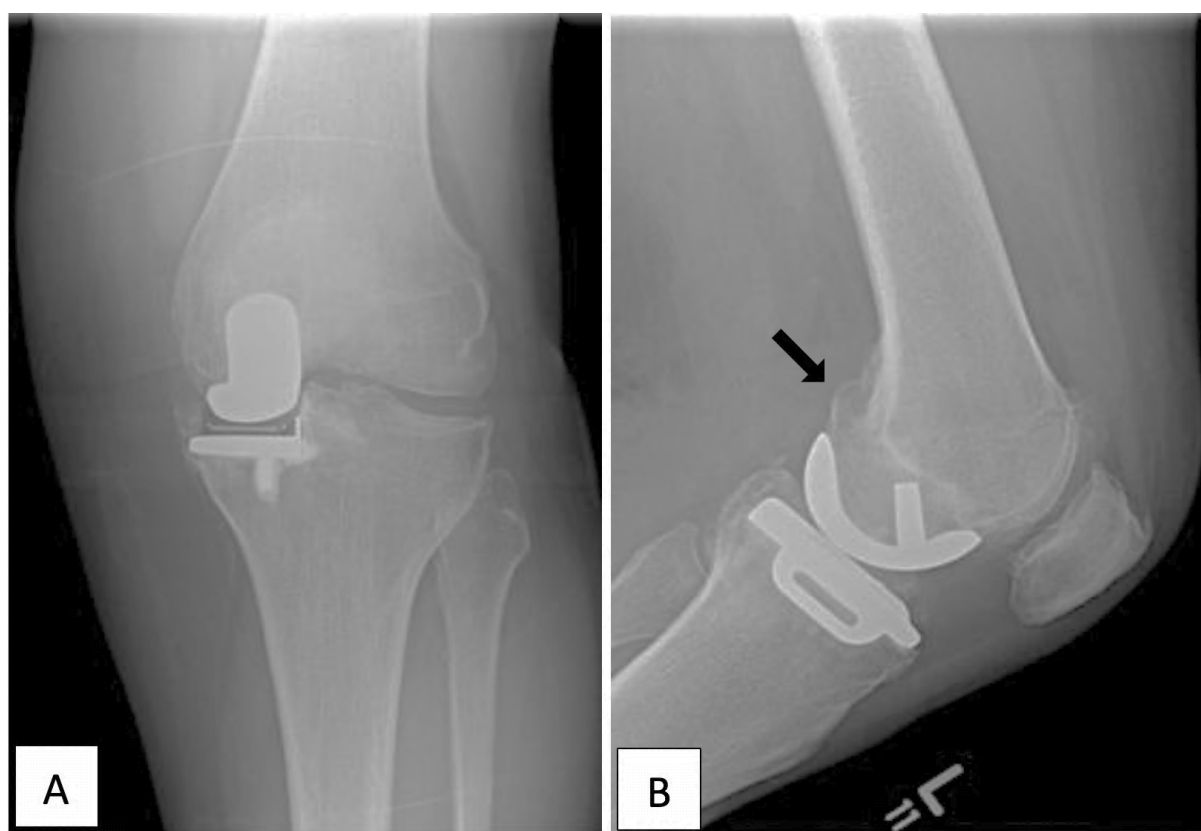


Figure 6.4. a) Anteroposterior and b) lateral radiographs of a wear outlier patient in the 1050 moulded group. Note that there is a posterior osteophyte, marked by an arrow, that would impinge on the bearing in flexion and cause increased wear.

6.3.3 The influence of femoral component size on wear

When all bearing types were combined, the wear rate was 44 $\mu\text{m}/\text{year}$ (SD 32) for small femoral components ($n = 18$), 59 $\mu\text{m}/\text{year}$ (SD 22) for medium femoral components ($n = 20$), 79 $\mu\text{m}/\text{year}$ (SD 32) for large femoral components ($n = 24$), and 178 $\mu\text{m}/\text{year}$ ($n = 1$) for extra-large femoral components. Spearman's coefficient of femoral component size and bearing wear rates was 0.53 ($p < 0.001$).

Using a linear regression model, there was a significant linear relationship between femoral component size and bearing wear; for each increase in femoral component size, the wear rate increased by 21 $\mu\text{m}/\text{year}$ (CI 12 to 30; $p < 0.001$). The strength of this relationship was influenced by bearing type ($p = 0.01$). For both machined bearings, there was increased wear with increased femoral component size; the wear increased by 35 $\mu\text{m}/\text{year}$ (CI 21 to 49) in the 1900 machined bearings ($p < 0.001$), and by 23 $\mu\text{m}/\text{year}$ (CI 10 to 35) in the 1050 machined bearings ($p = 0.001$). However, with the moulded bearings there was no significant increase in wear with increased size, at -0.5 $\mu\text{m}/\text{year}$ (CI -19 to 18; $p = 0.96$) (Figure 6.5).

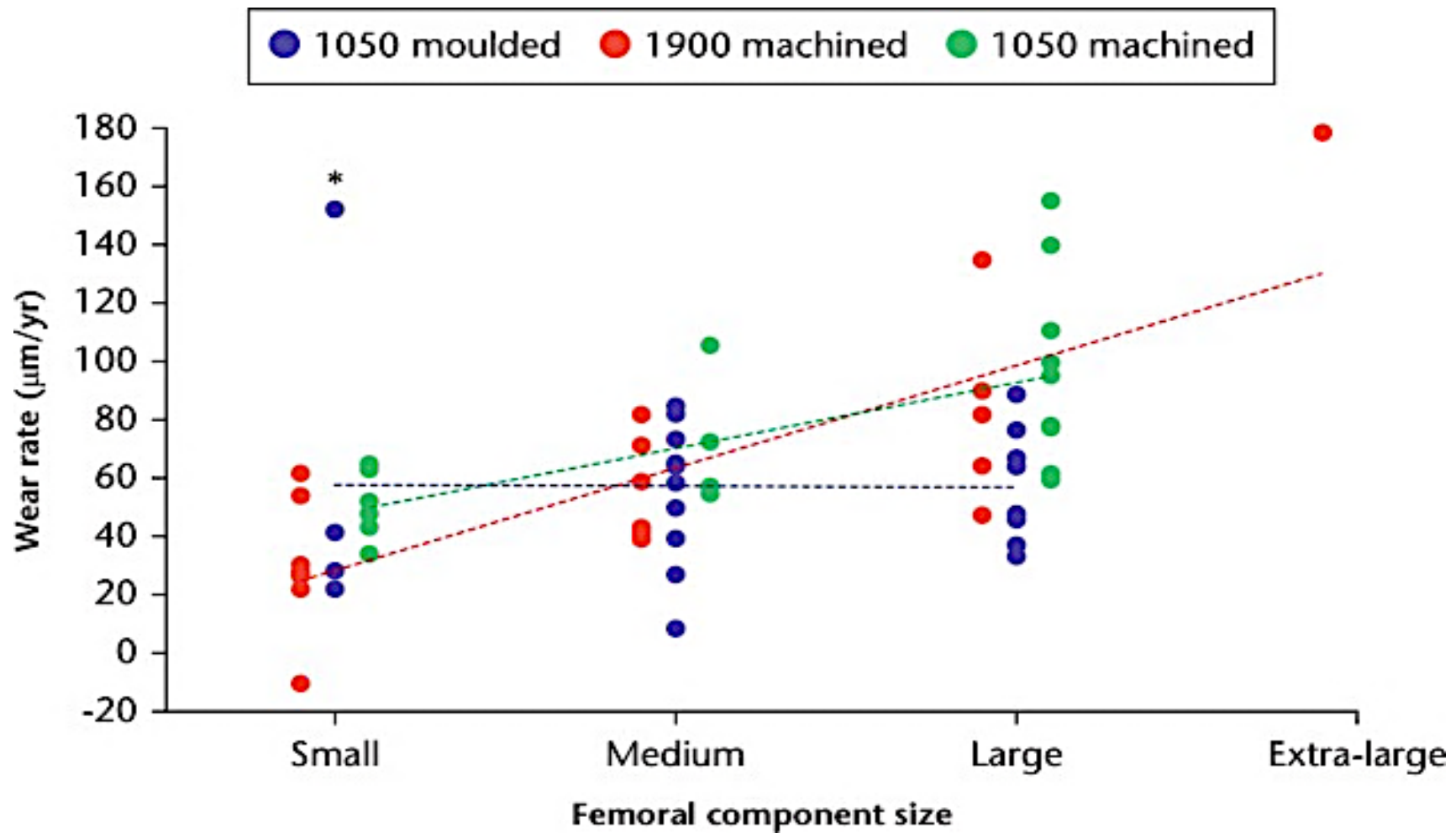


Figure 6.5. The relationship between femoral component size and polyethylene wear rate.

6.3.4 The influence of tibial component size on wear

When all bearing types were combined, the mean wear rate was 22 $\mu\text{m}/\text{year}$ for tibia A size components ($n = 1$), 46 $\mu\text{m}/\text{year}$ (SD 5) for tibia size B components ($n = 5$), 52 $\mu\text{m}/\text{year}$ (SD 32) for tibia size C components ($n = 20$), 57 $\mu\text{m}/\text{year}$ (SD 25) for tibia size D components ($n = 13$), 83 $\mu\text{m}/\text{year}$ (SD 32) for tibia size E components ($n = 11$), and 84 $\mu\text{m}/\text{year}$ (SD 43) for tibia size F components ($n = 13$). Spearman's coefficient of tibial component size and bearing wear rates was 0.46 ($p < 0.001$).

Using a linear regression model, there was found to be a significant linear relationship between tibial component size and bearing wear; for each increase in tibial component size, the wear rate increased by 12 $\mu\text{m}/\text{year}$ (CI 6 to 18; $p < 0.001$). The strength of this relationship was influenced by bearing type ($p = 0.003$). For both machined bearings, there was increased wear with increased tibial component size; the wear increased by 23 $\mu\text{m}/\text{year}$ (CI 12 to 35) in the 1900 machined bearings ($p = 0.001$) and increased by 14 $\mu\text{m}/\text{year}$ (CI 6 to 22) in the 1050 machined bearings ($p = 0.002$). However, with the moulded bearings, there was no significant increase in wear with increased size, at -2 $\mu\text{m}/\text{year}$ (CI -13 to 9; $p = 0.72$) (Figure 6.6).

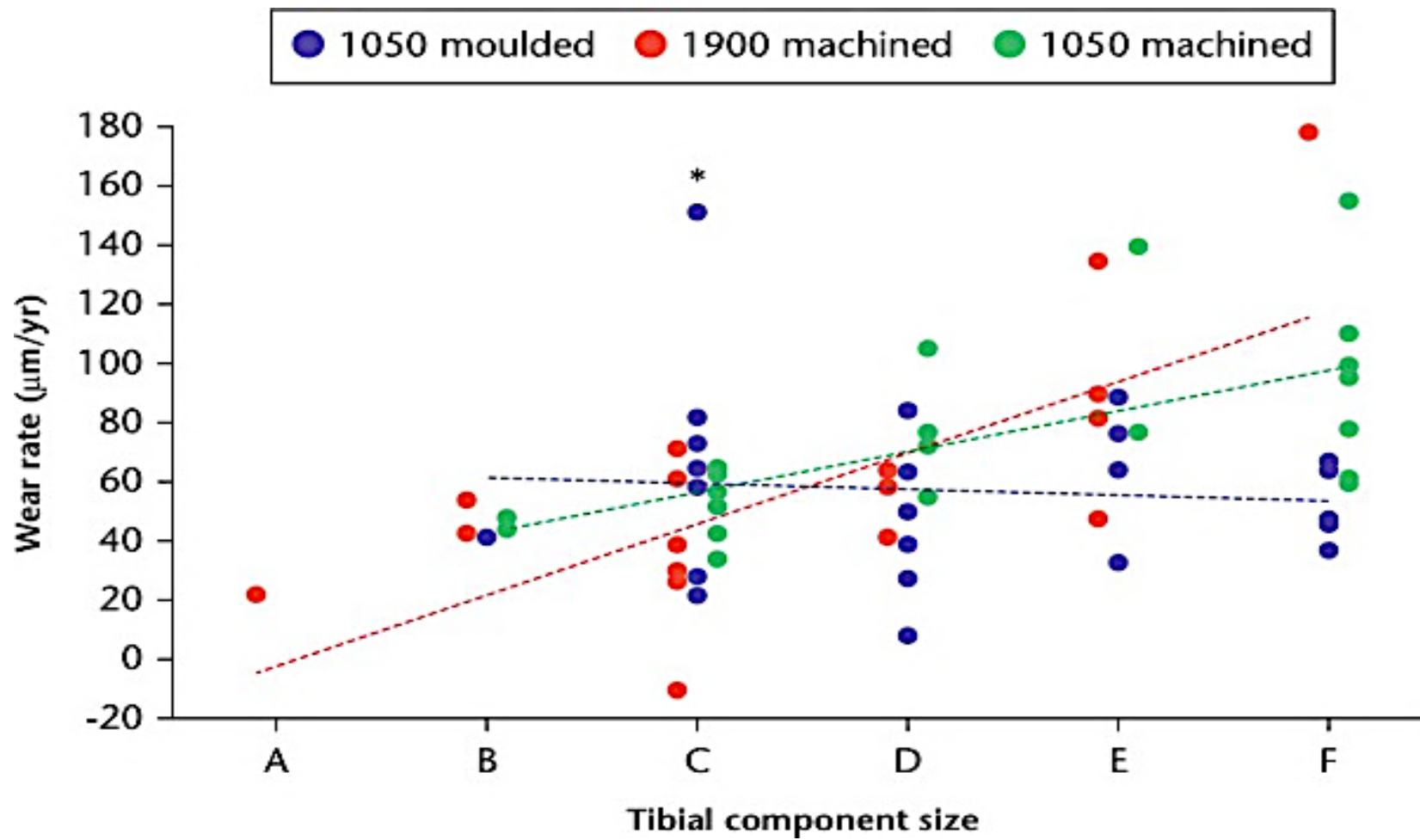


Figure 6.6. The relationship between tibial component size and polyethylene wear rate.

6.3.5 Other factors related to polyethylene wear

6.3.5.1 Sex and polyethylene wear

The mean age of males and females was 63.0 (SD 8.2) and 62.1 years (SD 9.4), respectively, with no significant differences ($p = 0.69$). The mean BMIs of males and females were 28.4 kg/m² (SD 3.5) and 27.9 kg/m² (SD 4.6), respectively, with no significant differences ($p = 0.69$).

The annual wear rate for males ($n=36$) was 75 $\mu\text{m}/\text{year}$ (SD 36) and was significantly higher ($p=0.004$) than the wear rate for females ($n=27$) which was 50 $\mu\text{m}/\text{year}$ (SD 29). Male sex was associated with significantly higher wear rates in the 1900 and 1050 machined groups, but not in the 1050 moulded groups (Table 6.3). These findings are likely explained by the observation that males had larger component sizes (Table 6.4) and that the wear rate increases with increased size with machined bearings but does not with moulded bearings.

Bearing type	Bearing wear rate $\mu\text{m}/\text{year}$		
	Males	Females	p-value
1900 machined	84 (SD 46); n=9	38 (SD 24); n=10	0.01
1050 machined	93 (SD 31); n=12	53 (SD 12); n=9	0.002
1050 moulded	55 (SD 21); n=15	60 (SD 43); n=8	0.72

Table 6.3. A comparison of wear rates between sex within each bearing group. Groups were compared using the unpaired t test.

Component size	Males (n = 36)	Females (n = 27)
Femoral		
Small	0 (0%)	18 (67%)
Medium	11 (31%)	9 (33%)
Large	24 (67%)	0 (0%)
Extra-large	1 (3%)	0 (0%)
Tibial		
A	0 (0%)	1 (4%)
B	0 (0%)	5 (19%)
C	4 (11%)	16 (59%)
D	8 (22%)	5 (19%)
E	11 (31%)	0 (0%)
F	13 (36%)	0 (0%)

Table 6.4. The sizes of UKR components stratified by sex.

6.3.5.2 Oxford knee score and polyethylene wear

There was no significant correlation between OKS and annual wear rate. Spearman's coefficient was 0.15 ($p = 0.23$). This is illustrated graphically in Figure 6.7.

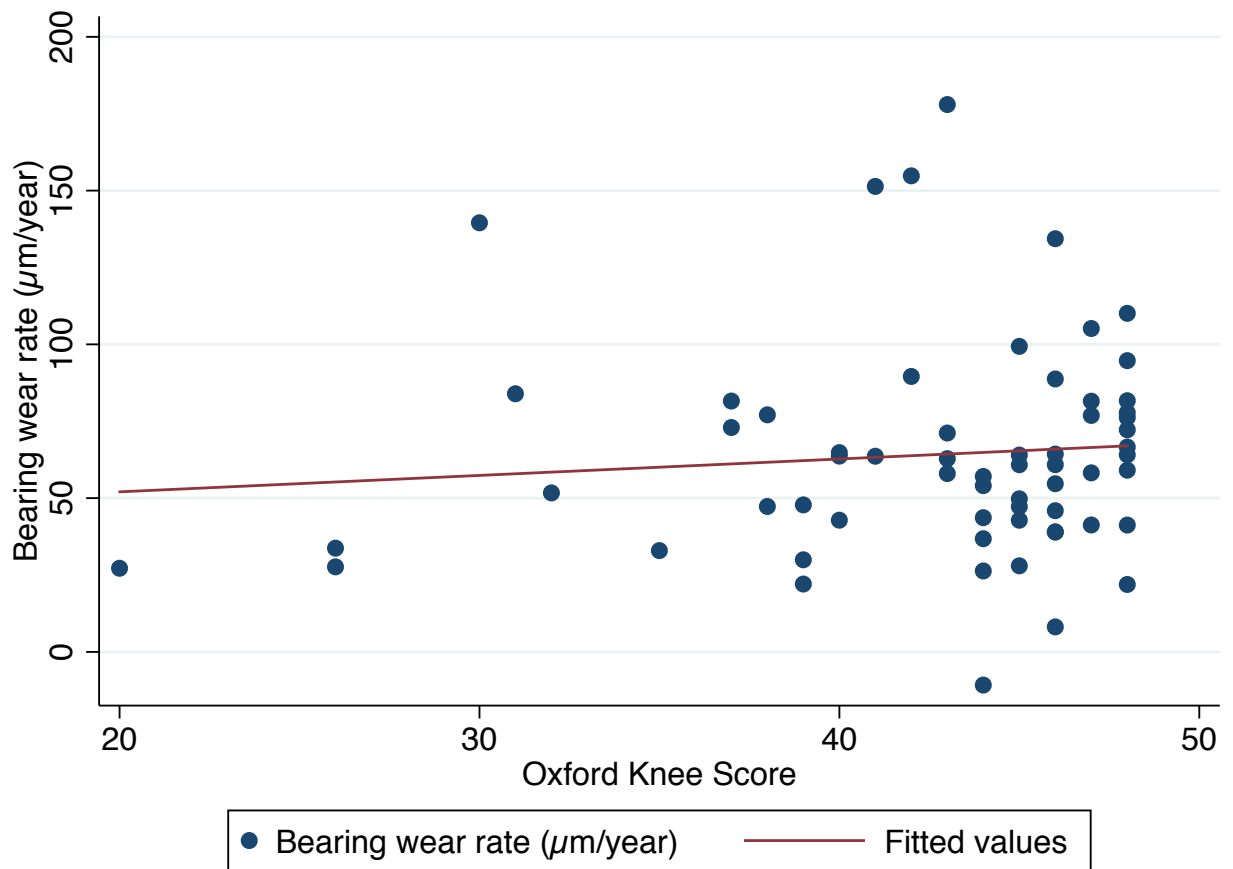


Figure 6.7. Scatterplot of bearing wear rate against OKS.

6.3.5.3 Age and polyethylene wear

No significant relationship existed between wear rate and age, although there was a trend towards increased wear in younger patients (Figure 6.8). At the time the RSA radiographs were taken, patients under 70 years of age ($n = 53$) had a wear rate of $68 \mu\text{m}/\text{year}$ (SD 34), while those over 70 years of age ($n = 10$) had a wear rate of $46 \mu\text{m}/\text{year}$ (SD 35). Spearman's correlation coefficient was -0.22 ($p = 0.08$).

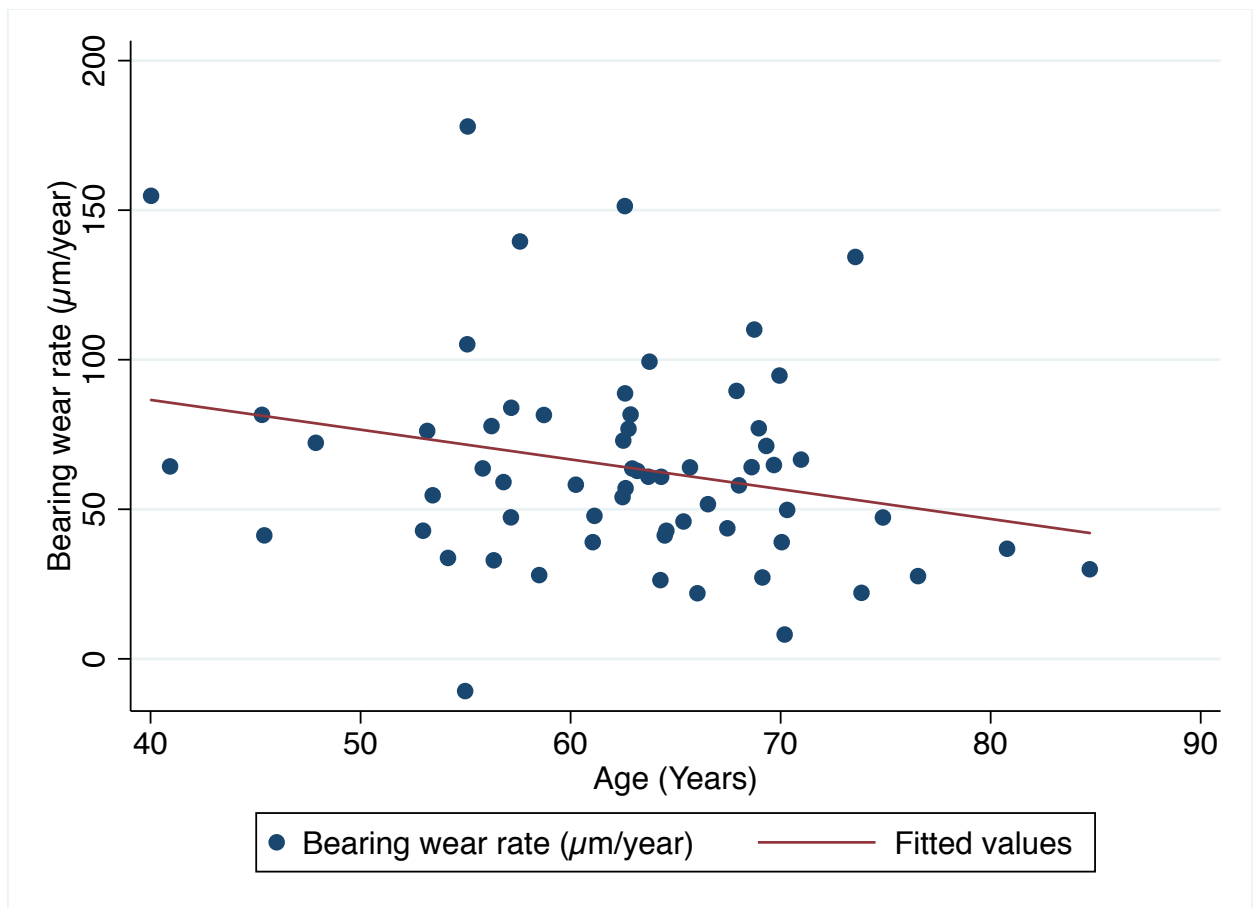


Figure 6.8. Scatter plot of bearing wear rate against age

6.3.5.4 Body mass index and polyethylene wear

Furthermore, no significant relationship between wear rate and BMI was observed (Figure 6.9). Patients with BMIs under 25 kg/m² (mean 23.3 kg/m²) had wear rates of 71 µm/year (SD 33, n = 11) and those with BMIs of 30 kg/m² or greater (mean 33.8 kg/m²) had wear rates of 72 µm/year (SD 40, n = 16). Spearman's coefficient was 0.05 (p = 0.69).

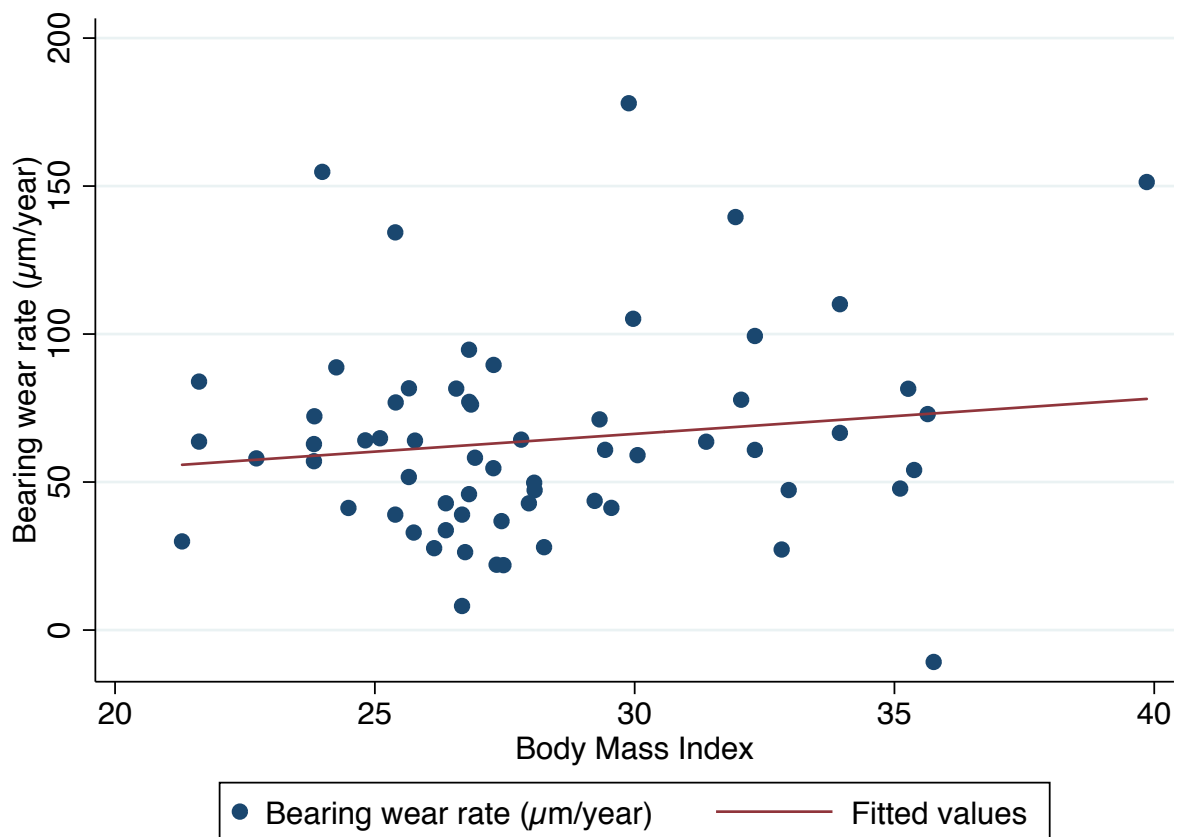


Figure 6.9. Scatterplot of bearing wear rate against BMI

6.3.5.5 Bearing thickness and polyethylene wear

The nominal bearing thickness varied from 3 mm to 6 mm. The mean linear wear rates of the thin (3 mm; $n = 17$) and thick (5 mm to 6 mm; $n = 16$) bearings were $59 \mu\text{m}/\text{year}$ (SD 28) and $56 \mu\text{m}/\text{year}$ (SD 27), respectively, with no significant difference between them ($p = 0.76$).

Direct correlation analyses between thickness and wear rate showed a Spearman's correlation coefficient of 0.02 ($p = 0.87$), showing no correlation (Figure 6.10).

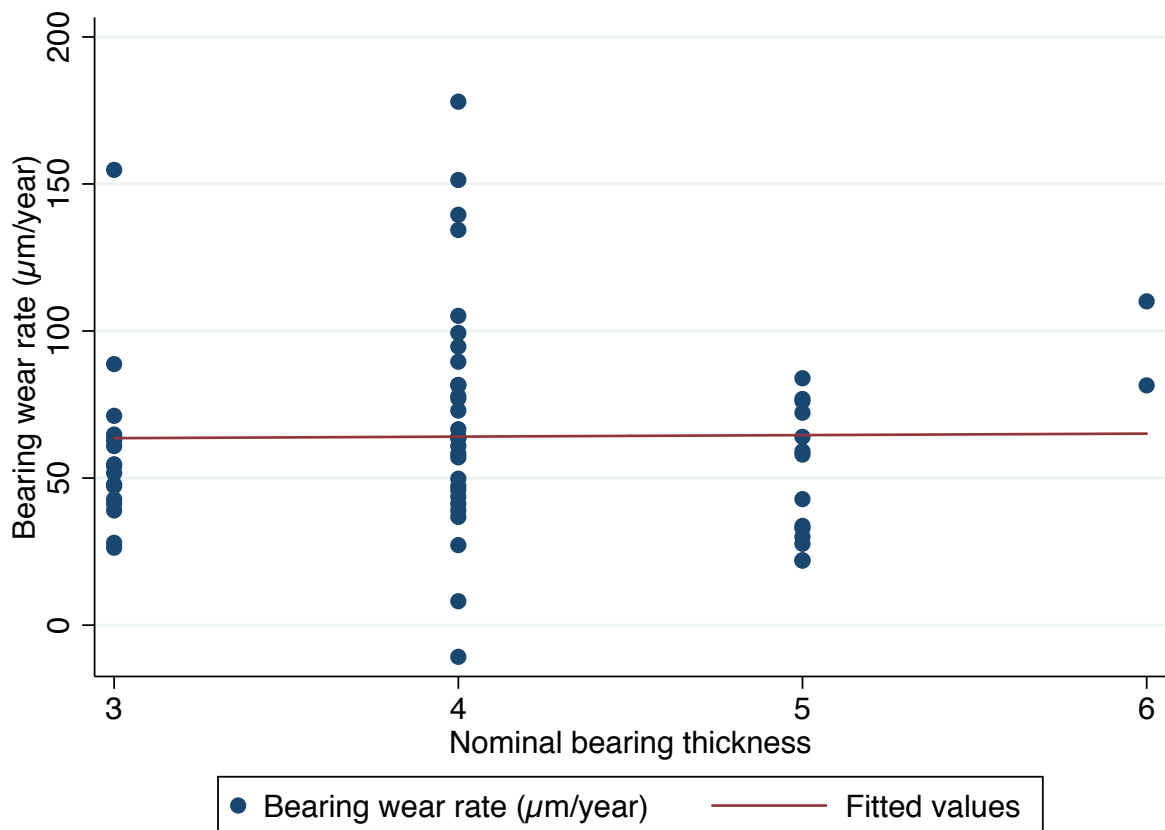


Figure 6.10. Scatterplot of bearing wear rate against nominal bearing thickness

6.4 Discussion

This chapter presents the first RSA wear study of the Phase 3 Oxford UKR and is the first to compare different polyethylene resin materials and manufacturing processes. The current wear rates in the Phase 3 Oxford UKR (1050 moulded resin) is 57 $\mu\text{m}/\text{year}$ and is much higher than the 20 $\mu\text{m}/\text{year}$ reported for the previous Phase 2 Oxford⁷⁷. No significant differences in wear rate of the 1900 and 1050 resins made with the same manufacturing process were observed. However the manufacturing processes did influence wear rates, with the moulded bearings having significantly lower wear rates than the machined. Wear rate increased with component size for machined but not moulded bearings.

The polyethylene resin used for the Phase 3 bearings changed from the 1900 to 1050 resin about 10 years ago²⁸⁸. Both 1900 and 1050 resin bearings have been manufactured using direct compression moulding but during the transition phase some were produced from machining bar stock²⁸⁸. With the same resin, the wear rate of the machined bearings were significantly higher than that of the moulded bearings and this is also suggested from studies of polyethylene wear in hip replacements²⁹⁴. There was no significant difference between the wear rates of the 1900 and 1050 machined resins and is the first time this has been shown in vivo. This is important, given all the current bearings are now made of 1050 resin, whereas the Phase 2 Oxford UKR used the 1900 resin.

Overall the wear rate increased with increasing component size, with the largest sizes having over twice the wear rate of the smallest. Larger patients tend to be heavier so apply larger loads, have larger components with larger surface areas and sliding distances for the same

amount of knee flexion. These factors are known to increase wear^{295, 296}. Subgroup analysis of bearing types yielded interesting results. For both machined bearings the wear rate increased with both tibial and femoral component size, but this was not observed for the moulded bearing. This explains why males who tend to be larger than females, have greater wear with machined bearings than females, whereas with moulded bearings there were no differences. Therefore the moulding process produces a material with different tribological properties to the machined process, perhaps because a surface skin is produced that reduces wear and oxidation. This requires further investigation.

The study found no significant relationship between wear rate and age, similar to the findings of Kendrick et al.⁷⁷. There was no relationship between wear rate and OKS or BMI. The findings relating to age and OKS are difficult to explain. Wear is related to the number of cycles and load with young and active patients expected to use their knees more often with greater loads. On the other hand, although obese patients apply greater loads, they are generally less active. It is likely that age and activity do in fact influence wear rates, but their effect is masked by other variables. Indeed, there was a trend towards increasing wear in younger patients and those with a higher OKS.

This RSA study has shown that the mean linear wear rate of the currently used 1050 resin-moulded bearings is 57 $\mu\text{m}/\text{year}$ and is independent of bearing thickness. This is lower than other knee replacements, whether partial or total²⁹⁷⁻²⁹⁹. Therefore the Oxford UKR can safely use thinner bearings, which helps to preserve bone stock.

The mean linear wear rate of the current Phase 3 bearings ($57 \mu\text{m}/\text{year}$) is higher than that reported for Phase 2 bearings ($20 \mu\text{m}/\text{year}$) but lower than the Phase 1 bearings ($70 \mu\text{m}/\text{year}$)⁷⁷. Bearing impingement on bone anterior to the femoral component was common in Phase 1 but less common in Phase 2, given surgeons were aware of the issue⁶⁷. Impingement is known to increase wear. Given the introduction of the minimally invasive approach with the Phase 3 Oxford, surgical errors that could contribute to wear, such as impingement may be more likely given the more difficult intraoperative visualisation. This could possibly contribute to the higher wear of Phase 3 than Phase 2. Although the Phase 2 used 1900 moulded bearings this study has shown that polyethylene resin type used has no effect on wear rates.

Although the Phase 3 bearing and tibial plateau shape are more anatomically shaped than the Phase 2, the difference is small, and unlikely to be the explanation. Given the minimally invasive approach with the Phase 3, patients tend to have higher levels of function and a better range of movement than those with Phase 2. The higher function (mean OKS in this study 42.6 (SD 6.1)) is likely to increase activity levels and therefore wear. Further study is needed to understand why the wear rates are higher with Phase 3.

Bearing fractures rarely occur with the Oxford UKR. Studies of the Phase 1 Oxford²⁸¹ found they most commonly occur in the third decade postoperatively. They can be easily revised by inserting a new bearing. A detailed study of ten fractured bearings found that fracture aetiology was multifactorial²⁸¹, but evidence of impingement with abnormally high wear and oxidation were observed in all cases²⁸¹. The 1050 moulded outlier presented in this chapter is a good example of how impingement from an osteophyte caused accelerated polyethylene

wear (Figure 6.4). New Microplasty instrumentation, introduced in Chapter 5, is now routinely used and is designed to prevent impingement⁶⁷. A finite element study³⁰⁰ demonstrated that thinner bearings were more likely to fracture, and approximately half of the retrieved fractured bearings in a study by Pegg et al.²⁸¹ were less than 2 mm thick. For the current Phase 3 bearings with a mean wear rate of 57 $\mu\text{m}/\text{year}$, this equates to 1.1 mm wear at 20 years. Therefore, the thinnest bearings available, which are size 3 with a minimum thickness of 3.5 mm, should be on average 2.4 mm thick at 20 years. Some of these will be substantially thinner than 2 mm and with marked oxidation and would be at risk of fracture. In contrast, if the bearing was initially 4.5 mm thick (size 4), it would be very unlikely to be worn thinner than 2 mm. Therefore, surgeons should aim to implant a size 4 bearing rather than a size 3 bearing in young active patients, unless they are small and require conservative resections. This can easily be guided with Microplasty instrumentation. Additionally it would also be sensible to consider having bearings made with highly crosslinked polyethylene to further reduce wear^{301, 302} and vitamin E to decrease oxidation^{303, 304}.

An important limitation of this chapter's work is that the change in bearing thickness between implantation and RSA is assumed to only be from bearing wear, whereas in reality it is due to both wear and creep. A single RSA measurement does not allow the contributions of creep and wear to be calculated. However creep mainly occurs in the first three months and therefore has minimal effect in long term wear studies³⁰⁵⁻³⁰⁷. Furthermore, had there been considerable creep, this would have resulted in overestimating, rather than underestimating wear. The precise bearing thickness at implantation was not known but previous work has found that measured bearing thickness with RSA postoperatively is virtually the same as that estimated from the bearing size using the methodology used in this study for both 1900 and 1050 bearings^{182, 283, 285}. Given the accuracy of the RSA system is 100 μm , at ten years, the

accuracy for measuring the wear rate would be about 10 $\mu\text{m}/\text{year}$ ⁷⁶. This is substantially less than the SD of the wear rate measurements, suggesting most of the variability in measurements was due to differences between the patients rather than the measurement accuracy. Another limit is that because there was difficulty identifying patients with bearing codes to allow the bearing type to be categorised, it was not possible to match patients in the three groups. As a result there were slight differences in age and gender across groups. However, there were no significant differences between the three groups in baseline characteristics. Additionally, given the three bearing types were used at slightly different time periods, this resulted in an inevitable difference of mean follow-up. However, given that all exceeded ten years and the annual wear rate was analysed, this should not have influenced the results. There was one outlier with high wear from the 1050 moulded group and the data from this may have influenced results. Therefore a sensitivity analysis was performed in which this case was excluded but the results and conclusions remained the same.

Therefore in conclusion, the Oxford UKR polyethylene bearing linear wear rate is similar with 1050 and 1900 resin but lower with direct compression-moulded rather than machined manufacturing processes. The wear rate of the Phase 3 bearings in current use is low (1050 resin moulded) but higher than those reported for the Phase 2 bearings (1900 resin moulded). Therefore, the fracture rate of Phase 3 bearings may be higher than that of Phase 2 bearings. It is not clear why the wear rate of Phase 3 is higher than Phase 2, but this may relate to the minimally invasive approach, which improves function and increases activity levels, but may also increase the risk of surgical errors, such as impingement, which can increase wear.

However, with the new Microplasty instrumentation introduced in Chapter 5, these errors should be avoided. In addition, it is simpler to select an appropriate bearing thickness and would be sensible to aim for 4 mm bearings rather than 3 mm bearings in young active patients, in all but small patients who need conservative bone cuts.

7. EXPERIMENTAL ASSESSMENT OF NEW SURGICAL INSTRUMENTATION ON RISK OF TIBIAL FRACTURES

7.1 Introduction

The cemented and cementless Oxford UKR components are similar except that the surfaces of cementless components in contact with bone are coated with porous titanium and hydroxyapatite to encourage bone ingrowth. Although clear advantages of cementless fixation have been highlighted in Chapters 3 and 4, they are reported to have more than twice the rate of tibial plateau fractures which are devastating complications often requiring complex revision surgery.

Primary fixation of the cementless UKR is dependent upon an interference fit between the prosthetic components and bony surfaces given there is no cement to support fixation. A keel slot is produced in the proximal tibia during surgery (Figure 7.1A) using a specially designed keel cut saw blade (Figure 7.1B). The cementless tibial component achieves its primary stability from the interference fit which is defined as the difference in thickness between the keel and keel slot it inserts into (Figure 7.2).

* This chapter has been published³⁰⁸. Mohammad HR, Campi S, Murray D, Mellon S. Instruments to reduce the risk of tibial fracture following cementless unicompartmental knee replacement. *Knee* 2018; 25(6): 988. (Appendix 1).

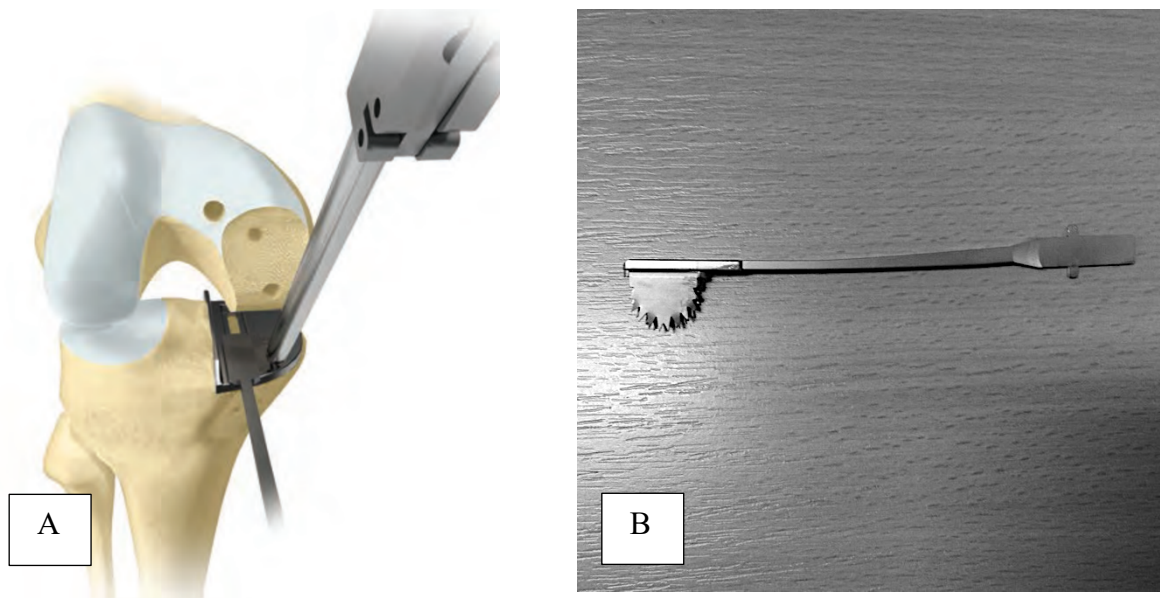


Figure 7.1. A) Tibial preparation during UKR surgery. Adapted from³⁰⁹ B) Keel saw blade.

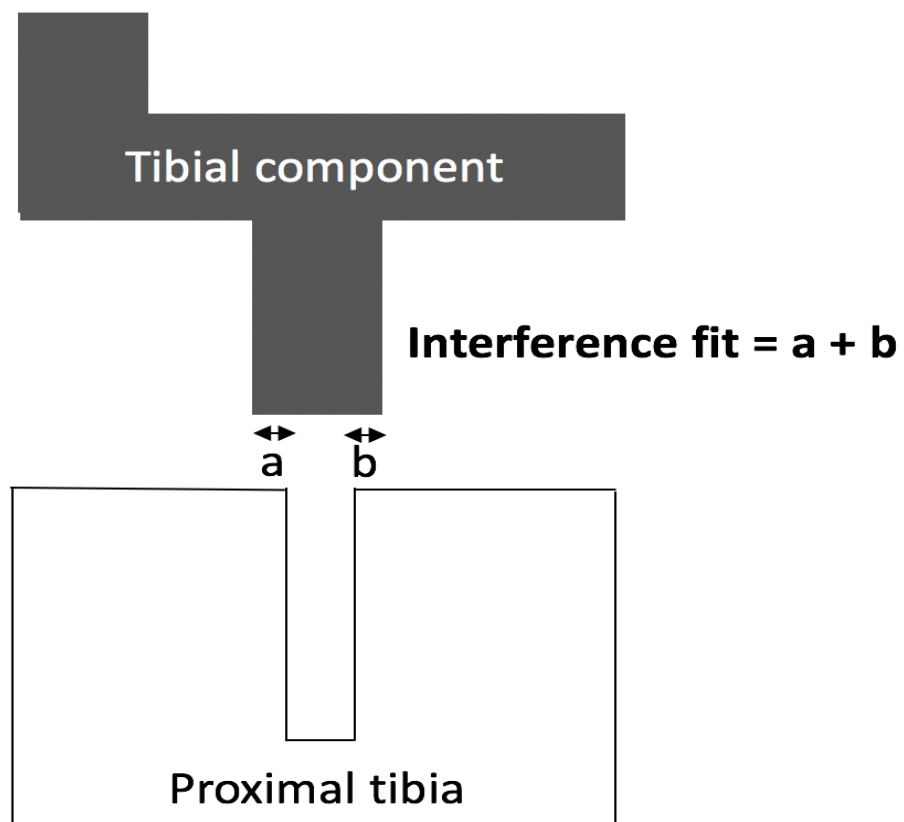


Figure 7.2. Interference fit of tibial component into proximal tibial bone.

Fractures of the tibial plateau usually present in the early postoperative period (Figure 7.3). Although the published incidence of tibial plateau fractures after the cementless Oxford UKR is low²⁰⁰ (<1%), it is believed to be underreported given that they are often treated by internal fixation and hence not recorded as a revision in the joint registries^{67, 310}. Additionally there are a number of anecdotal reports from surgeons having a higher incidence³¹¹⁻³¹⁵, particularly in patients with cementless implants^{190, 196, 310}, inexperienced hands³¹⁶ or in the Asian population⁶⁷. The incidence with cementless fixation appears higher than cemented with a cadaveric study¹⁹⁹ showing that reduced loads are required to fracture the tibial plateau with cementless compared to cemented UKRs. Given the tibial preparation is similar for both cemented and cementless fixation, it is likely that the higher rates of fracture with the cementless are due, at least in part, to the interference fit between the keel and the keel slot²⁶⁴.

The interference fit is established by pressing the tibial component into the tibia until it seats. The difference in width between the slot and the keel has consequences for the amount of force required to ‘seat’ the component i.e. the narrower the slot, the greater the amount of force required to seat the component. The amount of force used to seat the component is proportional to the normal forces on the walls of the slot³¹⁷. During surgery the keel impaction within the walls of the slot probably creates a normal force in the proximal tibia which can initiate a crack which later in the early post-operative period when the patient weight bears (Figure 7.4). This subsequently propagates resulting in a fracture.



Figure 7.3. Anteroposterior and lateral radiographs showing a tibial plateau fracture.

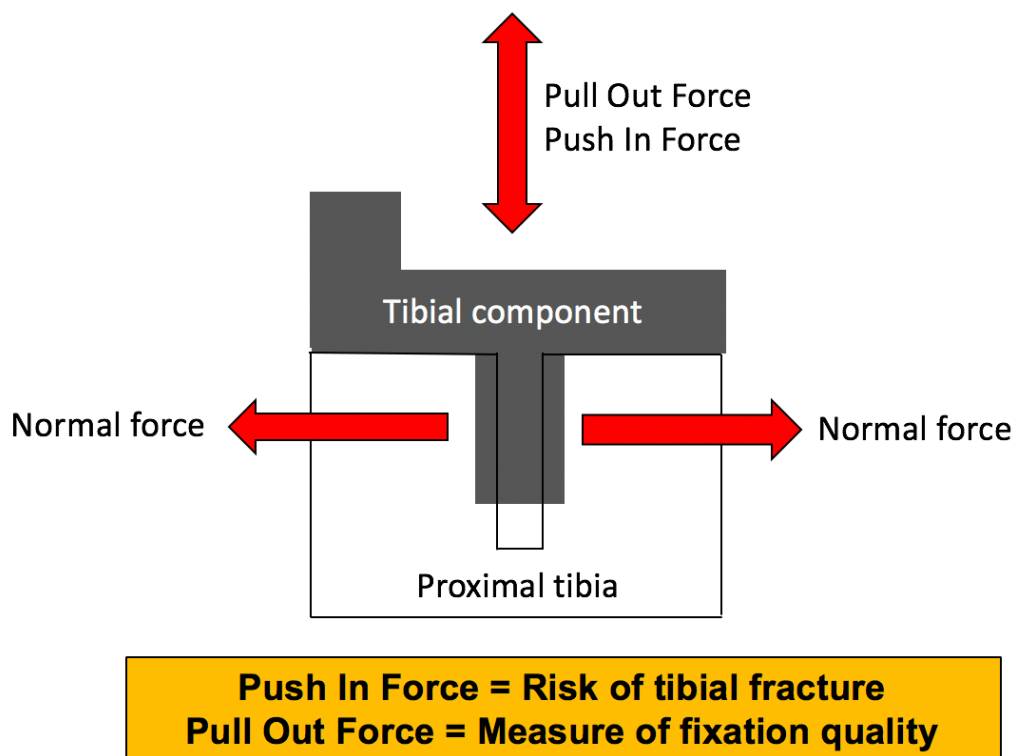


Figure 7.4. Schematic showing how push in forces are related to a splitting perpendicular normal force in the slot.

Campi et al.²⁶⁴ studied the relationship between interference, and the forces required to push-in and pull-out the tibial component into sawbones. Their assumption was that the maximum push-in force, which causes the splitting force in the tibia, was related to the risk of fracture and the maximum pull-out force was a surrogate of primary fixation and stability. Although overall both push-in and pull-out force increased with increasing interference, the relationships were non-linear with an optimal window with relatively low push-in force and high pull-out force (Figure 7.5). This optimal interference (between 0.5 to 0.7 mm) was less than that currently achieved using conventional Oxford UKR instrumentation (0.9 to 1.3 mm). Therefore the results of this study suggest that if the slot was further widened to reduce the interference, this may reduce the fracture risk without compromising the quality of fixation achieved.

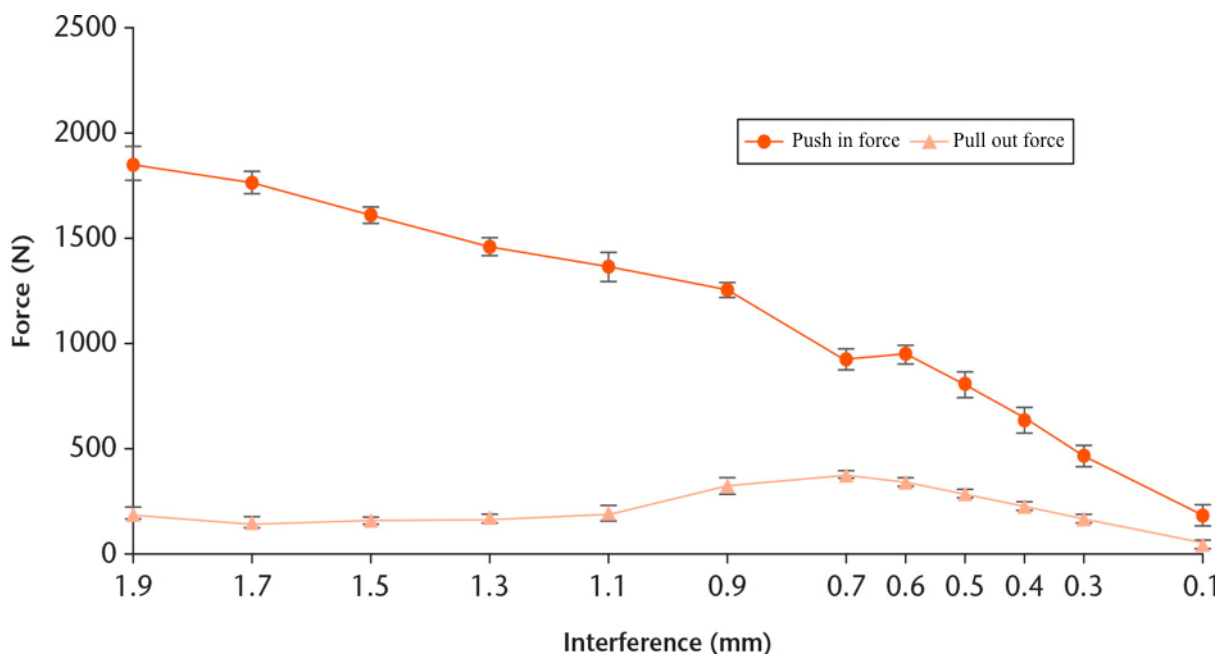


Figure 7.5. Mean push in and pull out forces across different interference fits using solid polyurethane foam observed by Campi et al. Taken from²⁶⁴.

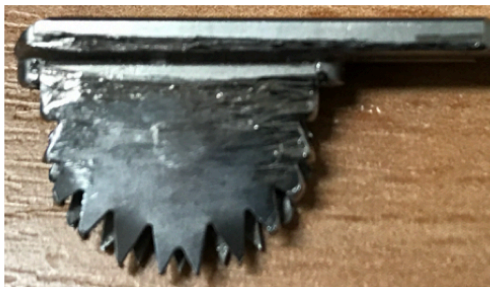
Options to slightly widen the slot, which have been used by different surgeons, include the use of a pick, which was originally designed for cemented fixation, a rasp, or a new saw blade³⁰⁹. The advantages and disadvantages of these options on the risk of fracture and quality of fixation achieved have not previously been studied.

The aim of this sawbone study was to determine which of the various instrumentation options for preparing the keel slot for the cementless Oxford UKR tibial component was most effective in reducing the risk of fracture without compromising primary fixation. To do this the push in and pull out forces would be measured, which in turn would inform of the risk of fracture and primary fixation quality respectively as per the work of Campi et al.²⁶⁴.

7.2 Methods

7.2.1 Surgical instruments used in the study

The keel slot in the proximal tibia is prepared with a keel cut saw blade, which has two parallel blades (Standard blade, Zimmer Biomet, Swindon, UK, Figure 7.6). The slot can be widened by using a pick (Zimmer Biomet, Swindon, UK, Figure 7.6), which was originally designed for use with the cemented Oxford UKR. This pick has smooth sides and a sharp end. A prototype rasp (Figure 7.6) has also been developed which has teeth on its side and bottom designed to widen the slot and smooth its bottom. Alternatively, a new wider and deeper saw blade (New Blade, Zimmer Biomet, Swindon, UK, Figure 7.6) is available.



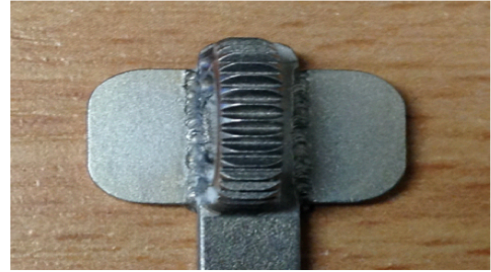
Standard blade



New blade



Pick



Rasp

Figure 7.6. Surgical instrumentation for creating and widening the tibial slot

The dimensions of the tibial component implanted and each instrument type were measured using a digital calliper (Mitutoyo, UK) using a previously established method described by Campi et al.³¹⁸. All surgical instrumentation was measured by two independent observers (Hasan Raza Mohammad and Stefano Campi) with reproducibility assessed (section 7.2.5 for additional details).

The tibial keel width of five size C components were all measured in 10 different positions on the keel with the use of a digital calliper and averaged to take into consideration the irregularity and non-homogeneity of the hydroxyapatite coating. Additionally the depth was measured in two places for each component to ensure that all the surgical instrumentation depths used in the study exceeded this depth to prevent impingement from influencing the implantation forces.

Five standard and new saw blades had their width measured at the proximal, middle and distal aspects of the blade and the maximum depth measured. The averages of these measurements were used to determine the instruments dimensions at each point. The most important width was the distal segment given this section of the blade is narrowest and comes into contact with all the bone cut. Therefore the mean of the distal blade width is the one reported for both the standard and new sawblades in the results. Additionally the maximum width and depth of the pick and rasp were measured.

7.2.2 Slot preparation for mechanical testing

Slots were cut into solid polyurethane foam (20 PCF, Sawbones, Malmö, Sweden), which are widely used as the analogue for trabecular bone, using the operating technique for the Oxford UKR³⁰⁹. Solid polyurethane foam 20 PCF has similar material properties (density 0.32 g/cm³, compressive modulus 210 MPa) to tibial bone (0.3 g/cm³, range 14–345 MPa)³¹⁹⁻³²¹.

Slots were prepared using standard and new blades and with the adjunctive use of either the cemented pick or the prototype rasp. Therefore there were six comparative groups in this study; (1) Standard Sawblade, (2) Standard Sawblade plus Pick, (3) Standard Sawblade plus Rasp, (4) New Sawblade, (5) New Sawblade plus Pick and (6) New Sawblade plus Rasp. Ten slots were cut for each comparative group given a power calculation revealed nine slots were required in each group (section 7.2.5 for additional details). Therefore in total there were 60 slots cut for mechanical testing.

A size C tibial template was clamped to the underlying sawbone blocks and the sawblades were used to cut a slot through the template using the same technique as is used clinically. Afterwards the template was removed and for the groups involving the pick or the rasp these instruments were subsequently used in the slot. A new blade was used for each study group to prevent wear of the blades having an effect on the results. However, one pick and rasp were used for all their respective groups given both instruments are designed for reuse³⁰⁹ and did not expect wear to change their dimensions for the number of slots on which they were used. Additionally this minimised any confounding factors from using different instruments unnecessarily.

7.2.3 Measuring push in and pull out forces

A custom-made boss was welded to the upper surface of standard cementless size C Oxford UKR components (Figure 7.7) by Zimmer Biomet (Swindon, UK), which allowed them to securely fasten to the materials testing machine. A Dartec materials testing machine (HC10) was used to implant and extract one component, at 0.01 mm/s, while measuring the push-in and pull-out forces at 250 Hz (Figure 7.8). Prior to push-in the starting position was determined by measuring the position of the tibial component when the bottom of the tibial keel was touching the upper surface of the sawbone block when offset so the keel was not above the slot. The height at which implantation was halted before the component was withdrawn was determined by bringing the under surface of the tibial tray into contact with the upper surface of the sawbone block. The vertical difference in position was calculated and used to calculate implantation distance.

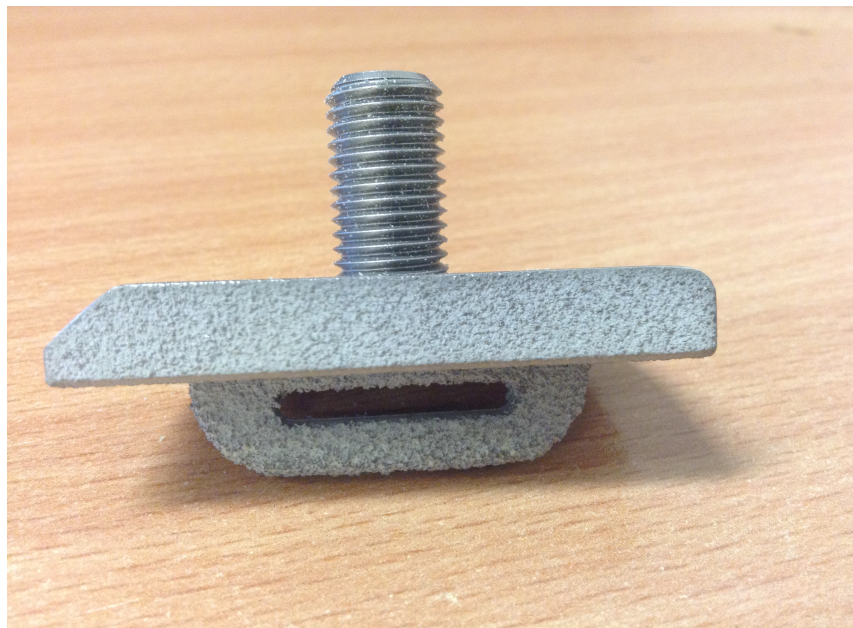


Figure 7.7. Custom made boss welded onto superior surface of the tibial component.

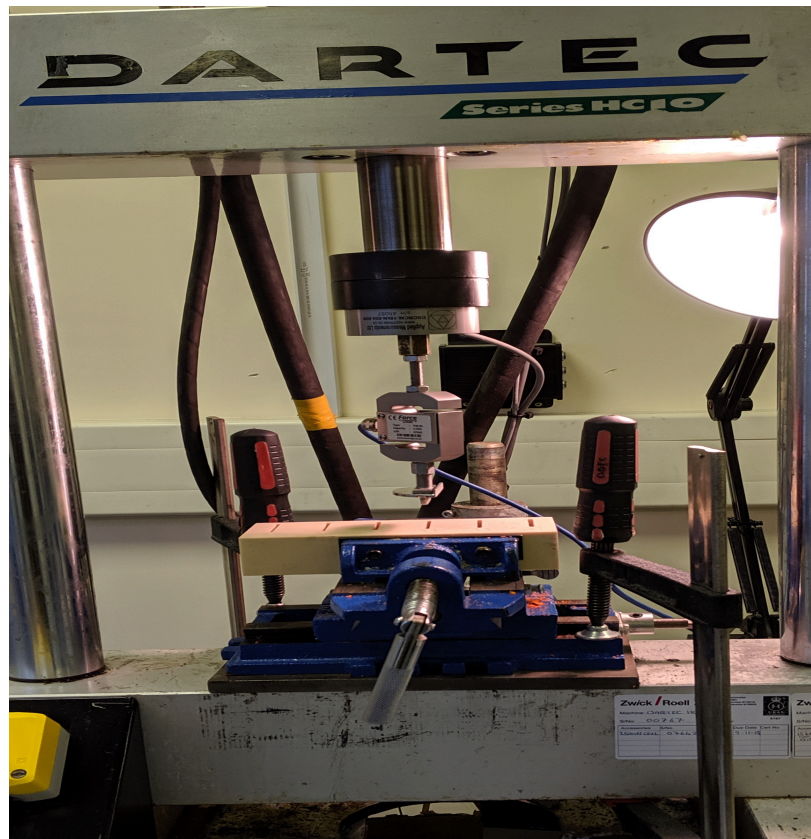


Figure 7.8. Dartec machine testing tibial components into cut slots.

An increase in the push-in load was noted in all experiments just before implantation was halted. The push-in value used as the maximum was obtained by determining the displacement at which zero load was registered during the pull-out phase of the experiment and finding the push-in load that was recorded at this level of displacement height. Maximum pull-out forces were also recorded. This can be illustrated using force displacement graphs of the average results of the standard (n=10) and new blade slots (n=10) in Figure 7.9. Although it is important to note that we this was performed for each individual slot tested rather than using average plots illustrated.

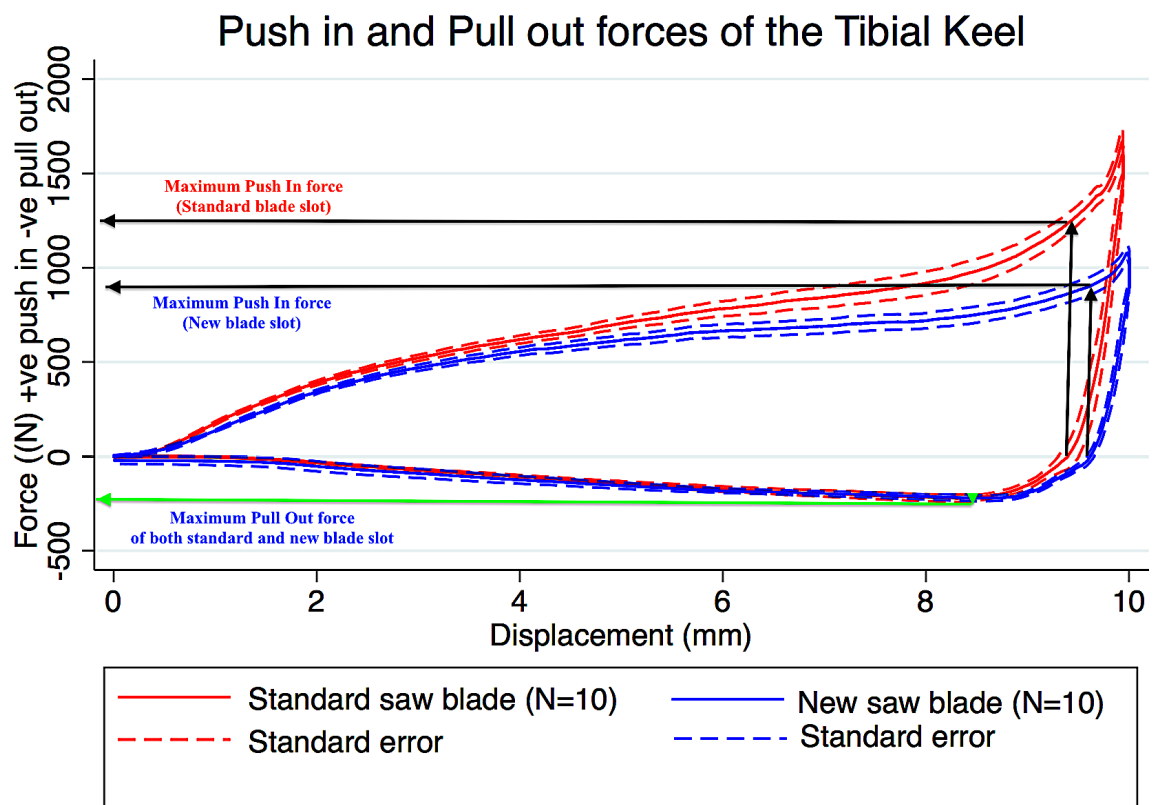


Figure 7.9. Force displacement curve for standard and new blade slots and how maximum push in and pull out forces were determined for each individual slot tested.

In between testing each slot the tibial component was cleaned with an air duster (Office Depot, Leicester, UK) to prevent debris influencing the push in and pull out forces of the subsequent slot to be tested.

7.2.4 Testing the effect of implant variation

To eliminate the chances that any differences found between the groups were specific to the dimensions of the keel of the tibial component used, 20 additional slots were made; 10 with the standard sawblade and 10 with the new sawblade. Ten different size C tibial components were randomly implanted and withdrawn from a standard sawblade slot or new sawblade slot while the maximum push-in and pull-out forces were recorded.

7.2.5 Slot dimension measurements of the standard and new blades

Three further slots were cut with the standard blade and three slots were cut with the new blade. Each of the six slots was cut into two mm slices. An image of each slice was captured with a digital camera against a dark background with a calibration object to provide scaling. The edge of each slice was detected with a custom routine in Matlab (Version 7.0.4.287; The MathWorks, Natick, Massachusetts, USA). All slots cut with the same blade were superimposed and the minimum slot width was then calculated for depths of 0.5, 2, 4, 6 and 8 mm.

7.2.5 Statistical analysis

A power calculation for the comparative groups with a power of 0.8, significance of 0.05 to detect a clinically meaningful difference of 250 N with a SD of 140 N from provisional data indicated that nine slots would be required in each group³²².

The intra class correlation coefficient was utilised to assess for both inter-rater and intra-rater reliability for the calliper measurements made on surgical instruments by two independent observers (Hasan Raza Mohammad and Stefano Campi).

Anova with the post hoc bonferroni procedure was performed to compare the maximum push-in forces and pull-out forces between groups. The paired t test was used to compare the push-in and pull-out forces to assess for the effect of implant variation. Statistical significance was defined as $p < 0.05$ for all tests. All statistical analyses were conducted using Stata (Version 14.2, Texas, USA).

7.3 Results

7.3.1 Instrumentation measurements

The inter-rater and intra-rater reliability for digital calliper measurements was 0.84 ($p=0.002$) and 0.92 ($p<0.001$) respectively showing excellent reproducibility, consistent with Campi et al.'s work³¹⁸.

The average width of the tibial components was 3.87 mm (SD 0.04) and depth was 9.7 mm (SD 0.16). The details of the width of the different surgical instruments are summarised in Table 7.1. The new blade was 0.2 mm wider than the standard blade at its distal tip although proximally there were no differences in width. The pick and rasp were respectively about 0.5 mm and 0.2 mm wider than the standard blade. The depth of all surgical instrumentation exceeded that of the tibial components used in this study. For full details of all the measurements taken please refer to Appendix 8.

Surgical instrument	Mean width (mm)
Standard blade tip	2.7 (SD 0.04)
New blade tip	2.9 (SD 0.04)
Pick	3.3 (SD 0.01)
Rasp	3.0 (SD 0.01)

Table 7.1. Width of surgical instruments used in the study.

7.3.2 Measured push in forces

The standard sawblade produced slots which had the highest maximum push-in loads averaging 1411 N (SD 180). The new sawblade slots had a lower average maximum push-in load that was almost half that of the standard sawblade at 789 N (SD 131) and this difference was statistically significant ($P < 0.001$).

Adjunctive use of the pick with the standard sawblade slots significantly reduced the push-in forces ($p < 0.001$) to 818 N (SD 388) compared to the standard sawblade alone. The use of the standard blade with the pick showed no significant difference in push-in force when compared to the slots made with the new sawblade alone. Adjunctive use of the rasp had no significant effect on the push-in forces for the standard sawblade group (Table 7.2).

Adjunctive use of the pick with slots made with the new sawblade did not significantly affect the push-in forces. Rasp usage with the new blades created a significant increase ($p < 0.001$) in the push-in forces to 1390 N (SD 202) (Table 7.2).

No significant differences in push-in forces were observed between the standard blade with adjunctive pick use and the new blade with adjunctive pick use. Similarly, no differences were observed between the standard blade with rasp and the new blade with rasp groups (Table 7.2). The average force displacement curves of the standard and new blades were previously illustrated in Figure 7.9. Figure 7.10 illustrates the different push-in forces between the groups.

	Standard blade 1441 N (SD 180)	Standard blade & pick 818 N (SD 388.2)	Standard blade & rasp 1368 N (SD 309)	New blade 789 N (SD 131)	New blade & pick 1001 N, (SD 156)	New blade & rasp 1390 N (SD 202)
Standard blade 1441 N		623 N (P < 0.001)	73 N (P > 0.9)	652 N (P < 0.001)	440 N (P < 0.05)	51 N (P > 0.9)
Standard blade & pick 818 N	623 N (P < 0.001)		550 N (P < 0.001)	29 N (P > 0.9)	183 N (P > 0.9)	572 N (P < 0.001)
Standard blade & rasp 1368 N	73 N (P > 0.9)	550 N (P < 0.001)		579 N (P < 0.001)	367 N (P < 0.05)	22 N (P > 0.9)
New blade 789 N	652 N (P < 0.001)	29 N (P > 0.9)	579 N (P < 0.001)		212 N (P > 0.9)	601 N (P < 0.001)
New blade & pick 1001 N	440 N (P < 0.05)	183 N (P > 0.9)	367 N (P < 0.05)	212 N (P > 0.9)		389 N (P < 0.05)
New blade & rasp 1390 N	51 N (P > 0.9)	572 N (P < 0.001)	22 N (P > 0.9)	601 N (P < 0.001)	389 N (P < 0.05)	

Table 7.2. The results of the mean push in force differences between groups. P values refer to the anova results with bonferroni adjustment.

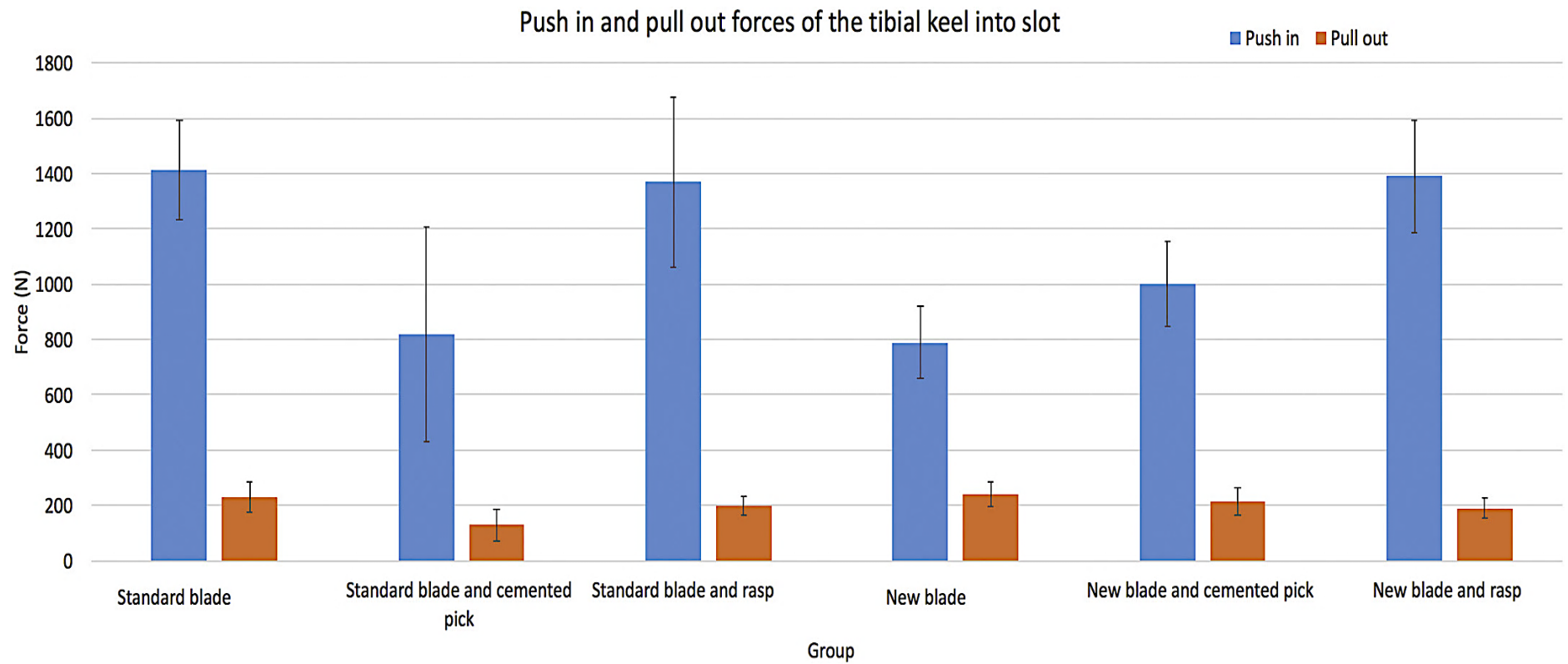


Figure 7.10. Bar chart of push in and pull forces.

7.3.3 Measured pull out forces

There were no significant differences in pull-out forces between the slots made with the standard and new blades. The highest pull-out force was the new saw blade group at 240 N (SD 47) and the second highest was the standard blade group at 230 N (SD 56) (Table 7.3).

For the standard blade the adjunctive use of the cemented pick significantly reduced the pull-out force to 128 N (SD 58). The rasp had no significant effect on the pull-out force (Table 7.3). In the new blade adjunctive use of the cemented pick or rasp had no significant effect on the pull-out forces when compared to the new blade alone (Table 7.3).

The pull-out forces for slots with the standard blade and pick were significantly lower ($P < 0.001$) 128 N (SD 58) than the new blade and pick 214 N (SD 48). No significant differences in pull-out load existed between the new blade with rasp and the standard blade with rasp (Table 7.3). See Figure 7.10 for graphical display of pull-out forces.

	Standard blade 230 N (SD 56)	Standard blade & pick 128 N (SD 58)	Standard blade & rasp 197 N, (SD 33)	New blade 240 N (SD 47)	New blade & pick 214 N (SD 48)	New blade & rasp 190 N, (SD 39)
Standard blade 230 N		102 N (P < 0.001)	33 N (P > 0.9)	10 N (P > 0.9)	16 N (P > 0.9)	40 N (P > 0.9)
Standard blade & pick 128 N	102 N (P < 0.001)		69 N (P < 0.05)	112 N (P < 0.001)	86 N (P < 0.05)	62 N (P = 0.1)
Standard blade & rasp 197 N	33 N (P > 0.9)	69 N (P < 0.05)		43 N (P > 0.9)	17 N (P > 0.9)	7 N (P > 0.9)
New blade 240 N	10 N (P > 0.9)	112 N (P < 0.001)	43 N (P > 0.9)		26 N (P > 0.9)	50 N (P = 0.5)
New blade & pick 214 N	16 N (P > 0.9)	84 N (P < 0.05)	17 N (P > 0.9)	26 N (P > 0.9)		24 N (P > 0.9)
New blade & rasp 190 N	40 N (P > 0.9)	62 N (P = 0.1)	7 N (P > 0.9)	50 N (P = 0.5)	24 N (P > 0.9)	

Table 7.3. The results of the mean pull in force differences between groups. P values refer to the anova results with bonferroni adjustment.

7.3.4 The effect of different implants

Using 10 different tibial size C components the mean maximum push-in force with the new blade was 905 N (SD 245) and was significantly lower ($P = 0.002$) than the standard blade at 1343 N (SD 219). There were no significant differences ($P = 0.37$) between the pull-out forces of the new blade 168 N (SD 67) and standard blade 195 N (SD 36).

7.3.5 Slot measurements

Figure 7.11 shows the difference between the minimum widths for slots cut with the standard blade and the new blade. At a depth of 0.5 mm the widths are approximately equal but at every subsequent depth (2, 4, 6 & 8 mm) the standard blade width decreased and was smaller than the corresponding width for the new blade. The widths for the new blade were generally more uniform throughout the depth of the slot. The slots were deeper with the new blade than the standard blade.

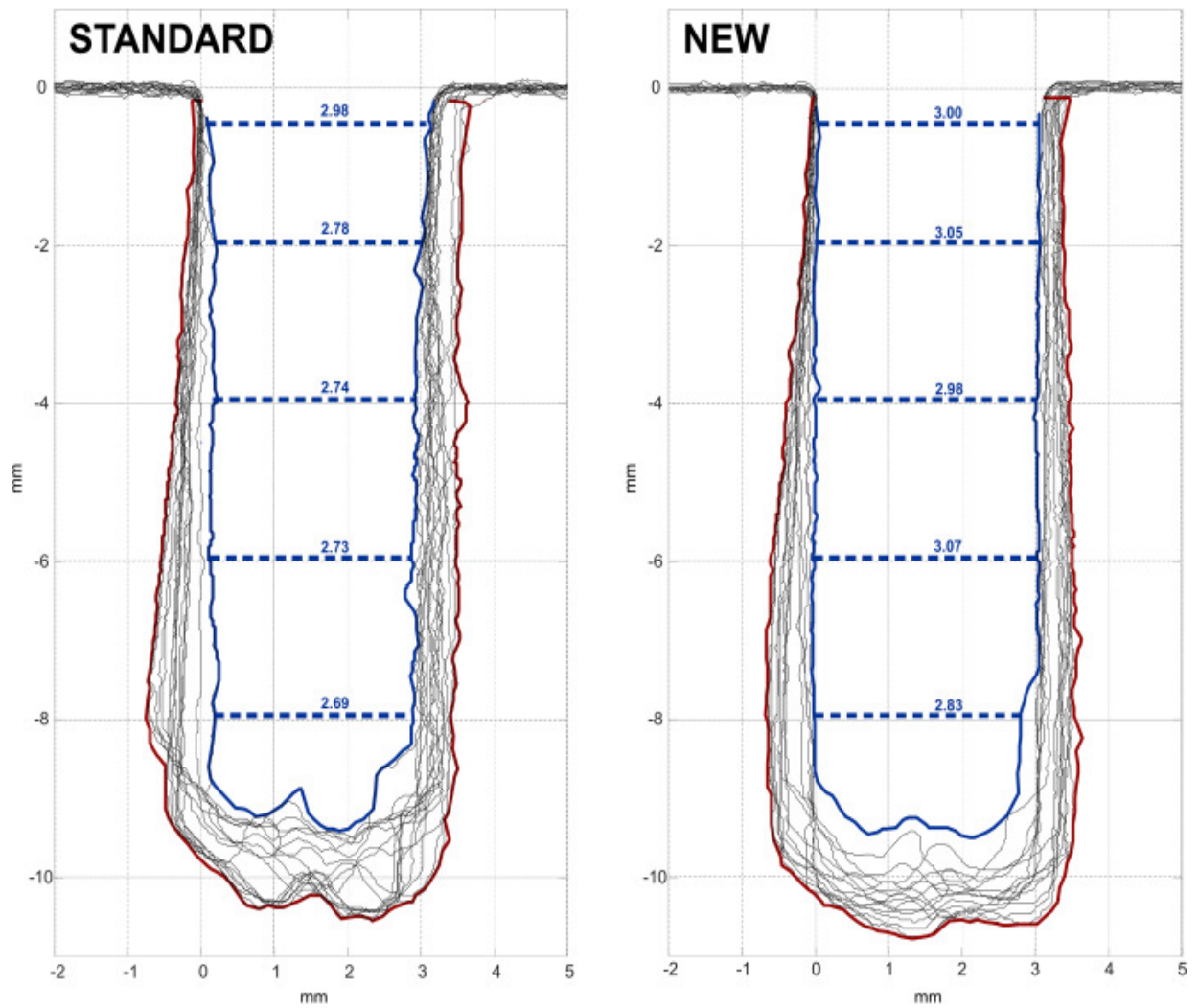


Figure 7.11. Three standard blade slots and three new blade slots were sectioned into two mm slices. The edges of the slots were superimposed, and the minimum slot width was determined.

7.4 Discussion

This chapter demonstrates that the push-in force is almost halved in the new blade compared to the standard sawblade, but the pull-out force is very similar. No combination of blade, pick or rasp significantly lowered the push-in force or increased the pull-out force compared to the new sawblade. Therefore the new blade should be used instead of the standard one without adjuvant instruments to minimise fracture risk whilst not compromising fixation. Saw blade usage is relatively straightforward for surgeons given they are completely guided by a tibial template. Adjuvant pick and rasp use are more susceptible to surgical errors given they have no such template and therefore rely completely on the judgement of the operating surgeon. This may be problematic for low volume surgeons (< 10 cases/year) as identified in Chapter 5, who tend to have much higher revision rates²⁶⁰. Given the results of this experiment, the new blade is now the only keel-cut blade available for surgeons.

When the keel is inserted into the cut slot, perpendicular forces to the keel act on the cavity walls (Figure 7.4). Bishop et al.³²³ demonstrate these perpendicular normal forces are proportional to the vertical push-in forces. If these normal forces are excessive, they can split the bone creating fractures^{317, 324}. This study suggests surgeons apply a force of 1400 N to seat the tibial component into slots cut by the standard blade. Although periprosthetic tibial fractures generally present a few weeks postoperatively rather than intraoperatively, the loading impact may initiate a crack below the keel which, can later propagate during physiological loading³²⁵.

The force displacement graph in Figure 7.9, provides a detailed insight into why the new blade is better than the standard. The load during the push-in phase for the standard and new blade slots remains similar until a depth of approximately four mm where the push in load

with standard blade slots increases at a steeper gradient than the new blade slots (Figure 7.9). This trend likely occurs because the new saw blade is wider at the tip (0.2 mm) than the standard saw and produces wider slots of a more consistent width (Figure 7.11).

Slot depth is likely to have an influence on the fracture risk given during the last millimetre of insertion the push-in force increased markedly for both blade slots (Figure 7.9). This increase was about twice as large with the standard blade slot compared to the new blade slot and may relate to the new blade being about 0.5 mm deeper. Even though the keel cut saws are deeper than the tibial keel, they have two blades meaning a segment of bone can remain in the slot centre which can impact the keel (Figure 7.11). It is important to note deeper slots may further weaken the tibia, but this would likely insignificant compared to the increased forces required to seat the tibial component, particularly for an increase in slot depth of only 0.5 mm. Another factor which could explain the rise in push in forces observed is the build-up of porous coating at the junction of the keel and underside of tibial tray. If this coating comes into contact with the slot edges at the final implantation stages, this could steeply elevate seating loads.

The results of this chapter suggest the pick should be used with caution. Although it reduced push-in forces when used with the standard blade, it also reduced the pull-out force thereby compromising fixation. The prototype rasp did not reduce push-in forces when used with the standard blade and in fact increased them with the new blade. This may be given it forced debris into the walls or the bottom of the slot increasing the push-in force. The rasp had no effect on pull-out loads and hence fixation achieved.

Tibial plateau fractures are devastating complications and likely multifactorial⁶⁷. During the preparation of the tibia, the subchondral bone plate has to be removed weakening the tibial plateau. Factors which unnecessarily further weaken the plateau and therefore need to be avoided include¹⁹⁸; (1) deep resection, (2) deep vertical saw cuts, (3) damage to the posterior cortex during keel preparation and (4) a too medial resection. The keel cut saw should be used carefully such that it reaches the ends in the anteroposterior direction and the inferior aspect of the slot whilst within the boundaries of the template tool. The blade should also be lifted up and down to remove all the bone from the slot. It is important to ensure that no retained bone is present within the keel slot. After slot preparation a trial tibial component should be inserted, but if it cannot be inserted with finger pressure alone, this suggests that there is retained bone which can be removed by reusing the keel cut blade or pulsatile lavage. All factors discussed need addressing to help to reduce the incidence of tibial plateau fractures.

This study is limited given it was performed on polyurethane foam which acted as a cancellous bone analogue. Although this material is well established for usage in orthopaedic fixation studies³²⁶⁻³²⁸, it is unclear how well the polyurethane foam can replicate bone during surgery where blood and fat likely affects friction. Additionally there is evidence that the friction coefficient for sawbones is significantly less than human bone³²⁹, although this would not affect comparisons made given the same polyurethane material was used. This chapter makes the assumption that the pull out force is a measure of primary stability. This is an oversimplification given in the knee joint the tibial component experiences both compressive and toggle forces which were not replicated in this study. However this limitation applies to all comparative groups in this study and is unlikely to affect their relative performances and hence the conclusions of this study. Bone remodelling and biology cannot be reproduced with

an inert testing material. The tibial components were implanted with a continuous force at 0.01 mm/s, whereas clinically they are impacted with a hammer at variable speeds depending on the operating surgeons' technique. Another limitation is that only size C tibial components were studied, which is the most commonly used size from NJR data (Chapter 4.1). Although the study was repeated with 10 different size C tibial components to test for any variability within each size, one cannot be certain that the results are completely generalisable to all sizes. However, given all tibial component sizes use the same instruments to prepare the keel slot and the keels have the same width and depth regardless of component size, the interference should be equivalent. As both push-in and pull-out forces are related to interference²⁶⁴ the results are likely to be generalisable to all sizes.

This experimental study suggests that the risk of tibial plateau fractures will reduce with the new keel cut saw blades compared to the standard blades without affecting the quality of fixation. With the new blade the cemented pick should not routinely be used given it probably will not reduce the risk of fracture and may in fact compromise fixation. Before the component is impacted it should be possible to insert the tibial trial with finger pressure alone and if this is difficult any retained bone probably preventing this should be removed.

8. CONCLUSIONS AND FUTURE WORK

8.1 Summary of the problem and thesis aims

Over 100,000 primary knee replacements are performed every year in the UK⁸, with the two main surgical treatment options for end stage medial compartment osteoarthritis being TKR and UKR. Previous work has shown that UKR offers significant advantages over TKR including faster recovery, reduced complications, improved function and lower mortality¹⁰⁻¹².

However the major issue with UKRs are their higher revision rates, which are reported to be several times higher than TKRs in various joint registries^{8, 16, 17}. Additionally there is significant variability in UKR results reported, secondary to inconsistent selection criteria, variable surgeon caseloads and different thresholds for revision surgery. Given this, UKR is only used in approximately 10% of primary knee replacements despite eligibility studies suggesting it can be used in up to 50% of cases⁸³.

In the UK, each operating surgeons' practice is audited by the NJR to monitor their joint replacement revision rates, with outliers detected at an early stage and forced to change their practice. Therefore it is logical for surgeons to avoid an implant with higher reported revision rates, given this can potentially adversely affect their orthopaedic practice. This is however problematic as many patients may not be presented with the benefits of UKR when considering treatment for their knee arthritis, both from when they initially present to their general practitioners and later when referred to an orthopaedic specialist. Therefore the only way to help to resolve this, is to identify modifiable factors that can lower UKR revision rates. This thesis studied the most commonly used UKR implant which is the Oxford UKR⁸. The main objectives of this thesis were to study the Oxford UKR's long term revision rates,

factors which influence revision and to develop new strategies to help improve the implants performance.

8.2 Summary of findings

This thesis has first allowed a consensus of the long term outcomes of the Oxford UKR to be achieved from Chapter 2, a systematic review of studies from all across the world. Using the endpoint revision, the 10 year implant survival was 93% (CI 91.9 - 93.3) which slightly lags behind those reported for TKR (usually between 94 - 97%). However using the endpoint reoperation, the 10 year implant survival was 91.1% (CI 89.8 - 92.3) which is better than those reported for TKR (86.7%¹⁴⁶). In terms of functional outcomes, the long term OKS was found to be 40 on average, which is much better than those reported for TKRs. However despite this, the issue remains that Oxford UKR revision rates were identified as being higher than TKR. Leading causes for revision included aseptic loosening which raised the question of whether cementless fixation could lower revision rates.

Given only a single cementless study was identified in Chapter 2, in Chapter 3 a prospective Oxford cohort of 1,000 consecutive cementless Oxford UKRs were studied. Using various endpoints; reoperation, revision, revision to TKR and major revisions, the respective 10 year implant survivals were 96.6%, 97.5%, 98.9% and 99.6%. These results were at least if not better than those reported for TKRs. However these results are from two operating surgeons in Oxford who were both involved in the design of the implant limiting its generalisability. However the study indicates the achievable results if the recommended indications and surgical technique are adhered to.

Given the promising results of the cementless Oxford UKR in Oxford, for Chapter 4.1, a propensity matched comparison of 14,814 cemented and cementless UKRs performed all across the UK was undertaken, using NJR data. Groups were matched for various patient, surgical and implant confounders to allow fair comparison. The 10-year cumulative implant survival rates were 93.2% (CI 89.7 - 95.6) and 90.2% (CI 87.5 - 92.3) for cementless and cemented groups respectively. Cementless UKRs had a significantly reduced revision rate compared with cemented UKRs (HR=0.76, p=0.002) given the rates for aseptic loosening, pain and lysis halved. These results were mirrored by the systematic review presented in Chapter 4.2 of all long term cemented and cementless UKRs which again found that cementless UKRs had significantly better implant survival (95.5% vs 92.7%, p<0.001), with rates of aseptic loosening significantly decreasing (p=0.02) for the cementless UKRs.

In Chapter 5.1, the analysis of the effect of surgeon caseload on UKR data (n=40,522) showed 10-year implant survival rates of 86.6% (CI 85.8 - 87.3), 90.8% (CI 90.1 - 91.5), and 94.1% (CI 93.2 - 94.8) for low, medium, and high-volume surgeons. The revision rates for medium and high-volume surgeons were significantly lower than those for low-volume surgeons, with hazard ratios of 0.67 (p<0.001) and 0.42 (p<0.001) respectively. High volume surgeons achieved outcomes similar to those reported for TKR and for cementless implants reached as high as 97.5% at 10 years. Additionally the propensity matched cemented and cementless UKRs (n=14,814) were used to determine the effect of surgeon caseload on the relative performances of cemented and cementless UKRs. For all caseloads, cementless implants had a lower revision rate than cemented implants. The rate of revision of cementless implants was 26% lower than that of cemented implants among low-volume surgeons (HR=0.74), 21% lower among medium-volume surgeons (HR=0.79) and 20% lower among high-volume surgeons (HR=0.80).

In Chapter 5.2, a matched comparison of Microplasty assisted and Non Microplasty UKRs (n=15,906) found five year cumulative implant survival rates were 96.7% (CI 96.0% - 97.2%) and 94.5% (CI 93.8 - 95.1%) respectively. The revision rates for Microplasty UKRs were significantly lower (HR=0.77, p=0.008). Additionally when the revision rates of Microplasty UKRs performed after one year of the instruments introduction, were compared to Non Microplasty UKRs the reduction in revision rate was even greater (HR 0.69, p=0.004). No adverse learning effect was observed with the Microplasty instrumentation when the results within the first year of its introduction were compared to Non Microplasty UKRs. Microplasty instrumentation has now replaced the conventional Phase 3 instruments (Non Microplasty instrumentation).

In Chapter 5.3, a matched comparison of Single and Twin Peg cemented Oxford UKRs (n=5,668) found that the five year cumulative all-cause implant survival rates were 94.8% (CI 93.6 - 95.8) for Single Peg UKRs and 96.2% (CI 95.1 - 97.1) for Twin Peg UKRs. The difference in cumulative revision rates between Twin Peg and Single Peg UKRs was statistically significant (HR=0.74, p=0.04). The revision rate for femoral component aseptic loosening was significantly lower (p=0.03) in the Twin Peg group compared to the Single Peg group. The Twin Peg has now replaced the Single Peg UKR.

Given anecdotal reports of bearing fracture and that bearing related revisions were listed amongst the most common causes for revision surgery in Chapter 2, for Chapter 6 a radiostereometric analysis study investigating long term polyethylene wear of the Phase 3 Oxford in three different bearing types (1900 resin machined, 1050 machined, 1050 moulded bearings) was performed (n=63). The wear rate of currently used Oxford UKR bearings, which are moulded from 1050 resin, is very low (0.06 mm/year) but is higher than that of the

previous Phase 2 bearings (0.02 mm/year). This may relate to the minimally invasive approach of the Phase 3 design making surgical errors, such as impingement, more likely.

Although cementless fixation offers clear advantages as identified from Chapters 3 and 4, a number of tibial plateau fractures have been reported, and deemed more common than in cemented fixation given cementless implant's reliance on interference fit for primary stability²⁶². In Chapter 7 an experimental study was performed to reduce the risk of tibial plateau fractures by modifying the width of the slot cut in the proximal tibia for the tibial component. A standard keel blade, a wider new blade and the adjuvant use of a rasp or pick to widen the slot further were assessed (n=60). The new blade almost halved the push in forces required to seat the component compared to the standard blade (1441 N vs 789 N, $p < 0.001$) with no significant differences in pull out forces (230 N vs 240 N, $p > 0.9$) suggesting no compromise in fixation. No advantages of the adjuvant use of a pick or rasp with either blade was detected, with in fact only evidence of adverse effects on the push in or pull out forces. These results suggest that the new blade should significantly reduce the risk of tibial plateau fractures and is supported from anecdotal evidence.

8.3 Limitations

There are important limitations from this thesis which require discussion. The systematic reviews of Chapter 2 and 4.2, have summarised all published UKR studies across the world. However, given only published studies are included, there is publication bias present which may influence the results. Additionally high volume centres are more likely to publish their positive results of an implant which may skew the results. However the systematic review

results of Chapter 4.2 presented the same findings as the NJR study which used knee replacement data from all across the UK.

Chapter 3 was performed on a consecutive series performed by surgeons involved in the design of the implant. This cohort was selected given it is the largest cohort available strictly using the recommended indications and operative techniques along with intraoperative, radiographic and outcome data independently assessed. Additionally this cohort represents the outcomes of two experienced surgeons, and therefore may result in less variability in outcomes from differing operative technique between cases than other series. However the inherent limitation of this is that the results may not be generalisable across the world, but rather inform of what results can be achieved if the recommended indications and techniques are used.

Chapters 4.1 and 5 used registry data to investigate the effect of cementless fixation, surgeon caseload, Microplasty instrumentation and femoral peg number on revision rates. Although registry data allows for large numbers of UKRs to be analysed which cannot be supplied from individual cohort studies, it does have limitations. First it only records the outcome revision when there is exchange, addition or removal of the primary procedure components and therefore does not collect information on reoperations such as MUAs, arthroscopies and internal fixation. Additionally no data on PROMs or radiographic outcomes are collected. As a result it does not comprehensively study all outcome measures which may be important for patients. Additionally, the reasons for revision in the NJR are those recorded at the time of surgery even if this subsequently changed from histopathology and microbiology data later available. Registries can underreport revisions although there is no reason to believe this would differ between comparative groups. Another limitation is that, despite matching, there

is potential for residual confounding. The only way to achieve true balance with respect to both known and unknown confounders is a randomised trial, but to compare revision rates would require very large numbers and long follow-up which is impractical.

Chapter 6 used RSA to compare long term polyethylene wear in three bearing types. A significant limitation is that patients from the three comparative groups were not matched, given it was difficult to find patients with available bearing codes in their notes, so that the bearing type could be identified. Given the three bearing types were used at slightly different time periods, this resulted in an inevitable difference in mean follow-up for each group. However, given that all groups exceeded 10 year follow up and annual wear rate was analysed, this should not have influenced the results. In this study there was an assumption that the change in bearing thickness between implantation and RSA was due to bearing wear, when it was actually due to both wear and creep. With a single RSA measurement, one cannot calculate the relative contributions of creep and wear. However creep mainly occurs in the first three months and has minimal effect in the long term and therefore, it is not unreasonable to assume, over a ten-year period, that the change in thickness was due to wear. Furthermore, had there been marked creep, this would have resulted in overestimating, rather than underestimating wear.

In Chapter 7 an experimental study testing the quality of fixation achieved with different surgical instruments was performed using solid polyurethane foam which acted as a cancellous bone analogue. Although the use of polyurethane foam for measuring push-in and pull-out forces is well established in orthopaedic fixation studies, it is unclear how well polyurethane foam can replicate bone during an operation where the presence of blood and fat is likely to affect the friction. Additionally, bone modelling cannot be reproduced. Another

issue is that the tibial components were implanted with a continuous force at 0.01 mm/s, whereas clinically they are impacted with a hammer.

8.4 Future work

This thesis has reported several novel findings, some of which require further investigation. In Chapter 2 and 4.2 most of the studies in these reviews were cemented in nature, with only a few being cementless. There is a need for more long term cohort studies of the cementless UKRs across the world to understand whether results vary significantly between surgical centres and countries where patient demographics may differ. Additionally from the work presented in Chapter 4.2 there is clearly a lack of non-Oxford UKR long term studies and these need to be encouraged so that the outcomes of all types of UKR can be understood.

Patient demographics undergoing knee replacement surgery are changing with more obese or younger and active patients requiring surgery^{229, 330}. These new demographics have created new challenges given cemented implants have higher failure rates in these groups^{331, 332} with the under 65 age group expected to represent the majority of cases by 2030²²⁹. Additionally, given the rise in life expectancy there is an increasing need for implants to provide a more physiological long-term fixation with current concerns that cemented implants will not last. In Chapter 3, although the long term outcomes were studied, the next steps would be to investigate long term outcomes stratified by different patient demographics such as age and BMI. Unfortunately currently too few patients were at risk at 10 years to be able to do this, but when more patients reach their 10 year follow up mark, this analysis will be performed.

The work in Chapter 4.1 comparing fixation types can also be expanded to compare fixation results in different subgroups of the population such as different age and BMI groups.

Additionally NJR data does not collect complete information on tibial plateau fractures, given that most tibial plateau fractures are treated by internal fixation, they are not documented as revisions in the NJR. However HES data may offer insight into this as well as allowing assessment of reoperations and PROMs which are not possible using NJR data alone. I have successfully obtained ethical approval, data linkage permissions and NHS Digital approval for this to be performed as a future study.

Chapter 5.1 investigated the effect of surgeon technical skills through assessing surgeons' caseload for all UKRs and its effect on the relative performances of cemented and cementless UKRs. However work published by Hamilton et al.²⁶⁵ suggest that non-technical skills associated with patient selection and the surgeons' decision making between TKR and UKR can also influence UKR revision rates. The decision of which implant to use (UKR or TKR) relates to the individual surgeons' indications and is reflected by the proportions of a surgeons' practice which is UKR and TKR. The proportion of UKRs which form a surgeons primary knee replacement practice has been defined as UKR usage²⁶⁵. Usage is particularly important given a surgeon can often not practically change their overall volume of practice but can change the percentage of knees which are UKRs. Although this could not be assessed in this thesis given, I did not have TKR registry data permissions. However, I have applied for and received NJR and ethical approvals to investigate the effect of UKR usage on revision rates in a future study.

Chapter 5.2 and 5.3 investigated the effect of Microplasty and a Twin Peg cemented femoral component on revision rates. A significant limitation of this work was that we were only able to assess the five year outcomes, given the relatively recent introduction of both interventions.

With time more patients will reach long term follow up and this will warrant more registry studies of their effects on the long term outcomes of the Oxford UKR.

The RSA study in Chapter 6 showed a wear rate of 0.06 mm/year which is much higher than those achieved by the Phase 2 Oxford UKR (0.02 mm/year). This wear rate will result in 1.2 mm of wear at 20 years follow up, making 3 mm thick bearings prone to fracture. Future work should use RSA to investigate the wear of vitamin E highly crosslinked polyethylene which will hopefully reduce the wear rate.

Finally in Chapter 7, the wider new blade significantly reduced the push in forces and did not affect quality of fixation compared to the standard blade by reducing the interference fit. The introduction of the new blade has already anecdotally reduced the incidence of fracture, but this needs to be studied using the last six months of available NJR and HES data.

Additionally the effect of depth and impingement of the tibial keel at the bottom of the slot may also have a role to play which requires further experimental slot testing which is currently under way.

8.5 Thesis conclusions

The aim of this thesis was to investigate methods of reducing the revision rate of the Oxford UKR. The data analyses have shown that surgeon caseload is a critical factor and ideally needs to be ≥ 30 cases/year which can be achieved by sticking to the recommended surgical indications. Additionally cementless fixation (all Twin Peg) has proven to lower revision rates independently of surgeon caseload. Using Microplasty instrumentation can help to further improve these results. Therefore the conclusion of this thesis is that surgeons should adhere to the recommended indications thereby achieving a high caseload and should use cementless fixation with Microplasty instrumentation. This should allow 10 year implant survivals similar to TKR and allow more patients benefit from the known advantages of UKRs including reduced mortality and better functional outcomes.

Two problems relating to bearing fracture and tibial plateau fractures from the analyses were identified and studied in detail. This thesis has shown that with a minimally invasive technique, higher levels of polyethylene wear occur, which may lead to bearing fracture. A definite reason for this higher wear has not been identified and therefore suggest the use of highly crosslinked polyethylene with vitamin E to address this. However an RSA study will be needed to investigate these bearing's wear rates. New surgical instrumentation (New blade) was developed to address tibial plateau fractures by reducing the forces required to seat the tibial component without compromising fixation. This instrumentation has been introduced clinically and has anecdotally reduced the fracture rate.

APPENDIX 1

A1.1 Awards

Henni Mester Scholarship – University of Oxford

Royal College of Surgeons Research Fellowship – Royal College of Surgeons of England

Goodfellow Fellowship – Nuffield Orthopaedic Centre

A1.2 Publications

Ten peer reviewed publications have come directly from work within this thesis. Additionally this work has been presented both nationally at the British Association of Surgeons of the Knee, British Orthopaedic Research Society and internationally at the American Academy of Orthopaedic Surgeons, World Arthroplasty Congress and the European Federation of National Associations of Orthopaedics and Traumatology.

A1.3 Publication list from this thesis

1. Mohammad HR, Strickland L, Hamilton TW, Murray DW. Long-term outcomes of over 8,000 medial Oxford Phase 3 Unicompartmental Knees—a systematic review. *Acta Orthop*. 2018;89(1):101-7.
2. Mohammad HR, Campi S, Murray D, Mellon S. Instruments to reduce the risk of tibial fracture following cementless unicompartmental knee replacement. *Knee*. 2018;25(6):988-96.
3. Mohammad HR, Kennedy JA, Mellon SJ, Judge A, Dodd CA, Murray DW. Ten-year clinical and radiographic results of 1000 cementless Oxford unicompartmental knee replacements. *Knee Surg Sports Traumatol Arthrosc* 2019:1-9.
4. Mohammad HR, Campi S, Kennedy JA, Judge A, Murray DW, Mellon SJ. Long-term in vivo wear of different bearing types used for the Oxford Unicompartmental Knee Replacement. *Bone Joint Res* 2019;8(11):535-43.
5. Mohammad HR, Kennedy JA, Mellon SJ, Judge A, Dodd CA, Murray DW. The clinical outcomes of cementless unicompartmental knee replacement in patients with reduced bone mineral density. *J Orthop Surg Res* 2020;15(1):1-6.
6. Mohammad HR, Matharu GS, Judge A, Murray DW. Comparison of the 10-year outcomes of cemented and cementless unicompartmental knee replacements: data from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man. *Acta Orthop* 2020;91(1):76-81.
7. Mohammad HR, Matharu GS, Judge A, Murray DW. The Effect of Surgeon Caseload on the Relative Revision Rate of Cemented and Cementless Unicompartmental Knee Replacements: An Analysis from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man. *J Bone Joint Surg Am* 2020;102(8):644-53.
8. Mohammad HR, Matharu GS, Judge A, Murray DW. New surgical instrumentation reduces the revision rate of unicompartmental knee replacement: A propensity score matched comparison of 15,906 knees from the National Joint Registry. *Knee* 2020; S0968-0160(20)30046-6.
9. Mohammad HR, Matharu GS, Judge A, Murray DW. A matched comparison of revision rates of cemented Oxford Unicompartmental Knee Replacements with Single and Twin Peg femoral components, based on data from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man. *Acta Orthop* 2020;1-6.
10. Mohammad HR, Bullock G, Kennedy JA, Mellon SM, Murray DW, Judge A. Cementless unicompartmental knee replacement achieves better ten year clinical outcomes than cemented – A systematic review. *Knee Surg Sports Traumatol Arthrosc* 2020; 1:1-7

Long-term outcomes of over 8,000 medial Oxford Phase 3 Unicompartmental Knees—a systematic review

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Background and purpose — There is debate as to the relative merits of unicompartmental and total knee arthroplasty (UKA, TKA). Although the designer surgeons have achieved good results with the Oxford UKA there is concern over the reproducibility of these outcomes. Therefore, we evaluated published long-term outcomes of the Oxford Phase 3 UKA.

Patients and methods — We searched databases to identify studies reporting ≥ 10 year outcomes of the medial Oxford Phase 3 UKA. Revision, non-revision, and re-operation rates were calculated per 100 component years (% pa).

Results — 15 studies with 8,658 knees were included. The annual revision rate was 0.74% pa (95% CI 0.67–0.81, n = 8,406) corresponding to a 10-year survival of 93% and 15-year survival of 89%. The non-revision re-operation rate was 0.19% pa (95% CI 0.13–0.25, n = 3,482). The re-operation rate was 0.89% pa (95% CI 0.77–1.02, n = 3,482). The most common causes of revision were lateral disease progression (1.42%), aseptic loosening (1.25%), bearing dislocation (0.58%), and pain (0.57%) (n = 8,658). Average OKS scores were 40 at 10 years (n = 3,417). The incidence of medical complications was 0.83% (n = 1,443).

Interpretation — Very good outcomes were achieved by both designer and non-designer surgeons. The PROMs, medical complication rate, and non-revision re-operation rate were better than those found in meta-analyses and publications for TKA but the revision rate was higher. However, if failure is considered to be all re-operations and not just revisions, then the failure rate of UKA was less than that of TKA.

Over 100,000 primary knee arthroplasties are conducted annually in the United Kingdom and demand is predicted to increase 6-fold by 2030 (UK National Joint Registry 2014). The 2 main treatments for severe knee osteoarthritis that has

Abbreviations

AMOA – anteromedial osteoarthritis
AKSS-O – American Knee Society Score (objective)
AKSS-F – American Knee Society Score (functional)
DVT – Deep vein thrombosis
HSS – Hospital for Special and Surgery Knee Score
OKS – Oxford Knee Score
pa – Per annum
PE – Pulmonary embolism
PROM – Patient-reported outcome measure
SONK – Spontaneous osteonecrosis of the knee
TKA – Total knee arthroplasty
UKA – Unicompartmental knee arthroplasty

failed non-operative management are total knee arthroplasty (TKA) and unicompartmental knee arthroplasty (UKA). UKA in appropriate patients has significant benefits over TKA including faster recovery, better patient-reported outcome measures (PROMs), and reduced risk of major complications, but has also been reported to have a higher revision rate (Liddle et al. 2014). There is therefore debate as to which is the most clinically effective.

The most commonly used UKA prosthesis in the United Kingdom is the Oxford Knee (Biomet, Swindon, UK) (UK National Joint Registry 2011). The primary indication for the Oxford Knee is anteromedial osteoarthritis (AMOA) with spontaneous osteonecrosis of the knee (SONK) being another rarer indication. In AMOA the patient should have bone-on-bone arthritis in the medial compartment, full -thickness lateral compartment cartilage, functionally normal medial collateral and anterior cruciate ligament, and a patellofemoral joint without lateral bone loss and grooving (Goodfellow et al. 1988, Beard et al. 2007). Other factors such as site of the pain, age, weight, activity, and chondrocalcinosis have been



Contents lists available at ScienceDirect

The Knee



Instruments to reduce the risk of tibial fracture following cementless unicompartmental knee replacement

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Background: Tibial plateau fracture is an important complication of cementless Oxford unicompartmental knee replacement. The press fit between the keel and the bone's keel slot is responsible for primary fixation and also contributes to fracture risk. This study investigates whether the fracture risk could be reduced without compromising primary fixation, by using different instruments to widen the keel slot.

Methods: Keel slots were made in polyurethane blocks ($n = 60$) using the standard keel cut saw blade or a new blade that was 0.2 mm wider, with adjuvant use of the cemented pick or a prototype rasp. A tibial component was pushed into and pulled out of the slots using a Dartec materials testing machine. It was assumed that the 'push-in' force was related to the risk of fracture and 'pull-out' force was related to fixation. Reproducibility studies with 10 different tibial components were undertaken.

Results: The new blade required significantly lower push-in forces than the standard blade (789 N SD 130, 1411 N SD 180; $P < 0.001$), but the pull-out forces were not different (240 N SD 47, 230 N SD 56; $P > 0.999$). With the standard blade the pick decreased the push-in (818 N SD 318; $P < 0.001$) and pull-out (128 N SD 58; $P < 0.001$) forces, but the rasp had no effect. With the new blade the pick had no effect, but the rasp increased the push-in force (1390 N SD 202; $P < 0.001$). **Conclusions:** This study suggests the fracture risk will be reduced with the new blades, with no compromise in fixation. If the new blades are used routine use of the cemented pick appears to be of no benefit.

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1. Introduction

Unicompartmental knee replacement (UKR) is an effective treatment for end stage knee osteoarthritis with advantages over total knee replacement (TKR) including faster recovery, fewer complications, superior patient reported outcomes and reduced mortality [1]. UKR does however have a higher revision rate. This is primarily due to a lower threshold for revision, which may in part relate to misinterpretation of radiolucent lines that are commonly seen around UKR. The cementless Oxford UKR has been shown to have a much lower incidence of radiolucent lines than the cemented, suggestive of improved fixation [2]. In the New Zealand Joint Registry the cementless Oxford UKR has a 96% 10-year survival which is better than that of the cementless Oxford UKR and is similar to that achieved by TKR [3].

The cemented and cementless Oxford UKR components are similar except that the surfaces of cementless components in contact with bone are coated with porous titanium and hydroxyapatite to encourage bony ingrowth [4,5]. Primary fixation is depen-

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Ten-year clinical and radiographic results of 1000 cementless Oxford unicompartmental knee replacements

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Abstract

Purpose Unicompartmental knee replacement (UKR) has substantial benefits over total knee replacement (TKR) but has higher revision rates. The cementless Oxford UKR was introduced to address this but there are concerns about fixation and tibial plateau fractures. The first long-term study of the device with clinical and radiographic outcomes is reported.

Methods The first 1000 medial cementless Oxford UKR were prospectively identified and followed up by independent physiotherapists. Survival was calculated using the endpoints reoperation, revision, revision to TKR, major revision requiring revision TKR components and patient mortality. The Oxford Knee Score (OKS), Tegner Activity Score and American Knee Society Score (AKSS) were recorded and radiographs analysed.

Results The ten year survival was 96.6% (CI 94.8–97.8), 97.5% (CI 95.7–98.5), 98.9% (CI 97.7–99.4) and 99.6% (CI 98.8–99.9) using reoperation, revision, revision to TKR and major revision as the endpoint, respectively. Commonest causes for revision were bearing dislocation ($n=7$, 0.7%), disease progression ($n=4$, 0.4%) and pain ($n=2$, 0.2%). There was one lateral tibial plateau fracture and one femoral component loosening. At 10 years, the mean OKS was 41.2 (SD 9.8), Tegner 2.8 (SD 1.3), AKSS-O 89.1 (SD 13.0) and AKSS-F 80.4 (SD 14.6). There were no pathological radiolucencies or complete radiolucent lines. There were no implant-related deaths.

Conclusions The cementless Oxford UKR is a safe procedure with excellent long-term clinical results. Our results suggest that reliable fixation was achieved with only one (0.1%) revision for loosening (femoral), no radiographic evidence of loosening in the remaining cases and no fractures related to implantation.

Level of evidence III.

Keywords Cementless fixation · Long-term outcomes · Unicompartmental knee replacement

Abbreviations

AKSS-F	American Knee Society Functional Score
AKSS-O	American Knee Society Objective Score
AMOA	Anteromedial osteoarthritis
CI	Confidence intervals
IQR	Interquartile range
OKS	Oxford Knee Score
RCT	Randomised controlled trial
SD	Standard deviation

TKR	Total knee replacement
UKR	Unicompartmental knee replacement

Introduction

The two main established treatments for end stage medial compartment osteoarthritis are total knee replacement (TKR) and unicompartmental knee replacement (UKR) [26]. UKR has substantial benefits over TKR including a faster recovery, better functional outcomes and cost effectiveness but has higher revision rates [3, 16, 28].

The most commonly used UKR is the Oxford UKR (Zimmer Biomet, Swindon, UK) [26]. The cemented version was introduced in 1998, and is implanted through a minimally invasive approach [7]. The most common causes for revision by the National registers are aseptic loosening and pain [1,

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■ KNEE

Long-term *in vivo* wear of different bearing types used for the Oxford Unicompartmental Knee Replacement

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Objectives

The aim of this study was to determine the polyethylene wear rate of Phase 3 Oxford Unicompartmental Knee Replacement bearings and to investigate the effects of resin type and manufacturing process.

Methods

A total of 63 patients with at least ten years' follow-up with three bearing types (1900 resin machined, 1050 resin machined, and 1050 resin moulded) were recruited. Patients underwent full weight-bearing model-based radiostereometric analysis to determine the bearing thickness. The linear wear rate was estimated from the change in thickness divided by the duration of implantation.

Results

The wear rate for 1900 resin machined ($n = 19$), 1050 machined ($n = 21$), and 1050 moulded bearings ($n = 23$) were $60 \mu\text{m}/\text{year}$ (sd 42), $76 \mu\text{m}/\text{year}$ (sd 32), and $57 \mu\text{m}/\text{year}$ (sd 30), respectively. There was no significant difference between 1900 machined and 1050 machined ($p = 0.20$), but 1050 moulded had significantly less wear than the 1050 machined ($p = 0.05$). Increasing femoral ($p < 0.001$) and tibial ($p < 0.001$) component size were associated with increasing wear.

Conclusion

Wear rate is similar with 1050 and 1900 resin, but lower with moulded bearings than machined bearings. The currently used Phase 3 bearings wear rate is low (1050 moulded, $57 \mu\text{m}/\text{year}$), but higher than the previously reported Phase 2 bearings (1900 moulded, $20 \mu\text{m}/\text{year}$). This is unlikely to be due to the change in polyethylene but may relate to the minimally invasive approach used with the Phase 3. This approach, as well as improving function and thus increasing activity levels, may increase the risk of surgical errors, such as impingement or bearing overhang, which can increase wear. Surgeons should aim to use 4 mm thick bearings rather than 3 mm thick bearings in young patients, unless they are small and need conservative bone resections.

Cite this article: *Bone Joint Res* 2019;8:535–543.

Keywords: Mobile bearing unicompartmental knee replacement, Polyethylene, Long-term wear

Article focus

- To determine the polyethylene wear rate of the Phase 3 Oxford Unicompartmental Knee Replacement bearings.
- To determine if the polyethylene resin type or manufacturing process influences the wear rate.

Key messages

- The wear rate of currently used Oxford Unicompartmental Knee Replacement

bearings, which are moulded from 1050 resin, is very low ($0.06 \text{ mm}/\text{yr}$) but is higher than that of the previous Phase 2 bearings.

- The wear rate is the same for bearings made of 1050 and 1900 resin, but is less when moulded rather than machined.

- With machined bearings, the wear rate increased with component size; with moulded bearings, it appeared to be

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RESEARCH ARTICLE

Open Access

The clinical outcomes of cementless unicompartmental knee replacement in patients with reduced bone mineral density



Hasan R. Mohammad^{1,2*} , James A. Kennedy¹, Stephen J. Mellon¹, Andrew Judge^{1,2}, Christopher A. Dodd³ and David W. Murray^{1,3}

Abstract

Background: Osteoporosis and osteopenia are conditions characterised by reduced bone mineral density (BMD). There is concern that bone with reduced BMD may not provide sufficient fixation for cementless components which primarily rely on the quality of surrounding bone. The aim of our study was to report the midterm clinical outcomes of patients with reduced BMD undergoing cementless unicompartmental knee replacements (UKR). Our hypothesis was that there would be no difference in outcome between patients with normal bone and those with reduced BMD.

Methods: From a prospective cohort of 70 patients undergoing cementless UKR surgery, patients were categorised into normal ($n = 20$), osteopenic ($n = 38$) and osteoporotic groups ($n = 12$) based on their central dual-energy X-ray absorptiometry (DEXA) scans according to the World Health Organization criteria. Patients were followed up by independent research physiotherapists and outcome scores; Oxford Knee Score (OKS), Tegner score, American Knee Society Score Functional (AKSS-F) and Objective (AKSS-O) were recorded preoperatively and at a mean of 4 years postoperatively. The prevalence of reoperations, revisions and mortality was also recorded at a mean of 5 years postoperatively.

Results: There were no significant differences in the midterm postoperative OKS ($P = 0.83$), Tegner score ($P = 0.17$) and AKSS-O ($P = 0.67$). However, the AKSS-F was significantly higher ($P = 0.04$) in normal (90, IQR 37.5) compared to osteoporotic (65, IQR 35) groups. There were no significant differences ($P = 0.82$) between normal and osteopenic bone (80, IQR 35). The revision prevalence was 5%, 2.6% and 0% in the normal, osteopenic and osteoporotic groups respectively. The reoperation prevalence was 5%, 7.9% and 0% respectively. There were no deaths in any group related to the implant.

Conclusions: We found that patients with reduced BMD could safely undergo cementless UKR surgery and have similar clinical outcomes to those with normal BMD. However, larger studies with longer follow-up are needed to confirm our findings and ensure that cementless fixation is safe in patients with reduced BMD.

Keywords: Bone mineral density, Cementless, Oxford UKR

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Comparison of the 10-year outcomes of cemented and cementless unicompartmental knee replacements: data from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man

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Background and purpose — Unicompartmental knee replacement (UKR) offers advantages over total replacement but has higher revision rates, particularly for aseptic loosening. The cementless Oxford UKR was introduced to address this. We undertook a registry-based matched comparison of cementless and cemented UKRs.

Patients and methods — From 40,552 Oxford UKRs identified by the National Joint Registry for England, Wales, Northern Ireland and Isle of Man (NJR) we propensity score matched, based on patient, surgical, and implant factors, 7,407 cemented and 7,407 cementless UKRs (total = 14,814).

Results — The 10-year cumulative implant survival rates for cementless and cemented UKRs was 93% (95% CI 90–96) and 90% (CI 88–92) respectively, with this difference being significant (HR 0.76; $p = 0.002$). The risk of revision for aseptic loosening was less than half ($p < 0.001$) in the cementless (0.42%) compared with the cemented group (1.00%), and the risk of revision also decreased for unexplained pain (to 0.46% from 0.74%; $p = 0.03$) and lysis (to 0.04% from 0.15%; $p = 0.03$). However, the risk of revision for periprosthetic fracture increased significantly ($p = 0.01$) in the cementless (0.26%) compared with the cemented group (0.09%). 10-year patient survival rates were similar (HR 1.2; $p = 0.1$).

Interpretation — The cementless UKR has improved 10-year implant survival compared with the cemented UKR, independent of patient, implant, and surgical factors. This improved survival in the cementless group was primarily the result of lower revision rate for aseptic loosening, unexplained pain, and lysis, suggesting the fixation of the cementless was superior. However, there was a small increased risk of revision for periprosthetic fracture with the cementless implant.

Over 100,000 primary knee replacements are performed annually in the United Kingdom, with these numbers rapidly increasing (National Joint Registry 2018). This includes both total knee replacement (TKR) and unicompartmental knee replacement (UKR). Although UKR offers significant advantages over TKR including faster recovery, fewer complications, improved function, and lower mortality (Liddle et al. 2014, 2015, Burn et al. 2018), its revision rate is higher in the National Registries (New Zealand Joint Registry 2016, Australian Orthopaedic Association 2018, National Joint Registry 2018).

The most commonly used UKR is the Phase 3 Oxford (Zimmer Biomet, Swindon, UK), which has a fully congruent mobile bearing and is implanted using a minimally invasive approach (Pandit et al. 2006). The cemented version was introduced in 1998. The commonest reasons for revision include aseptic loosening and pain (Mohammad et al. 2018). Radiolucent lines, also known as physiological radiolucencies, are indicative of fibrocartilage at the interface and are seen in over half of cemented UKR tibial components (Gulati et al. 2009). In the presence of pain, these can be misinterpreted as aseptic loosening and lead to revisions despite studies showing no relation (Gulati et al. 2009). In an attempt to decrease the revision rate a cementless version was introduced in 2004, with the only changes to the implant being a porous coating of titanium and hydroxyapatite, and the femoral component having an additional peg.

Randomized controlled trials comparing cemented and cementless UKRs found no statistically significant difference in functional outcomes, but the prevalence of partial and complete radiolucencies was reduced with cementless implants (Pandit et al. 2013). These trials were too small to compare revision rates. However, data from the New Zealand Joint Reg-



A commentary by Per-Henrik Randsborg, MD, PhD, is linked to the online version of this article at jbjs.org.

The Effect of Surgeon Caseload on the Relative Revision Rate of Cemented and Cementless Unicompartamental Knee Replacements

An Analysis from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man

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Investigation performed at the Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Nuffield Orthopaedic Centre, University of Oxford, Oxford; and the Musculoskeletal Research Unit, Bristol Medical School, University of Bristol, Southmead Hospital, Bristol, United Kingdom

Background: Unicompartamental knee replacement (UKR) offers substantial benefits compared with total knee replacement (TKR) but is associated with higher revision rates. Data from registries suggest that revision rates for cementless UKR implants are lower than those for cemented implants. It is not known how much of this difference is due to the implant or to other factors, such as a greater proportion of high-volume surgeons using cementless implants. We aimed to determine the effect of surgeon caseload on the revision rate of matched cemented and cementless UKRs.

Methods: From a group of 40,522 Oxford (Zimmer Biomet) UKR implants (30,814 cemented, 9,708 cementless) recorded in the National Joint Registry, 14,814 (7,407 cemented, 7,407 cementless) were propensity-score matched. Surgeons were categorized into 3 groups: low volume (<10 cases/year), medium volume (10 to <30 cases/year), and high volume (≥30 cases/year). The effect of caseload on the relative risk of revision was assessed with use of Cox regression.

Results: The 10-year survival rates for unmatched cementless and cemented UKR implants were 93.3% (95% confidence interval [CI] = 89.8% to 95.7%) and 89.1% (95% CI = 88.6% to 89.6%), respectively, with the difference being significant (hazard ratio [HR] = 0.59; $p < 0.001$). Cementless UKR implants had a greater proportion of high-volume surgeon users than cemented implants (30.4% compared with 15.1%). Following matching, the 10-year survival rates were 93.2% (95% CI = 89.7% to 95.6%) and 90.2% (95% CI = 87.5% to 92.3%), which were still significantly different (HR = 0.76; $p = 0.002$). The 10-year survival rates for matched cementless and cemented UKR implants were 86.8% (95% CI = 73.6% to 93.7%) and 81.8% (95% CI = 73.0% to 88.0%) for low-volume surgeons, 94.3% (95% CI = 92.2% to 95.9%) and 92.5% (95% CI = 89.9% to 94.5%) for medium-volume surgeons, and 97.5% (95% CI = 96.5% to 98.2%) and 94.2% (95% CI = 90.8% to 96.4%) for high-volume surgeons. The revision rate for cementless implants was lower for surgeons in all 3 caseload groups (HR = 0.74, 0.79, 0.80, respectively).

Conclusions: Cementless fixation decreased the revision rate by about a quarter, whatever the surgeon caseload. Caseload had a profound effect on implant survival. Low-volume surgeons had a high revision rate with cemented or cementless fixation and therefore should consider either stopping or doing more UKR procedures. High-volume surgeons performing cementless UKR demonstrated a 10-year survival rate of 97.5%, which was similar to that reported in registries for the best-performing TKRs.

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

Disclosure: Zimmer Biomet provided grant support for this work. The funding source did not play a role in the investigation. On the **Disclosure of Potential Conflicts of Interest** forms, which are provided with the online version of the article, one or more of the authors checked "yes" to indicate that the author had a relevant financial relationship in the biomedical arena outside the submitted work and "yes" to indicate that the author had a patent and/or copyright, planned, pending, or issued, directly relevant to this work (<http://links.lww.com/JBJS/F714>).



Contents lists available at ScienceDirect

The Knee



New surgical instrumentation reduces the revision rate of unicompartmental knee replacement: A propensity score matched comparison of 15,906 knees from the National Joint Registry

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Non-Microplasty

Unicompartmental knee arthroplasty

Background: Unicompartmental knee replacement (UKR) offers advantages over total knee replacement but has higher revision rates. New instrumentation known as Microplasty was introduced to address this. The aim was to compare the revision rates of UKRs implanted with Microplasty and traditional instrumentation (Non-Microplasty).

Methods: National Joint Registry (NJR) data was used to propensity score match 15,906 UKRs (7953 Microplasty and 7953 Non-Microplasty) for important patient, implant and surgical factors. Implant survival rates were determined using the Kaplan–Meier method and compared using Cox regression models in a multilevel model.

Results: The five-year implant survival for Microplasty and Non-Microplasty UKRs were 96.7% (95% CI: 96.0%–97.2%) and 94.5% (CI: 93.8–95.1%), respectively. The revision rate for Microplasty UKR was significantly lower than that of Non-Microplasty UKRs (hazard ratio [HR] = 0.77, $p = 0.008$). Compared with Non-Microplasty UKRs, the revision rate of Microplasty UKRs implanted during the year after the introduction of Microplasty was lower, but the difference was not significant (HR: 0.86, CI: 0.67–1.10, $p = 0.23$), whereas for those implanted more than a year after introduction, the difference was significant (HR: 0.69, CI: 0.54–0.89, $p = 0.004$).

Conclusion: The use of Microplasty instrumentation has resulted in an improved five-year UKR survival. Microplasty UKR implanted during the first year after introduction had a small, non-significant decrease in revision rate. As the revision rate did not increase, this suggests that there is no adverse learning curve effect. Microplasty UKRs implanted after this transition period had a revision rate 31% lower than the Non-Microplasty group.

Level of evidence: II.

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1. Introduction

Total and unicompartmental knee replacement (TKR, UKR) are the two main treatments for knee osteoarthritis that has failed to respond to conservative therapy, with evidence that UKR is appropriate in up to 50% of cases [1]. Although UKR is more cost-

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A matched comparison of revision rates of cemented Oxford Uni-compartmental Knee Replacements with Single and Twin Peg femoral components, based on data from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man

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Background and purpose — Registries report high revision rates after unicompartmental knee replacement (UKR) due, in part, to aseptic loosening. In an attempt to improve Oxford UKR femoral component fixation a new design was introduced with a Twin rather than a Single peg. We used the National Joint Registry (NJR) to compare the 5-year outcomes of the Single and Twin Peg cemented Oxford UKRs.

Patients and methods — We performed a retrospective observational study using NJR data on propensity score matched Single and Twin Peg UKRs (matched for patient, implant and surgical factors). Data on 2,834 Single Peg and 2,834 Twin Peg were analyzed. Cumulative implant survival was calculated using the Kaplan–Meier method and comparisons between groups performed using Cox regression models.

Results — In the matched cohort, the mean follow up for both Single and Twin Peg UKRs was 3.3 (SD 2) and 3.4 years (SD 2) respectively. The 5-year cumulative implant survival rates for Single Peg and Twin Peg were 94.8% (95% CI 93.6–95.8) and 96.2% (CI 95.1–97.1) respectively. Implant revision rates were statistically significantly lower in the Twin Peg (hazard ratio [HR]) = 0.74; $p = 0.04$). The revision rate for femoral component aseptic loosening decreased significantly ($p = 0.03$) from 0.4% ($n = 11$) with the Single Peg to 0.1% ($n = 3$) with the Twin Peg. The revision rate for pain decreased significantly ($p = 0.01$) from 0.8% ($n = 23$) with the Single Peg to 0.3% ($n = 9$) with the Twin Peg. No other reasons for revision had significant differences in revision rates.

Interpretation — The revision rate for the cemented Twin Peg Oxford UKR was 26% less than the Single Peg Oxford UKR. This was mainly because the revision rates for femoral loosening and pain more than halved. This suggests that the Twin Peg component should be used in preference to the Single Peg design.

Unicompartmental knee replacement (UKR) for anteromedial knee arthritis has many advantages over total knee replacement (TKR) (Wilson et al. 2019). However, national registries suggest that UKR revision rates are several times higher than TKR, with aseptic loosening a leading cause (New Zealand Joint Registry 2016, National Joint Registry 2018).

The most commonly used UKR is the Phase 3 Oxford UKR. The initial Phase 3 femoral component, like its predecessors, was spherical and cemented. It had a single peg that was thought to be helpful as it allowed the component to seat optimally (Figure 1). However, as 25–50% of aseptic loosening was femoral (Mohammad et al. 2018), it was felt that the introduction of a Twin Peg component that might improve fixation would be advantageous. During surgery a small hole is made in the femur anterior to the main peg hole to stabilize the femoral saw guide. A second peg, which would fit in the small hole, was therefore added, allowing the new component to be used with standard instrumentation. In order to support the peg, the spherical part of the component was extended about 15° further anteriorly. To accommodate this extension more bone is removed anteriorly, which decreases the risk of the bearing impinging. This also allows the femoral component to be implanted in increased flexion.



Figure 1. The Oxford UKR with Single and Twin Peg femoral component.

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Cementless unicompartmental knee replacement achieves better ten-year clinical outcomes than cemented: a systematic review

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Abstract

Purpose The aim of this study was to report and compare the long-term revision rate, revision indications and patient reported outcome measures of cemented and cementless unicompartmental knee replacements (UKR).

Methods Databases Medline, Embase and Cochrane Central of Controlled Trials were searched to identify all UKR studies reporting the ≥ 10 year clinical outcomes. Revision rates per 100 component years [% per annum (% pa)] were calculated by fixation type and then, subgroup analyses for fixed and mobile bearing UKRs were performed. Mechanisms of failure and patient reported outcome measures are reported.

Results 25 studies were eligible for inclusion with a total of 10,736 UKRs, in which there were 8790 cemented and 1946 cementless knee replacements. The revision rate was 0.73% pa (CI 0.66–0.80) and 0.45% pa (CI 0.34–0.58) per 100 component years, respectively, with the cementless having a significantly ($p < 0.001$) lower overall revision rate. Therefore, based on these studies, the expected 10-year survival of cementless UKR would be 95.5% and cemented 92.7%. Subgroup analysis revealed this difference remained significant for the Oxford UKR (0.37% pa vs 0.77% pa, $p < 0.001$), but for non-Oxford UKRs there were no significant differences in revision rates of cemented and cementless UKRs (0.57% pa vs 0.69% pa, $p = 0.41$). Mobile bearing UKRs had significantly lower revision rates than fixed bearing UKRs in cementless ($p = 0.001$), but not cemented groups ($p = 0.13$). Overall the revision rates for aseptic loosening and disease progression were significantly lower ($p = 0.02$ and $p = 0.009$ respectively) in the cementless group compared to the cemented group (0.06 vs 0.13% pa and 0.10 vs 0.21% pa respectively).

Conclusions Cementless fixation had reduced long-term revision rates compared to cemented for the Oxford UKR. For the non-Oxford UKRs, the revision rates of cementless and cemented fixation types were equivalent. Therefore, cementless UKRs offer at least equivalent if not lower revision rates compared to cemented UKRs.

Level of evidence III.

Keywords Arthroplasty · UKA · Unicondylar

Abbreviations

AKSS-O American Knee Society Score (Objective)
AKSS-F American Knee Society Score (Functional)
CENTRAL Cochrane Central of Controlled Trials

CI Confidence interval
HSS Hospital for Special Surgery knee score
KSS Knee Society Score
MINOR Methodological index for evaluation of non-randomised studies
OKS Oxford Knee Score
pa Per annum
PROM Patient-reported outcome measure
PRISMA Preferred reporting items for systematic reviews and meta-analyses
TKR Total knee replacement
WOMAC Western Ontario and McMaster universities arthritis index
UKR Unicompartmental knee replacement

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APPENDIX 2

A2.1 Ovid Medline search strategy

- 1 exp knee arthroplasty/
- 2 "knee replace*".ti,ab.
- 3 "knee arthroplasty".ti,ab.
- 4 "knee reconstruction".ti,ab.
- 5 1 or 2 or 3 or 4
- 6 partial.ti,ab.
- 7 unicompartmental.ti,ab.
- 8 unicondylar.ti,ab.
- 9 uni.ti,ab.
- 10 UKA.ti,ab.
- 11 UKR.ti,ab.
- 12 UCA.ti,ab.
- 13 UCR.ti,ab.
- 14 PKA.ti,ab.
- 15 PKR.ti,ab.
- 16 PCA.ti,ab.
- 17 Oxford.ti,ab.
- 18 meniscal.ti,ab.
- 19 mobile.ti,ab.
- 20 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
- 21 5 and 20
- 22 1 and 20
- 23 21
- 24 limit 23 to yr="2008 -Current"
- 25 exp treatment outcome/
- 26 exp follow up/
- 27 (ten or "10-year" or "10 year" or "10year").ti,ab.
- 28 (fifteen or "15-year" or "15 year" or "15year").ti,ab.
- 29 long*.ti,ab.
- 30 25 or 26 or 27 or 28 or 29
- 31 5 and 20 and 30
- 32 31
- 33 limit 32 to yr="2008 -Current"
- 34 33

35 medial.mp. [mp=title, abstract, original title, name of substance word, subject heading word,
keyword heading word, protocol supplementary concept word, rare disease supplementary concept
word, unique identifier]

36 34 and 35

37 exp Cohort Studies/

38 25 or 27 or 28 or 29 or 37

39 5 and 20 and 35 and 38

40 39

41 limit 40 to yr="2008 -Current"

A2.2 EMBASE search strategy

1 exp knee arthroplasty/
2 "knee replace*".ti,ab.
3 "knee arthroplasty".ti,ab.
4 "knee reconstruction".ti,ab.
5 1 or 2 or 3 or 4
6 partial.ti,ab.
7 unicompartmental.ti,ab.
8 unicondylar.ti,ab.
9 uni.ti,ab.
10 UKA.ti,ab.
11 UKR.ti,ab.
12 UCA.ti,ab.
13 UCR.ti,ab.
14 PKA.ti,ab.
15 PKR.ti,ab.
16 PCA.ti,ab.
17 Oxford.ti,ab.
18 meniscal.ti,ab.
19 mobile.ti,ab.
20 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21 5 and 20
22 1 and 20
23 21
24 limit 23 to yr="2008 -Current"
25 exp treatment outcome/
26 exp follow up/

27 (ten or "10-year" or "10 year" or "10year").ti,ab.
 28 (fifteen or "15-year" or "15 year" or "15year").ti,ab.
 29 long*.ti,ab.
 30 25 or 26 or 27 or 28 or 29
 31 5 and 20 and 30
 32 31
 33 limit 32 to yr="2008 -Current"
 34 33
 35 medial.mp. [mp=title, abstract, heading word, drug trade name, original title, device
 manufacturer, drug manufacturer, device trade name, keyword, floating subheading] (144350)
 36 33 and 35

A2.3 CENTRAL search strategy

ID	Search Hits
#1	MeSH descriptor: [Arthroplasty, Replacement, Knee] explode all trees
#2	"knee replace*"
#3	"knee arthroplasty"
#4	"knee reconstruction"
#5	#2 or #3 or #4 or #1
#6	partial or unicompartmental or unicondylar or uni or UKA or UKR or UCA or UCR or PKA or PCR or Oxford or meniscal or mobile
#7	medial
#8	#5 and #6 and #7

A2.4 Abstracts from Oxford Partial Knee 40 Year Symposium

Multi-Center Study of 825 Phase III Oxford Medial Compartmental Arthroplasty Knees:

An Average Ten-Year Survival Analysis in the United States

Omar K. Alnachoukati MS, Keith Berend MD, Mike Kolczun MD, Roger Emerson MD, Adolf Lombardi MD, David Mauerhan MD, John Barrington MD

Abstract

Background Since its creation in the 1970's, the Oxford partial knee system has evolved into the most recent Phase III Oxford medial compartmental knee design. 40 years of development has resulted in a non-fixated meniscal bearing implant, with several size variations, that has again raised the bar in regards to fixation and function, in comparison to its predecessor designs. This study seeks to provide the first long-term survivorship, large patient sample size study in the United States looking at the various aspects of the Phase III Oxford design while also addressing recent advancements that can help aid the UKA process and improve partial knee survivorship.

Methods Five Surgeons from across the United States; four joint replacement sites, two from Ohio, one from North Carolina, and one from Texas, implanted the phase III Oxford medial compartmental partial knee system (Zimmer Biomet, Warsaw, IN) in a combined 825 knees, between 2004 and 2006, while utilizing phase III instrumentation.

Results 825 knees were implanted with the Oxford implant. Ten-year survivorship for the implant was 90%, calculating revisions related to implant fixation and function as the endpoint. The ten-year survivorship for the unicompartmental knee replacement procedure, calculating all revisions as the endpoint, was 85%. Survivorship was calculated utilizing the Life Table Method. Average range of motion across all sites was 122 degrees, average Knee Society Score was 90, and average Knee Society Function Score was 77. 53% of patients were female, and 47% were male. Average age for all patients was 64, with an average BMI of 32.

Conclusions The most recently upgraded Oxford partial knee design, incorporating a non-fixated meniscal bearing, has clearly proven greater survivorship in comparison to its predecessor. The unicompartmental knee arthroplasty is proving to be a viable option for both patients and surgeons to consider for those who meet AMOA criteria. Being the first Oxford Phase III multi-center study in the United States, and of this size, the long term results of the Oxford implant demonstrate good survivorship long-term. Appropriate patient selection, the use of radiographic valgus stress tests, and the improved Microplasty instrumentation, provide new advancements that have the potential to further better UKA survivorship.

The Twin Peg Oxford Knee – 10 Year Survivorship and Surgical Principles

Author: Stephen H White, Jan Herman Kuipers, Sharon Roberts

The Robert Jones and Agnes Hunt Orthopaedic Hospital NHS Foundation Trust, Oswestry, Shropshire. SY10 7AG

Abstract

Concerns over the risk of femoral loosening with the single peg Oxford knee led us to use the Twin Peg Oxford knee since 2003. There were additional theoretical advantages of better congruency in high flexion. We describe the surgical principles which we used and the survivorship at 10 years of a cohort of 455 patients (563 implants), treated with the Oxford Twin Peg cemented knee replacement. In all, 16 implants needed revision, and the 10 year survivorship was 95%. The results were most favourable for anteromedial osteoarthritis. There were no failures due to femoral loosening but there was a higher revision rate for patients with extended indications.

In this independent series, the 10 year survivorship of the Oxford Twin Peg knee was comparable with the excellent outcomes published by the Oxford Group for the single peg implant.

Long-term survival of a Single-surgeon Consecutive series of The Oxford Partial Knee Arthroplasty

Kendall RW

Abstract:

BACKGROUND: Long term success of partial knee replacements remains controversial. A 15-year single surgeon series of the Oxford Partial knee replacement is discussed.

Methods: This study reviewed a consecutive series of 414 patients who underwent 523 Oxford Medial Partial knee replacements between 2001 and 2016. The average age at the time of implantation was 66 years, 8 months (range 42-89 years). Females 59.5% and Males 40.5%. Median time to follow-up was 40 months (Range 1 to 163 months). 31 patients were deceased and a further 23 were lost to follow-up. Implant survival and major complications will be reviewed.

Results: The 15 year cumulative survival rate was 95.9%. There were 21 conversions to total knee (20 patients). Reasons for revision include 6 revisions for unexplained pain; 5 for lateral OA (2 late diagnosis inflammatory arthritis); 5 for tibial component loosening; 3 for both tibial and femoral loosening; 1 for femoral loosening, and 1 for infection. The average time to revision was 54 month (9 to 129 months). An additional 17 knees remained at risk for suspected component loosening without revision (8 knees), symptomatic lateral OA (6 knees) or symptomatic patellofemoral OA (3 knees).

Re-operation rate for all causes was 7.3%. Re-operation included 21 conversion to total knee (4%), 1 Femoral re-implantation for dislocation (0.2%) (with subsequent dislocation and conversion to TKA), 2 single-stage bearing exchange and debridement for acute infection (0.4%), 5 manipulation under anaesthetic for arthrofibrosis (0.95%), 6 arthrotomy with bearing exchange (3 unexplained pain, 2 retained cement removal and one bearing subluxation with locking 1.1%), 3 wound revision (2 dehiscence and 1 pre-tibial rotation flap for skin necrosis).

There was a 9.5% major post-operative complication rate which included: 22 persistent medial knee pain greater than 6 months (4.2%); 6 Superficial infections (1.1%); 6 persistent post-op effusion or recurrent haematoma greater than 6 months (1.1%); 5 arthrofibrosis requiring remanipulation (.95%); 4 DVT/PE (0.76%, none fatal); 3 deep infection requiring re-operation (.57%: one 2-stage exchange to TKA and 2 single stage bearing exchange, debridement and wash out); 3 wound dehiscence

(0.57%); 1 transfusion (0.2%); no bearing dislocations. No deaths in the first 3 month peri-operative period attributable to post-operative complications.

Conclusion: The Oxford partial knee arthroplasty is a predictable, durable implant with a low complication and revision rate at mid term follow-up.

Nikolai N. Kornilov¹, Taras A. Kuliaba¹, Ruslan E. Fedorov², Alexey S. Fill¹,
Alexander V. Selin¹.

Causes and time of surgical interventions after “Oxford” unicompartmental knee arthroplasty: results of a 15 years Vreden Institute experience.

(1) Knee surgery departments N 17 & 10, Russian Research Institute of Traumatology and Orthopaedics n.a. R.R.Vreden, Akademika Baikova street 8, 195427 Saint-Petersburg, Russia

(2) Trauma and orthopedic surgery department, Smolensk Regional Hospital, Gagarina avenue 27, 214018 Smolensk, Russia

Corresponding author – Nikolai Kornilov

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Abstract

Aim: To retrospectively analyze the causes and time of any surgical intervention after “Oxford” unicompartmental knee arthroplasty (UKA) during the last fifteen years in the biggest Russian arthroplasty center.

Materials and Methods: Regarding Vreden Institute database 254 “Oxford” UKA’s were performed in 249 patients from the first implantation in 2001 till the December of 2015. The primary diagnosis was knee osteoarthritis (OA) in 203 (79,9%) and osteonecrosis of medial femoral condyle in 51 (20,1%) patients. The medial knee compartment was replaced in 252 (99,2%) and lateral – only in 2 (1,8%) patients. The surgical interventions were required only after medial UKA in 21 (8,3%) cases.

Results: The main reasons for surgical interventions after “Oxford” UKA were loosening of tibial component (8 (38,1%)) and knee injuries (8 (38,1%)), while PJI or OA progression happened more rarely – 3 (14,3%) and 2 (9,5%) correspondently. In 19 (90,5%) patients full revision to total knee arthroplasty was performed, while in 2 (9,5%) arthroscopic procedures resolved the problem.

The mean time from the primary procedure till second surgery was 4,2 years. The majority of traumatic accidents happened during sport activities in the first 5 years after surgery while loosening spread more uniformly across mid- and long-

term period. 80,9% of re-operations took place in the first 5 years after primary surgery.

During UKA revisions the necessity of varus-valgus constrained implants was rare (1 (5,3%)), while in most surgeries CR (68,4%) or PS (26,3%) implants were used. Bone deficiency of medial tibial or femoral condyles were substituted by autologous graft from the lateral plato in 3 (15,8%) and by modular metal block also in 3 (15,8%) patients.

Conclusion: Consider that various sport-associated traumatic accidents along with aseptic loosening of tibial component are the leading reasons of re-operation after “Oxford” UKA the special prevention program may be beneficial for patients who like to maintain the high level of physical activity. The importance of the proper patient selection and meticulous surgical technique in UKA can not be underestimated as well.

Level of evidence: IV

Key words: Unicompartmental knee arthroplasty, revision, complication, failure.

SP15

TEN-YEAR SURVIVAL OF MINIMALLY INVASIVE CEMENTLESS OXFORD PHASE 3 UNICOMPARTMENTAL KNEE REPLACEMENT

Campi S.¹, Pandit H.G.^{1,2}, Hooper G.³, Snell D.³, Jenkins C.², Dodd C.A.F.², Maxwell R.³, Murray D.W.^{1,2}

¹Nuffield Dept. of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford;

²Nuffield Orthopaedic Centre, Oxford University Hospital NHS Foundation Trust, Oxford, UK; ³Dept. of Orthopaedic Surgery and Musculoskeletal Medicine, University of Otago, Christchurch, New Zealand

Introduction: Cementless fixation is an alternative to cemented Oxford Unicompartmental Knee Replacement (OUKR), with potential advantages including avoidance of cementation errors, reduced incidence of radiolucencies and faster surgical time. However, no 10-year survival and outcome studies have been published so far. The aim of the study is to determine the 10-year survival, the clinical outcome and modes of failure of the cementless OUKR.

Materials and Methods: This prospective study describes the outcome of 1000 consecutive cementless OUKRs implanted using a minimally invasive surgical approach for the recommended indications in two centres and followed up independently. Patients were clinically assessed using the Oxford knee score (OKS). Survival was determined with life table analysis. Revision was defined as exchange or addition of a new component in the knee.

Results: The mean follow-up of was 7.0 years (range 4.7 to 12.1 years). The mean OKS improved from 23 (SD 8) preoperatively to 42 (SD 7) at the last follow-up ($p < 0.001$). Considering revisions for any cause, the survival at 10 years of follow-up was 97% (CI 95%: 93.1-100%) with 87 patients at risk in the tenth year. Twenty-two cases (2.5%) needed revision surgery. The most common reason for revision was progression of arthritis in the retained compartment in 11 cases (1.1%) followed by dislocation of the bearing in 8 cases (0.8%). Out of the 11 knees needing further surgery for progression of arthritis 5 were treated with revision to a total knee replacement (TKR) and 6 with addition of a UKR. The 6 cases of bearing dislocation were treated with insertion of a new bearing. There were two tibial fractures and two tibial component loosening, all revised to TKR. Two further patients required revision to TKR, one for impingement caused by tibial component overhang and one for persistent pain.

Conclusions: The cementless OUKR is a safe and effective procedure in patients with end-stage anteromedial osteoarthritis of the knee, with excellent survival and clinical outcome at long-term follow-up.

A2.5 Additional tables for Chapter 2

Study	Year	Country	Reason for exclusion
Kumar et al. ³³³	2015	United Kingdom	Uses subgroup of cohort completely used in Pandit et al. ⁸² .
Hamilton et al. ²⁴⁹	2016	United Kingdom	Uses subgroup of cohort completely used in Pandit et al. ⁸² .
Mercier et al. ³³⁴	2010	France	Study using the Oxford phase 2 prosthesis.
Price et al. ²³⁰	2011	Sweden/United Kingdom	Uses cohort of Oxford phase 1,2 and 3. Reports results of all implants combined.
Faour-Martin et al. ³³⁵	2015	Spain	Uses subgroup previous cohort from Faour-Martin et al. ¹⁶³ .
Emerson et al. ³³⁶	2008	USA	Cohort using the Oxford Phase 2 implant
Pandit et al. ³³⁷	2010	United Kingdom	Uses same cohort as more recent paper published ²⁴⁷ .
Jones et al. ³³⁸	2012	United Kingdom	Uses same cohort as paper published by Bottomley et al. ¹⁵⁹ .

Table A1. List of excluded studies from systematic review with reasons.

Study	No of revisions	Causes of revisions	No of reoperations	Causes of reoperations	No of non-revision reoperations
Alnachoukati et al. ¹⁵⁸	93	19 tibial loosening 5 tibial and femoral loosening 6 tibial collapse 22 arthritic progression 2 tibial overload 1 loose body removal 7 femoral loosening 13 unknown 5 bearing dislocation 1 tibial fracture 1 instability 1 car accident 1 infection 3 pain 1 RA 3 chronic haemarthrosis 2 polywear impingement	n.r	n.r	n.r
Aly et al. ¹⁵⁷	2	2 revisions to TKR (1 fracture of medial tibial plateau after fall, 1 aseptic loosening)	n.r	n.r	n.r
Bottomley et al. ¹⁵⁹	46	12 aseptic loosening 13 lateral progression 7 infection 5 unexplained pain 7 bearing dislocation 1 tibial fracture 1 unknown	69	Same as revisions. Additionally: 15 exploratory arthroscopy 3 washout of wound and evac of haematoma 3 MUA 1 excision wound neuroma 1 open exploration impingement	23
Campi et al. ¹⁶⁰	25	11 progression of arthritis in lateral compartment 7 bearing dislocation 2 tibial fractures	29	Revisions plus; 2 washout 1 MUA 1 Arthroscopy	4

		2 tibial component loosening 1 persistent pain 1 impingement 1 ACL tear			
Edmonson et al. ¹⁶¹	26	9 Lateral compartment OA 5 Combination of lateral and patellofemoral OA 6 Aseptic loosening 4 Dislocated bearing 2 Unexplained medial pain	29	Revisions plus 1 washout 2 MUA	3
Emerson et al. ¹⁵⁸	20	3 chronic haemarthrosis 2 loose femoral components 2 loose tibial components 9 progression of OA in lateral compartment 1 bearing dislocation 1 polyethylene wear 2 unknown	n.r	n.r	n.r
Faour-Martin et al. ¹⁶³	29	15 infection 2 bearing exchange 8 persistent pain 4 aseptic loosening tibial component	31	Revisions plus 2 MUA	2
Kendall et al. ¹⁶⁴	29	6 unexplained pain 5 lateral OA 5 tibial component loosening 3 tibial and femoral component loosening 1 Femoral loosening 1 Infection 2 single stage bearing exchange with debridement for infection 6 arthrotomy with bearing exchange	38	Revisions plus 1 femoral reimplantation for dislocation 5 MUA 3 wound revisions	9
Kornilov et al. ¹⁶⁶	19	8 loosening of tibial component, 3 Periprosthetic joint infection, 2 OA progression,	21	Revisions plus 1 lateral meniscus tear	2

		3 fracture of medial tibial/femoral condyle, 2 bearing dislocation with ACL and MCL rupture 1 complete rupture ACL and MCL		1 loose body formation	
Kim et al. ¹⁶⁵	16	7 bearing dislocations 1 bearing wear and breakage 1 MCL rupture with bearing dislocation 3 Femoral component loosening 1 Femoral and tibial component loosening 1 Component loosening with bearing dislocation 1 Tibial condylar fracture 1 Infection	n.r	n.r	n.r
Kristensen et al. ¹⁶⁷	51	8 aseptic loosening of tibial component 1 aseptic loosening of femoral component 2 aseptic loosening of both components 14 Progressive OA in lateral compartment 2 Progression of retropatellar OA 10 Pain without loosening 4 Deep infection 2 Periprosthetic fracture 2 Malposition 4 Instability 2 Other	n.r	n.r	n.r
Lisowski et al. ¹⁶⁸	11	4 pain 6 disease progression laterally 1 bearing dislocation	n.r	n.r	n.r

Pandit et al. ⁸²	52	25 Progressive OA in lateral compartment 7 bearing dislocation 7 unexplained pain 1 unknown 6 infection 1 ACL injury 1 ANV lateral femoral condyle 1 Tibial malposition 1 aseptic loosening femur 1 aseptic loosening tibia 1 instability	n.r	n.r	n.r
White et al. ¹⁶⁹	16	6 progressive arthritis 4 instability 3 unexplained pain 1 aseptic loosening 1 infection 1 periprosthetic fracture	n.r	n.r	n.r
Yoshida et al. ¹⁷⁰	25	1 bearing rotation, 2 periprosthetic fracture tibia, 9 bearing dislocation, 12 tibial subsidence of component, 1 progression lateral OA	n.r	n.r	n.r
TOTAL:	460 revisions out of 8658 cases (5.3%)		217 reoperations out of 3734 cases (5.8%)		43 non revision reoperations out of 3734 cases (1.2%)

Table A2. Specific reasons for revision and reoperations in all included studies for systematic review.

APPENDIX 3

A3.1 Operation proforma collected for each patient

<i>Please attach patient sticky label here</i>		NOC	
Completed forms in top red tray on Vicky's desk (Bone Bank office) please			
OXFORD UKA OPERATION FORM			
Patient's name	Hospital Number	Side: R / L	Medial / Lateral
Operation Date: / / 201	Operation type: Primary / Revision	Diagnosis: OA / AVN	
Operating surgeon:	Operating surgeon grade:		
Assistant surgeon:	Assistant surgeon grade:		
Consultant surgeon:	Operation approach: MIS UKA	Funded: NHS	
Anaesthesia: 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% bupivacaine			
SURGICAL FINDINGS			
ACL: Normal / 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
Involved Femur			
Involved Tibia			
* Partial thickness cartilage loss		** Full Thickness cartilage loss	
	Normal	Superficial Damage	PTCL*
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/Domed lateral			
Tibia Size: AA / A / B / C / D / E / F or 26x38 / 26x41 / 28x44 / 30x47 / 32x50 / 34x53 or 28x40 / 28x44 / 28x48 / 31x48 / 31x52			
Cement: CMW1 / CMW3 / Palacos/ Optipac		CEMENTED CEMENTLESS	
Additional procedures: 1. RSA Y / N 2. Mosaicplasty Y / N			
PLEASE ATTACH IMPLANT STICKERS ON REVERSE - THANK YOU			

A3.2 PROMs questionnaires used for study

Oxford Knee Score questionnaire

PROBLEMS WITH YOUR KNEE										
During the past 4 weeks..					✓tick <u>one</u> box for <u>every</u> question					
1	<i>During the past 4 weeks.....</i> How would you describe the pain you <u>usually</u> have from your knee? <table style="width: 100%; margin-top: 10px;"> <tr> <td style="text-align: center;">None ☐</td> <td style="text-align: center;">Very mild ☐</td> <td style="text-align: center;">Mild ☐</td> <td style="text-align: center;">Moderate ☐</td> <td style="text-align: center;">Severe ☐</td> </tr> </table>					None ☐	Very mild ☐	Mild ☐	Moderate ☐	Severe ☐
None ☐	Very mild ☐	Mild ☐	Moderate ☐	Severe ☐						
2	<i>During the past 4 weeks.....</i> Have you had any trouble with washing and drying yourself (all over) <u>because of your knee</u> ? <table style="width: 100%; margin-top: 10px;"> <tr> <td style="text-align: center;">No trouble at all ☐</td> <td style="text-align: center;">Very little trouble ☐</td> <td style="text-align: center;">Moderate trouble ☐</td> <td style="text-align: center;">Extreme difficulty ☐</td> <td style="text-align: center;">Impossible to do ☐</td> </tr> </table>					No trouble at all ☐	Very little trouble ☐	Moderate trouble ☐	Extreme difficulty ☐	Impossible to do ☐
No trouble at all ☐	Very little trouble ☐	Moderate trouble ☐	Extreme difficulty ☐	Impossible to do ☐						
3	<i>During the past 4 weeks.....</i> Have you had any trouble getting in and out of a car or using public transport <u>because of your knee</u> ? (whichever you would tend to use) <table style="width: 100%; margin-top: 10px;"> <tr> <td style="text-align: center;">No trouble at all ☐</td> <td style="text-align: center;">Very little trouble ☐</td> <td style="text-align: center;">Moderate trouble ☐</td> <td style="text-align: center;">Extreme difficulty ☐</td> <td style="text-align: center;">Impossible to do ☐</td> </tr> </table>					No trouble at all ☐	Very little trouble ☐	Moderate trouble ☐	Extreme difficulty ☐	Impossible to do ☐
No trouble at all ☐	Very little trouble ☐	Moderate trouble ☐	Extreme difficulty ☐	Impossible to do ☐						
4	<i>During the past 4 weeks.....</i> For how long have you been able to walk before <u>pain from your knee</u> becomes severe ? (<i>with or without a stick</i>) <table style="width: 100%; margin-top: 10px;"> <tr> <td style="text-align: center;">No pain/ More than 30 minutes ☐</td> <td style="text-align: center;">16 to 30 minutes ☐</td> <td style="text-align: center;">5 to 15 minutes ☐</td> <td style="text-align: center;">Around the house <u>only</u> ☐</td> <td style="text-align: center;">Not at all - pain severe when walking ☐</td> </tr> </table>					No pain/ More than 30 minutes ☐	16 to 30 minutes ☐	5 to 15 minutes ☐	Around the house <u>only</u> ☐	Not at all - pain severe when walking ☐
No pain/ More than 30 minutes ☐	16 to 30 minutes ☐	5 to 15 minutes ☐	Around the house <u>only</u> ☐	Not at all - pain severe when walking ☐						
5	<i>During the past 4 weeks.....</i> After a meal (sat at a table), how painful has it been for you to stand up from a chair <u>because of your knee</u> ? <table style="width: 100%; margin-top: 10px;"> <tr> <td style="text-align: center;">Not at all painful ☐</td> <td style="text-align: center;">Slightly painful ☐</td> <td style="text-align: center;">Moderately painful ☐</td> <td style="text-align: center;">Very painful ☐</td> <td style="text-align: center;">Unbearable ☐</td> </tr> </table>					Not at all painful ☐	Slightly painful ☐	Moderately painful ☐	Very painful ☐	Unbearable ☐
Not at all painful ☐	Slightly painful ☐	Moderately painful ☐	Very painful ☐	Unbearable ☐						
6	<i>During the past 4 weeks.....</i> Have you been limping when walking, <u>because of your knee</u> ? <table style="width: 100%; margin-top: 10px;"> <tr> <td style="text-align: center;">Rarely/ never ☐</td> <td style="text-align: center;">Sometimes, or just at first ☐</td> <td style="text-align: center;">Often, not just at first ☐</td> <td style="text-align: center;">Most of the time ☐</td> <td style="text-align: center;">All of the time ☐</td> </tr> </table>					Rarely/ never ☐	Sometimes, or just at first ☐	Often, not just at first ☐	Most of the time ☐	All of the time ☐
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.

/P.T.O

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
☐

American Knee Society Score questionnaire

PART B (American Knee Soc. 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

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

Knee Score

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

COMMENTS & CHARNLEY ABC:

A: knee only B: other joints C: systemic illness

Please file safely in patient notes

Tegner Activity Score questionnaire

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

Level 10	Competitive sports: football/rugby – national and international.
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 (eg 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 (eg 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 eg 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.

A3.3 Letter from Research Ethics Committee



Oxfordshire REC C
2nd Floor, Astral House
Chaucer Business Park
Granville Way
Bicester
OX26 4JT

03 October 2008

Hemant Pandit
C/O ODEC
C/O Botnar Research Centre,
Windmill Road,
Headington
Oxford OX3 7LD

Dear Hemant,

Full title of project: Prospective follow up of all unicompartmental knee replacements.

Thank you for seeking the Committee's advice about the above project.

Following your discussion with the Chair, Janet Burton regarding the issue of regular follow up of patients (after joint replacement - clinical and radiological), she advised that the proposal is an audit. Therefore it does not require ethical review by a NHS Research Ethics Committee.

You can find a copy of our leaflet, "Defining Research", which explains how we differentiate research from other activities, at the following web address:
<http://www.nres.npsa.nhs.uk/rec-community/guidance/#researchoraudit>.

You should check with the Oxford Radcliffe Hospitals NHS Trust what other review arrangements or sources of advice apply to projects of this type. Guidance may be available from the clinical governance office.

This letter should not be interpreted as giving a form of ethical approval to the project or any endorsement of the project, but it may be provided to a journal or other body as evidence that ethical approval is not required under NHS research governance arrangements.

However, if you, your sponsor/funder or any NHS organisation feels that the project should be managed as research and/or that ethical review by a NHS REC is essential, please write setting out your reasons and we will be pleased to consider further.

This Research Ethics Committee is an advisory committee to South Central Strategic Health Authority
The National Research Ethics Service (NRES) represents the NRES Directorate within
the National Patient Safety Agency and Research Ethics Committees in England.



Where NHS organisations have clarified that a project is not to be managed as research, the Research Governance Framework states that it should not be presented as research within the NHS.

Yours sincerely

A handwritten signature in black ink, appearing to read 'Sabrina Harris'.

Sabrina Harris
Committee Co-ordinator

A4.1 NJR approval letter



National Joint Registry

www.njrcentre.org.uk

Working for patients, driving forward quality

Dawson House
5 Jewry Street
London EC3N 2EX

T 020 3857 5030
F 020 7997 7398

05 July 2018

Dear ,

Study title; 'Factors affecting the outcome of the Oxford Knee NJR';
University of Oxford; NJR REF RSC2017/17 – External application

Thank you for resubmitting the above named research application to the NJR Research Subcommittee (RSC) for further evaluation. The RSC chair reviewed this research application on 02.07.2018, and I can confirm that the committee is satisfied that all points raised in our previous feedback letter have since been addressed.

I am pleased to inform you the RSC is able to recommend **approval** of this study, which has been classified as an **external** NJR supported project.

Conditions of Approval:

A condition of this approval is that you agree to provide 6 monthly progress reports to the NJR. Please submit these to me electronically within 30 days of the review date. These progress reports will be circulated to the NJR RSC and the final report summary will be published on the NJR website. I enclose a copy of the NJR's 'Terms and Conditions of approval'. Please return a signed copy of each document to me. Subject to RSC approval, the application will then be referred to HQIP DARG for final approval of data release.

Please note that due to data protection issues beyond our control, there is a temporary delay in release of data of applications which involve mortality data. We are actively addressing this as a priority, but are unable to provide timelines at this time.

Wishing you all the best with this research study.

Yours sincerely,

A. J. M.

Chris Boulton

Associate Director-Research & Governance (NJR)
On behalf of the NJR Research Sub-committee

Registered Charity No. 1127049
Company Limited by guarantee
Registered in England No. 6498947
Registered Office:
70 Wimpole Street, London W1G 8AX

A4.2 NJR patient consent form

National Joint Registry: Patient Consent Form



National Joint Registry
www.njrcentre.org.uk
Working for patients, driving forward quality

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 provides information and evidence to:

- Help surgeons choose the best artificial joints (implants) for patients
- Empower patients by helping them find out more about the implants available to them
- Improve patient safety by checking how well implants, surgeons and hospitals perform and take action where it is needed
- Giving hospitals, surgeons and implant manufacturers feedback about their performance to help them improve patient care
- Help surgeons quickly decide whether patients need to return to hospital if implant problems are found

What information is collected?

Details of your operation and your implants will be recorded on the NJR by your hospital. 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, hospitals and surgeons are doing. **Without using personal details to link operations, the NJR cannot find out about problems with implants, hospitals or surgeons.**

Personal details needed by the NJR are:

- ✓ Name
- ✓ Date of birth
- ✓ Postcode
- ✓ NHS 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.

NJR and research

Operation and patient information in the NJR may be used for medical research. The purpose of this research is to improve our understanding and treatment of joint problems.

The majority of our research uses only anonymised information that means it is impossible to identify individuals. From time to time researchers may wish to gather further information. In these cases we would seek your approval prior to disclosing your contact details. You do not have to take part in any research study you are invited to take part in and saying no does not affect the care you receive.

Please be reassured that the storage, release and use of this data are subject to very strict controls.

You can find examples of how we use data for research at www.njrcentre.org.uk as part of our Research library.



Giving your consent is voluntary and more information is available if you are unsure.
Whether you choose to consent or not, please sign this form on the back.

NJR data and other healthcare information

Operation and patient information in the NJR is used to link to other healthcare information. It is also analysed and made available to surgeons, hospitals and manufacturers - without any of your personal details - as part of our feedback services.

Doing this improves the NJR's ability to monitor patient safety and patient outcomes. It also means that people and organisations involved in improving joint replacement surgery can better understand and develop improved or more cost-effective medical treatments.



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' below.



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

E-mail
enquiries@njrcentre.org.uk



National Joint Registry

www.njrcentre.org.uk

Working for patients, driving forward quality

NJR Helpline

Tel: 0845 345 9991

Mon-Fri, 9am to 5pm (excluding public holidays)

NJR Centre

Peoplebuilding 2, Peoplebuilding Estate, Maylands Avenue, Hemel Hempstead HP2 4NQ

This form should be kept as part of the patient record. DO NOT send this form to the NJR Centre

Patient Details (all mandatory)

Surname

Forename

Date of birth

Postcode (home)

To be completed by the hospital

Hospital

NHS or national patient number

Height m & 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. 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

Giving your consent is voluntary and more information is available if you are unsure.

Version 6.0 August 2014

A4.3 NJR data collection form

 National Joint Registry www.njrcentre.org.uk Working for patients, driving forward quality		MDS VERSION 7.0 Form: MDSv7.0 K1 v3.0 Knee Operation	
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			
NJR Patient Consent Obtained	Yes ☐	No ☐	Not Recorded ☐
If 'Yes' or 'No' was selected for patient consent above, was consent provided by a consultee on behalf of the patient?	Yes ☐	No/Not Known ☐	
Body Mass Index (enter either H&W OR BMI OR tick Not Available box)	Height (IN M) Weight (IN KG)	BMI	Not Available ☐
PATIENT IDENTIFIERS			
Forename(s)			
Surname			
Gender	Male ☐	Female ☐	Not Known ☐
Date of Birth	DD/MM/YYYY		
Patient Postcode	Overseas Address ☐		
NHS Number OR National Patient Identifier (if available)			
Patient Hospital ID			
Patient email address (optional)			
Patient mobile phone number (optional)			
OPERATION DETAILS			
Hospital			
Operation Date	DD/MM/YYYY		
Anaesthetic Types	General ☐	Regional – Nerve Block ☐	
	Regional - Epidural ☐	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 (AVN) ☐	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 ☐				
	Unicompartmental Knee Replacement (select all that apply) ☐				
	Medial ☐	Lateral ☐	Patello-Femoral ☐		
	Primary Total Prosthetic Replacement Not Classified Elsewhere (e.g. Hybrid) ☐				
Approach	Medial Parapatellar ☐	Mid-Vastus ☐			
	Lateral Parapatellar ☐	Other ☐			
	Sub-Vastus ☐				
Minimally Invasive Technique Used?	Yes ☐	No ☐			
Computer Guided Surgery Used?	Yes ☐	No ☐			
Robotic Surgery Used?	Yes ☐	No ☐			
If Yes, Name of Robot					
Patient Specific Instruments?	Yes ☐	No ☐			

THROMBOPROPHYLAXIS REGIME (intention to treat)					
Chemical (In Hospital)	Aspirin ☐	Direct Thrombin Inhibitor (e.g. Dabigatran) ☐			
	LMWH ☐	Factor Xa Inhibitor (e.g. Rivaroxaban/Apixaban) ☐			
	Pentasaccharide (e.g. Fondaparinux) ☐	Other ☐			
	Warfarin ☐	None ☐			
Mechanical	Foot Pump ☐	Other ☐			
	Intermittent Calf Compression ☐	None ☐			
	TED Stockings ☐				

BONE GRAFT USED					
Was Femoral Bone graft used?	Yes ☐	No ☐			
Femoral - Form	Structural ☐	Morsellised/chips ☐			
Femoral - Type	Autograft ☐	Allograft ☐	Synthetic ☐	Other ☐	
Was Tibial Bone graft used?	Yes ☐	No ☐			
Tibial - Form	Structural ☐	Morsellised/chips ☐			
Tibial - Type	Autograft ☐	Allograft ☐	Synthetic ☐	Other ☐	

SURGEON'S NOTES**INTRA-OPERATIVE EVENT**

Untoward Intra-Operative Event	None	☐	Ligament Injury	☐
	Fracture	☐	Other	☐
	Patella Tendon Avulsion	☐		

Minimum Dataset Form - COMPONENT LABELS

1. Please affix any component labels to this sheet and ensure any extra component label sheets are attached to the main Minimum Dataset Form.
2. Ensure all component details are provided, including cement.
3. The NJR DOES NOT record the following: wire, mesh, cables, plates, screws, surgical tools, endoprotheses or bipolar heads.

Femoral Component (or unicondylar femoral component)	Tibial Tray (or unicondylar tibial component)
Meniscal Component	Cement (if used)
Patella (if used) Needed in Patello-femoral replacement	Accessories

APPENDIX 5

A5.1 Ovid Medline search strategy

- 1 Knee/ or exp Knee Joint/ or Osteoarthritis, Knee/
- 2 knee*.tw.
- 3 1 or 2
- 4 Knee Prosthesis/ or Arthroplasty, Replacement, Knee/
- 5 (knee* and (arthroplast* or implant* or replace* or prosth* or endoprosth*)).tw.
- 6 4 or 5
- 7 "Prostheses and Implants"/
- 8 3 and 7
- 9 6 or 8
- 10 Cementation/
- 11 Bone Cements/
- 12 exp Hydroxyapatites/
- 13 (cement* or uncement* or hydroxyapatite or durapatite or hybrid or porous* or coat* or press-fit* or fixation or implant*).tw.
- 14 10 or 11 or 12 or 13
- 15 9 and 14
- 16 15
- 17 limit 16 to english language
- 18 Osteoarthritis, Knee/
- 19 osteoarthr*.tw.
- 20 18 or 19
- 21 17 and 20

A5.2 Embase search strategy

- 1 knee/
- 2 knee*.tw.
- 3 1 or 2
- 4 exp knee arthroplasty/
- 5 exp knee prosthesis/
- 6 (knee* adj2 (arthroplast* or implant* or replace* or prosth* or endoprosth*)).tw.
- 7 4 or 5 or 6
- 8 exp implantation/
- 9 3 and 8
- 10 7 or 9
- 11 cementation/
- 12 hydroxyapatite/
- 13 (cement* or uncement* or hydroxyapatite or durapatite or hybrid or porous* or coat* or press-fit* or fixation or implant*).tw.
- 14 11 or 12 or 13
- 15 knee osteoarthritis/
- 16 (knee and osteoarthr*).ti,ab.
- 17 15 or 16
- 18 10 and 14 and 17

- 19 18
20 limit 19 to english language

A5.3 Central search strategy

- ID Search Hits
#1 MeSH descriptor: [Knee] explode all trees
#2 MeSH descriptor: [Knee Joint] explode all trees
#3 knee*
#4 #1 OR #2 OR #3
#5 MeSH descriptor: [Arthroplasty, Replacement, Knee] explode all trees
#6 MeSH descriptor: [Knee Prosthesis] explode all trees
#7 (knee* and (arthroplast* or implant* or replace* or prosth* or endoprosth*))
#8 #5 OR #6 OR #7
#9 MeSH descriptor: [Prostheses and Implants] explode all trees
#10 #4 AND #9
#11 #8 OR #10
#12 MeSH descriptor: [Cementation] explode all trees
#13 MeSH descriptor: [Bone Cements] explode all trees
#14 MeSH descriptor: [Durapatite] explode all trees
#15 (cement* or uncement* or hydroxyapatite or durapatite or hybrid or porous* or coat* or press-fit* or fixation or implant*)
#16 #12 OR #13 OR #14 OR #15
#17 osteoarthr*
#18 #11 AND #16 AND #17

APPENDIX 6

A6.1 Additional tables for Chapter 4.2

Study	No of revisions	Details of revisions
<u>Cemented studies</u>		
Alnachoukati et al. (2018) ²³⁵	93	19 tibial loosening, 5 tibial and femoral loosening, 6 tibial collapse, 22 arthritis progression, 2 tibial overload, 1 loose body removal, 7 femoral loosening, 13 unknown, 5 bearing dislocation, 1 tibial fracture, 1 instability, 1 car accident, 1 infection, 3 pain, 1 RA, 3 chronic haemarthrosis, 2 polywear impingement
Aly et al. (2010) ¹⁵⁷	2	1 fracture of medial tibial plateau, 1 aseptic loosening
Argenson et al. (2013) ²³¹	19	9 OA progression, 2 aseptic loosening, 3 patellafemoral prosthesis because of OA progression, 5 polyethylene wear
Chattelard et al. (2013) ²³²	14	5 loosening, 5 tibial component wear, 2 lateral OA, 2 infection
Edmonson et al. (2015) ¹⁶¹	26	9 Lateral compartment OA 5 Combination of lateral and patellofemoral OA 6 Aseptic loosening 4 Dislocated bearing 2 Unexplained medial pain
Emerson et al. (2016) ¹⁵⁸	20	3 chronic haemarthrosis 2 loose femoral components 2 loose tibial components 9 progression of OA in lateral compartment 1 bearing dislocation 1 polyethylene wear 2 unknown
Faour Martin et al. (2013) ¹⁶³	29	15 infection 2 bearing exchange for dislocation 8 persistent pain 4 aseptic loosening tibial component
Foran et al. (2013) ²³³	3	2 patellofemoral and lateral OA, 1 lateral OA
Kim et al. (2015) ¹⁶⁵	16	7 bearing dislocations 1 bearing wear and breakage 1 MCL rupture with bearing dislocation 3 Femoral component loosening 1 Femoral and tibial component loosening 1 Component loosening with bearing dislocation 1 Tibial condylar fracture 1 Infection
Kristensen et al. (2013) ¹⁶⁷	51	8 aseptic loosening of tibial component 1 aseptic loosening of femoral component 2 aseptic loosening of both components 14 Progressive OA in lateral compartment 2 Progression of retropatellar OA 10 Pain without loosening 4 Deep infection 2 Periprosthetic fracture 2 Malposition

		4 Instability 2 Other
Lim et al. (2018) ²³⁷	11	2 aseptic loosening, 6 OA progression, 1 poly fracure, 1 poly wear and progressive arthritis, 1 medial condylar fracture
Lisowski et al. (2016) ¹⁶⁸	11	4 pain 6 disease progression 1 bearing dislocation
Pandit et al. (2015) ⁸²	52	25 Progressive OA in lateral compartment 7 bearing dislocation 7 unexplained pain 1 unknown 6 infection 1 ACL injury 1 ANV lateral femoral condyle 1 Tibial malposition 1 aseptic loosening femur 1 aseptic loosening tibia 1 instability
Schlueter-Brust et al. (2014) ²³⁴ (cemented arm)	7	4 pain, 3 bearing dislocation
Song et al. (2016) ²⁴⁰	3	1 tibial plateau fracture, 1 tibial plateau collapse, 1 pain
Venkatesh et al. (2016) ²³⁹	7	4 unexplained pain, 2 aseptic loosening, 1 poly wear
White et al. (2018) ²³⁶	16	6 progressive arthritis, 4 instability, 3 unexplained pain, 1 aseptic loosening of tibia, 1 infection, 1 periprosthetic fracture
Winnock de Grave et al. (2018) ²³⁸	11	4 infection, 2 lateral pain and overload, 2 pain and patellar chondropathy, 2 lateral OA, 1 synovitis
Yoshida et al. (2013) ¹⁷⁰	25	1 bearing rotation, 2 periprosthetic fracture tibia, 9 bearing dislocation, 12 tibial subsidence of component, 1 progression lateral OA
<u>Cementless studies</u>		
Campi et al. (2018A) ¹⁴⁸	19	1 Pain, 2 tibial loosening, 5 lateral disease progression, 1 patellofemoral dx, 2 tibial plateau fractures, 1 tibial overhang/impingement, 7 bearing dislocation
Hall et al. (2013) ²⁴¹	7	4 aseptic loosening, 1 sepsis, 2 OA progression
Lecuire et al. (2014) ²⁴²	11	1 knee rheumatoid degeneration, 1 OA in lateral compartment, 1 increased pain, 1 ACL rupture, 3 polyethylene fracture, 4 bearing exchange for wear
Mohammad et al. (2019) ¹⁷¹	18	7 bearing dislocation, 4 disease progression, 2 pain, 2 infections, 1 AVN, 1 femoral component loosening, 1 tibial plateau fracture
Schlueter-Brust et al. (2014) ²³⁴ (cementless arm)	2	1 pain, 1 bearing dislocation

Table A3. The specific revision indications for the included studies for the mechanisms of failure analysis.

APPENDIX 7

A7.1 Research ethics approval for RSA study


Health Research Authority

Prof David Murray
Professor of Orthopaedic Surgery
University of Oxford
Botnar Research Centre, Windmill Road
OX3 7LD

02 December 2016

Dear

Letter of HRA Approval

Study title: In vivo wear of Oxford Unicompartmental knee replacement
Phase 3 bearings made of three different polyethylene resins
IRAS project ID: 201795
REC reference: 16/SC/0456
Sponsor Clinical Trials and Research Governance

I am pleased to confirm that HRA Approval has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications noted in this letter.

Participation of NHS Organisations in England

The sponsor should now provide a copy of this letter to all participating NHS organisations in England.

Appendix B provides important information for sponsors and participating NHS organisations in England for arranging and confirming capacity and capability. **Please read *Appendix B* carefully**, in particular the following sections:

- *Participating NHS organisations in England* – this clarifies the types of participating organisations in the study and whether or not all organisations will be undertaking the same activities
- *Confirmation of capacity and capability* - this confirms whether or not each type of participating NHS organisation in England is expected to give formal confirmation of capacity and capability. Where formal confirmation is not expected, the section also provides details on the time limit given to participating organisations to opt out of the study, or request additional time, before their participation is assumed.
- *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

It is critical that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details

Page 1 of 8

A7.2 Participant consent form for RSA study

 UNIVERSITY OF OXFORD	Oxford University Hospitals  NHS Foundation Trust Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences	
<u>PARTICIPANT CONSENT FORM</u>		
Study Title: In vivo wear of Oxford Unicompartmental knee replacement Phase 3 bearings made of three different polyethylene resins Short Title: Polyethylene wear of the Oxford Knee replacement IRAS ID: 201795		
Name of Researchers: Professor David Murray & Mr Stefano Campi		
Identification Number: _____	Please initial each box	
1. I confirm that I have read and understand the information sheet dated [22/11/2016 V3] for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐	
2. I understand that my participation is voluntary and that I am free to withdraw at anytime, without giving any reason, without my medical care or legal rights being affected.	☐	
3. I understand that relevant sections of any of my medical notes and data collected during the study may be looked at by responsible individuals from the Oxford University Hospitals NHS Trust, the Regulatory Authorities, and members of the research team where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	☐	
4. I consent to personal details about me being kept on a secure database for a maximum of 12 months after completion of the study. Data will be available only to staff and researchers directly involved with the project.	☐	
5. I understand that my answers to questions may be used for publication within a research article, but that no information by which I may be identified will be published.	☐	
6. I understand that the information collected about me may be used in an anonymous form to support other research in the future. It will not be possible for me to be identified by it.	☐	
7. I agree to take part in the above study.	☐	
_____ Name of Patient	_____ Date	_____ Signature
_____ Name of Person taking consent (if different from researcher)	_____ Date	_____ Signature
An original copy of the participant information sheet and completed informed consent form is to be given to the participant, in addition to the original copy that is filed in the investigator file.		

A7.3 Participant information sheet for RSA study



Oxford University Hospitals **NHS**
NHS Foundation Trust

**Nuffield Department of Orthopaedics, Rheumatology and
Musculoskeletal Sciences**
University of Oxford
Nuffield Orthopaedic Centre
Botnar Research Centre
Windmill Road
OXFORD, OX3 7LD
UNITED KINGDOM

PARTICIPANT INFORMATION SHEET

Study Title: In vivo wear of Oxford Unicompartmental knee replacement Phase 3 bearings made of three different polyethylene resins

Short Title: Polyethylene wear of the Oxford Knee replacement

IRAS ID: 201795

We'd like to invite you to take part in our research study. Before you decide, it is important that you understand why the research is being done and what it would involve for you. Please take time to read this information, and discuss it with others if you wish. If there is anything that is not clear, or if you would like more information, please ask us.

What is the Purpose of the Study?

We are conducting a study to compare the amount of wear in three types of plastic bearing (the bit between the two metal components) of the Oxford Knee.

The Oxford Knee (OUKR) was designed to produce extremely low wear rates. The studies that we have done have shown that although the wear rate is very low, there are differences in wear between different polyethylene, which is the material in the bearing. The aim of the study is to determine which is the best bearing material. Retrieval studies have shown that the very low wear rates predicted from the design are achievable in practice with linear penetration rates (LPR) as low as 0.01 mm/year. With an average penetration rate of 0.02 mm/year, it would take 75 years for the metal component to wear through half the bearing width.

We have developed an X-ray system using two X-rays taken at once (RSA) that can measure the wear rate of the polyethylene bearing in the Oxford Knee. This allows us to identify the outlines of the metal implants on X-ray and to reconstruct where they are in space and thus to measure the distance between them which tells us how thick the plastic bearing is.

Why am I being sent this information sheet?

You are being sent this information sheet as you had an Oxford Knee at the Nuffield Orthopaedic Centre and have a plastic bearing of the type we wish to study. If you do decide to take part you would be given this information sheet to keep and be asked to sign a consent form. Seventy-five patients will be recruited for this study.

Do I have to take part?

No. If you decide to take part you are still free to withdraw at any time and without giving a reason. This would not affect the standard of care you receive.

What would happen to me if I take part?

If you agree to take part you will be contacted to arrange an appointment to come for an RSA X-ray of your knee on a Wednesday afternoon at the Nuffield Orthopaedic Centre. Before any procedures are performed, you will be asked by a clinical member of the research team to give your written consent.

The dose of radiation per RSA X-ray is similar to that of a normal X-ray, and poses no significant risk to your health. The radiographer will explain the procedure to you.

During the same appointment, a member of the research team will ask you to complete an Oxford Knee Score questionnaire to assess the pain and function of your knee.

This appointment would be expected to take around 20 - 30 minutes.

Expenses and payments

Taking part is voluntary. Reasonable travel expenses for any visit additional to normal care will be reimbursed upon presentation of valid receipts.

Are there any side effects?

The amount of X-ray's you are exposed to is very small and is well within accepted levels, this does not pose a significant risk to your long-term health. By participating in the study the performance of your knee is not affected in any way. The X-ray exposure over the period of the study is equivalent to the natural background radiation experienced over three weeks.

What if there is a problem?

The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study you can contact: Professor David Murray, Botnar Research Centre, Nuffield Orthopaedic Centre, Windmill Road, Oxford, OX3 7LD or email: _____ or you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on _____ or the head of CTRG, email _____ or the Patient Advice and Liaison Service (PALS) of the Nuffield Orthopaedic Centre on _____

What if relevant new information becomes available?

During the course of this research your treating surgeon would have access to your X-ray images. If we discovered something relevant to your health/treatment we would inform you, and your GP if appropriate.

What will happen to the results of the research study?

The results will be analysed and findings subsequently published in scientific journals. You will not be identified in any publication. You are very welcome to receive an update of the project or a copy of any publication resulting from this work. You will be provided with the details of how to request copies of the reports.

Who has reviewed this study?

This study has been reviewed and given favourable opinion by South Central – Oxford B Research Ethics Committee.

What are the possible benefits of taking part?

By participating in this study you will be contributing to our understanding of the wear rates of plastic bearings. This information about your knee may give your surgeon more information to benefit other patients in the future. In addition, you may benefit from early identification of any problem with your knee replacement.

Would my taking part in this study be kept confidential?

All the information which is collected about you during the course of the research would be kept strictly confidential. When we store the results of your answers, we would identify you by a number rather than a name; only the people you meet when you come into the hospital would know your name. Where necessary, anonymised or encrypted data will be electronically transferred from the NHS to the University premises by computer networks and external media to secure University computers and will be available only to staff and researchers involved directly with the project.

Additionally Responsible members of the Oxford University and Oxford University Hospitals NHS Foundation Trust and Regulatory Authorities may be given access to data for monitoring and/or audit of the study to ensure we are complying with regulations. We may use the anonymised data we collect from the study for use in future ethically approved studies so that we can compare the results.

Where can I get further information?

For general information about participation in medical research as a volunteer, please see:

www.arec.org.uk/documents/research-participants/medical-research-and-you.doc

For more information about our research department and the work that we do, please see:

www.ndorms.ox.ac.uk

What to do next?

If you agree to take part in the study, please complete and return the enclosed reply slip. If you do not wish to take part it would be helpful if you could let us know.

Whether you decide to take part or not will not impact in any way on the routine treatment you will receive.

If you have any doubts or queries please do not hesitate to contact us on

or write to:

A7.4 Participant invitation letter for RSA study



Oxford University Hospitals **NHS**
NHS Foundation Trust

**Nuffield Department of Orthopaedics, Rheumatology and
Musculoskeletal Sciences**

University of Oxford
Nuffield Orthopaedic Centre
Botnar Research Centre
Windmill Road
OXFORD, OX3 7LD
UNITED KINGDOM

PARTICIPANT INVITATION LETTER

Dear

Study Title: In vivo wear of Oxford Unicompartmental knee replacement Phase 3 bearings made of three different polyethylene resins

Short Title: Polyethylene wear of the Oxford Knee replacement

Name of Researchers: Professor David Murray & Mr Stefano Campi

We would like to inform you about a research study which is organized by Professor David Murray & Mr Stefano Campi at the University of Oxford based at the Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences. They are conducting a study to compare the amount of wear in three types of plastic bearing (the bit between the two metal components) of the Oxford Knee replacement. From our records, we have identified that you have one of the types of bearing and maybe eligible to take part in this study. We have not passed on your details to the research team.

Please find enclosed an information sheet with some more details about what the project involves. Please take time to read this and see if you would like to take part. You are under no obligation to take part in the study and are free to withdraw at any time. Involvement would in no way compromise any future care that you receive, data would be kept confidential and you would be kept fully informed at all times.

Enclosed with this letter, is a return slip and a stamped address envelope. If you would like to be involved in the study send this back to the researchers and one of the team will contact you to arrange an appointment to come for an X-ray on a Wednesday afternoon. If we haven't heard from you within 14 days one of the clinical team will contact you to see if you are interested in taking part. It is entirely up to you to decide whether you would like to take part in this study, and whether you decide to take part or not will not affect the treatment you receive.

Thank you very much for taking the time to read through this letter and the information sheet. If there are any questions please do not hesitate to contact us on _____ or write to the address at the top of the page.

Thank you for your time and consideration.

Professor David Murray
Clinical Care Team

Study Title: In vivo wear of Oxford Unicompartmental knee replacement Phase 3 bearings made of three different polyethylene resins

Name.....

Address.....

.....

.....

Contact phone number.....

Contact email.....

Please tick the relevant box:

I am interested in taking part, please contact me by telephone.....

☐

When is it convenient to contact you? (Please circle)

Morning

Afternoon

Evening

I am interested in taking part, please contact me by email.....

☐

I am not interested in taking part.....

☐

Please return in the enclosed addressed envelope, thank you.

APPENDIX 8

A8.1 Raw instrumentation measurements taken for Chapter 7

Tibial component measured	Mean width (mm)	Mean depth (mm)
1	3.88	9.68
2	3.83	9.65
3	3.88	9.97
4	3.83	9.84
5	3.92	9.56
Average	3.9mm (SD 0.03)	9.7mm (SD 0.16)

Table A4. Tibial component measurements taken.

Standard saw blade no	Mean proximal blade width	Mean middle blade width	Mean distal blade width	Mean blade depth
1	2.91	2.84	2.71	11.22
2	2.91	2.90	2.77	11.81
3	3.0	2.81	2.68	11.82
4	2.91	2.82	2.77	11.80
5	2.92	2.81	2.69	11.90
Average	2.9mm (SD 0.04)	2.8mm (SD 0.04)	2.7mm (SD 0.04)	11.7mm (SD 0.28)

Table A5. Standard keel blade measurements taken.

New saw blade no	Mean proximal blade width	Mean middle blade width	Mean distal blade width	Mean blade depth
1	2.92	2.90	2.81	12.32
2	2.93	2.90	2.83	12.42
3	2.93	2.91	2.90	12.46
4	2.96	2.93	2.89	12.40
5	2.89	2.88	2.86	12.46
Average	2.9mm (SD 0.03)	2.9mm (SD 0.02)	2.9mm (SD 0.04)	12.4mm (SD 0.06)

Table A6. New keel blade measurements taken.

Surgical adjunct tool	Mean width	Mean depth
Pick	3.3 mm (SD 0.01)	11.4 mm (SD 0.09)
Rasp	3.0 mm (SD 0.01)	10.0 (SD 0.2)

Table A7. Pick and Rasp measurements taken.

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