Influence of age on knee replacement selection and outcomes

A dissertation submitted to the University of Oxford in partial fulfilment of the requirements for the degree of

Doctor of Philosophy



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Abstract

Influence of age on knee replacement selection and outcomes
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Knee replacement is a very successful procedure and implantation rates continue to increase. Due to the success of the intervention the indications have been stretched to include patients historically considered too young and too old. Accusations of designer centre bias are used by some to explain discrepancies between national register outcome data and cohort data. This thesis examines the influence of age on selection and outcome for different types of knee replacement and attempts to untangle designer centre bias.

The first section of this thesis examines the influence of age on selection of patients for partial and total knee replacement using a combination of designer and non-designer centres. In patients sufficiently symptomatic to be offered replacement, about half of patients are eligible for partial replacement, with younger patients more likely to be eligible for medial replacement whilst older patients are more eligible for total replacement. The eligibility for partial replacement is far higher than current national usage in all age groups.

Outcomes following partial replacement were examined in designer and non-designer centres and found to be excellent in all age groups and did not vary significantly with age, or between centres. In particular revision rates for those under 55 years of age were found to be lower than that seen for total replacement. A finding strongly contrasting with national registers.

Finally, comparisons were undertaken for outcomes between partial and total replacement of the knee. In a matched comparison, partial replacement had better function and similar implant survival to total. Lifetime revision risk was determined using novel methodology, and was found to be similar in older age groups, but lower in younger age groups (<60 years) with partial replacement.

This thesis has not examined the use of partial replacement in early arthritis, and comparisons with total replacement may be confounded by indication. Possible explanations for the discrepant findings to registers include the use of partial replacement as a ‘pre-total replacement’ in young patients. Further work should examine morbidity and mortality benefits against revision risk in older patients alone (as opposed to all age groups combined).

In conclusion, this thesis rejects ‘designer’ bias, and supports the use of partial replacement in the severely arthritic knee in all age groups, provided appropriate indications are followed, and surgeons have appropriate expertise.

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Thank you for taking the time to read this thesis. I hope it can inspire further work and understanding. The words and ideas contained in this thesis represent but a fraction of my life in Oxford. I will be forever thankful for my time as a member of the University and of the NHS Trust.

Abbreviations

ACL	Anterior cruciate ligament
AP	Anteroposterior
CI	Confidence interval
CTIR	Component time incidence rate
EQ5D	EuroQuol 5 Dimension: a patient reported outcome score related to quality of life.
IQR	Interquartile range
FLO	Fixed lateral Oxford (a type of partial knee replacement)
GIRFT	Getting It Right First Time (a national campaign in the UK)
NHS	National Health Service
NJR	National Joint Registry of England, Wales, Northern Ireland and the Isle of Man
NOC	Nuffield Orthopaedic Centre, Oxford
OA	Osteoarthritis
OKS	Oxford Knee Score: a patient reported outcome related to knee pain and function
PA	Posteroanterior
PKR	Partial knee replacement (synonymous with UKR)
PROM	Patient reported outcome measure
SD	Standard deviation
TKR	Total knee replacement
UK	United Kingdom
UKR	Unicompartmental knee replacement (synonymous with PKR)
USA	United States of America

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1. Introduction

1.1. Background

Knee replacement is increasingly performed and the knee is now the most commonly replaced joint in the human body[1]. It is widely successful in the treatment of arthritic conditions, predominantly osteoarthritis and rheumatoid arthritis[2]. However there is a physiological insult during the surgery which can lead to morbidity and even mortality[3], and after the surgery there are persistent risks of infection, further surgery and dissatisfaction, the latter of which is estimated to be around 20%[4].

Historically knee replacement was performed in elderly patients due to concern over implant wear and requirements for revision surgery. The disease process, most commonly osteoarthritis, was severe. The implants designed at the time performed well, and surgeons and manufacturers stretched the indications to cater for more patients, both in terms of disease severity and in patient age, with knee replacement being performed at one end of the spectrum in increasingly young patients, and at the other, in increasingly frail, elderly patients.

In 2018, over 100,000 knee replacements were performed in the UK[1]. This is approximately 40% more than were performed in 2008 (n = 70 thousand)[5]. The UK population grew by 7% in the same period[6]. Further, this number is projected to continue to increase over time, with projections estimating an increase of between 38% and 916% by the year 2035 in the United Kingdom[7]. Similar estimates exist for Australia[8], and the United States of America[9]. In the USA and Canada, the most rapid increase in provision

has been in those under 50 years of age, a group of patients that would have historically been considered too young for the procedure[10]. Far more commonly performed are knee replacements in those aged 65 to 80 (Figure 1-1).

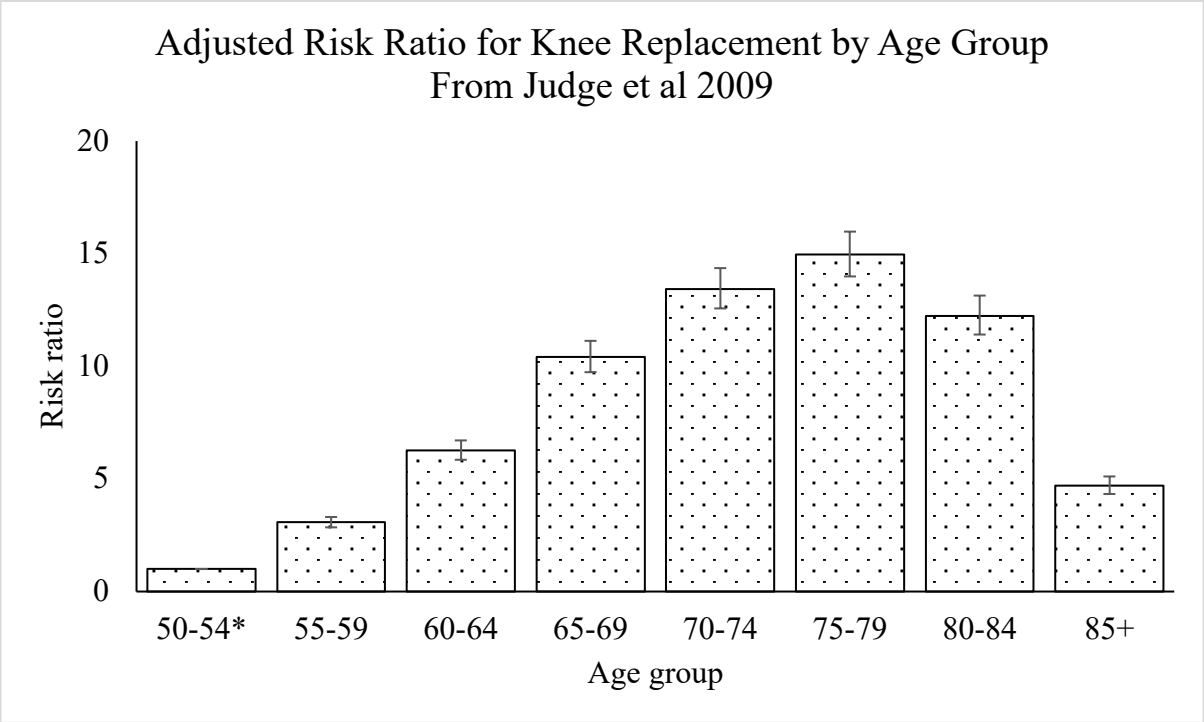


Figure 1-1 Risk of knee replacement by age
The adjusted risk ratio for knee replacement by age group relative to 50-54 year olds produced from Judge et al[11]. Those in the 75-79 year old age group are 15 times more likely to receive a joint replacement than those aged 50-54. Bars indicate 95% confidence interval. *This age group is the reference category, with Risk Ratio of 1.

Whilst considered a very successful intervention[2], about one in five patients report being dissatisfied with knee replacement[4, 12-15]. Many theories have been developed to address the high dissatisfaction rate: Some authors suggest that patient factors are to blame[4, 16], whilst others suggest that implant design or alignment may be the cause[17-19]. The deficit in quality of life is such that an improvement in satisfaction would lead to far more cost

effective treatments than improvements in implant survival[20]. Clearly, it is in the interests of patients, surgeons and policy makers to optimise the outcome of knee replacement.

1.2. Age

Age presents an interaction with the goals of knee replacements. Younger age at replacement causes concern about the longevity of the implant, with many surgeons considering that most, if not all, will require further surgery on the knee during their lifetime (Figure 1-2). At the other end of the spectrum, the aim is to have one surgery only in their lifetime for those at older age at replacement. A bigger priority is managing perioperative frailty and reducing the physiological burden from the replacement surgery to minimise perioperative morbidity and mortality.

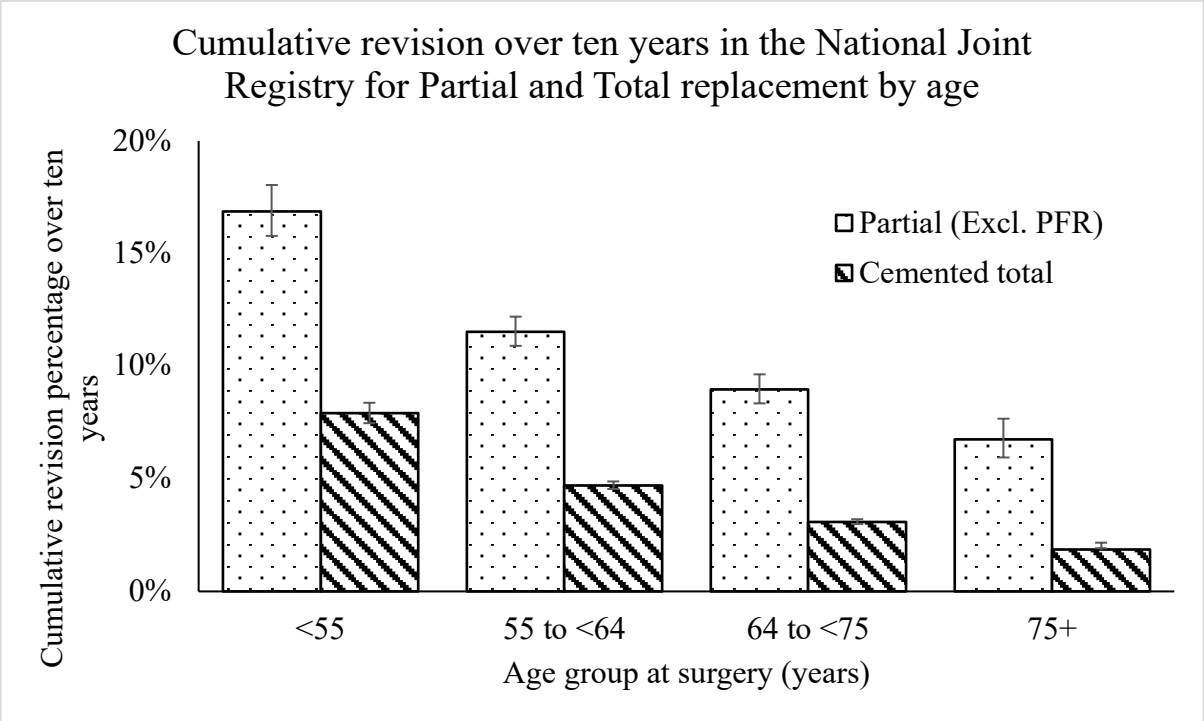


Figure 1-2 Cumulative ten year revision from NJR
Figure adapted from NJR annual report 2019[21]. PFR patellofemoral replacement.

The mean age at knee replacement in the United Kingdom is 67 years of age[1]. When considered for knee replacement, this age group represents those of 'middle age' and roughly corresponds to patients between 60 and 75 years of age at primary replacement. These patients represent the largest proportion of knee replacement and have competing goals of surgery. On the one hand, they will require a knee of reasonable durability: average life expectancy for a 67 years old in the United Kingdom is about 18 years (Figure 1-3), with an average age at death of 85 years[22]. On the other hand, they will require a safe procedure, with quick recovery and minimal perioperative complications[23]. As they age, they are more likely to have comorbidities, and increased frailty[23-25]. Finally, as functional demand decreases over time the stress on the prosthesis will reduce, and the requirement of a highly durable prosthesis reduces[26].

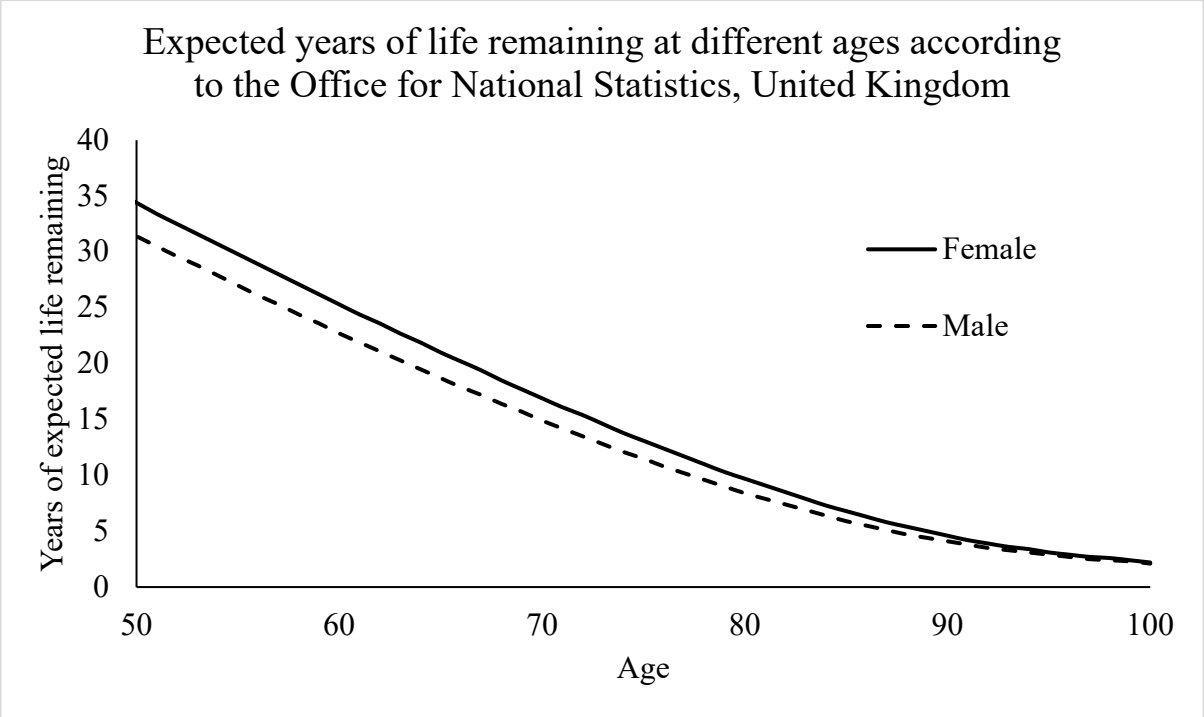


Figure 1-3 Life expectancy at different ages
Figure created from data from the Office for National Statistics[22]

Young age at primary replacement causes concern for the knee replacement surgeon. In this context, young age is often defined as patients younger than 60 years of age at knee replacement. They are much more active than their elderly peers, placing greater strains on the prosthesis[27], and a higher revision rate is seen in this age group compared to their older peers (Figure 1-2). Further, they have a significantly longer life expectancy (Figure 1-3). Mean life expectancy at 50 years of age is a further 33 years[22]. They tend to be more robust physiologically, and can survive more involved operations, but incongruously it is beneficial in young patients to conserve bone stock to allow for potential later revision

surgery[28]. Durability of the prosthesis is of such concern that almost all patients in this age group are counselled to expect revision surgery in their lifetime.

Elderly patients, for the purpose of this thesis, are those older than 75 or 80 years of age at primary replacement. Life expectancy is shorter: on average an 80 year old is expected to live 9 years[22]. They have a lower functional demand on their knee and tend to be limited in their activities due to the physiological ageing process[23-25]; they have a higher prevalence of comorbidities and frailty[23-25]. In individuals aged 70 or older undergoing elective orthopaedic surgery, frailty is estimated to be present in 35% to 41% of patients, depending on the measure used[29], and is associated with a relative increase in mortality of 1.63-6.03 times[30-33].

With particular regard to knee replacement there is an increased prevalence of osteoporosis[34], with subsequent concerns about knee replacement fixation and periprosthetic fracture[35]. The goals of surgery in this age group are to minimise perioperative physiological insult[24], whilst providing a functional knee that will last their lifetime. Revision surgery in this age group can be a disaster, and in some cases it is preferable to leave the patient on medical treatment than risk further surgical and anaesthetic intervention[36, 37]. In this context the type of revision surgery undertaken is crucially important, as a bearing exchange is a fundamentally different operation to a two stage stemmed, constrained, revision knee prosthesis, or indeed an amputation[38]. Perhaps worse, a patient can be in pain and discomfort but is left unrevised owing to concerns over physiological tolerance for further intervention[38]. Generally, these elderly patients prioritise quality of life over other outcome measures.

Table 1-1 Risk of death and complication by age
From a cohort of Orthopaedic patients from Japan[39]

Age group	Risk of death*	Adjusted odds ratio for death#	Risk of complication*	Adjusted odds ratio for complication#
<65	0.03%	Reference	3.01%	Reference
65-80	0.06%	2.58 (1.36-4.89)	4.07%	1.22 (1.09-1.36)
80+	0.11%	5.88 (2.93-11.8)	4.85%	1.51 (1.31-1.75)
*Absolute risk estimated from 41,060 total knee replacements #Estimated from 107,104 patients who had undergone cervical laminoplasty, lumbar decompression, lumbar arthrodesis or total knee replacement. Adjustments made via regression for comorbidity (Charlson Comorbidity Index), sex, and surgical procedure.				

In conclusion, age alters the priorities of surgery in a non-linear way. It is thus important to examine the age groups independently of each other to determine the appropriateness of interventions.

1.3. Selection

Broadly, knee replacement can be classified as partial (also known as unicompartmental) and total knee replacement. Partial knee replacement replaces only the diseased portion of the joint and requires the rest of the joint to be functionally intact, whilst total knee replacement replaces the entire knee and will often require the resection of normal parts of the knee.

Partial knee replacements replace only the diseased part of the joint. This can be medial, lateral or patellofemoral. Medial PKR is by far the most common, and is used where the disease process affects the medial compartment. Beyond the anatomic region of replacement, there are different designs of PKR. A major difference is whether the polyethylene bearing is fixed to the tibial tray, with designation as fixed and mobile bearing designs. There are small differences in indication (described below), with surgeons often having a preference based on outcome (further discussed in 1.4 Outcome). Other design differences include tibial component design (all polyethylene or metal backed, different shapes and coverage of the tibial plateau), femoral component design (mono- or polyradial), and implant to bone fixation (cemented or cementless, keel or peg).

A requirement for medial Oxford PKR is that the cartilage has completely eroded on both femur and tibia, leading to bone-on-bone arthritis. Further, the rest of the joint must be functionally intact. The lateral compartment must have full thickness cartilage, the anterior cruciate ligament must resist anterior translation, and the medial collateral ligament resist valgus deformity. In contrast, total knee replacement excises all articular surfaces and the anterior cruciate ligament.

Debate continues regarding precise indications[40], and PKR can be considered in patients outside the indications described above. For example, fixed bearing PKR may be considered in patients who are ACL deficient[41, 42], or a deficient ACL in appropriately selected patients may be reconstructed at or before PKR insertion[43].

The Oxford PKR (Zimmer Biomet, Warsaw, Indiana, USA) is used exclusively in this thesis owing to the availability of data, the longevity of data, and its widespread use. Selecting one device minimises potential sources of bias that can be introduced with multiple designs, but limits the generalisability to other designs of PKR. Where PKR is used in text, it tends to refer to Oxford PKR.

Eligibility for PKR has traditionally been based on the disease pathoanatomy described above[44], and for medial Oxford UKR it is recommended that these are assessed with plain weight-bearing anteroposterior and lateral radiographs[45]. Routinely acquired should be further assessment of the lateral compartment with either a valgus stress radiograph, or a fixed flexion weight-bearing posteroanterior (PA) radiograph (a Rosenberg view[46]). If bone-on-bone arthritis is not demonstrated in the medial compartment, further investigation with varus stress radiographs, Rosenberg views, or arthroscopy may be undertaken. The pathoanatomy identified via the investigations should then be confirmed at time of operation, in particular, the status of the anterior cruciate ligament, patella and lateral compartment. The radiographic assessment has been published as a Decision Aid[47] (Figure 1-4 and Figure 1-5).

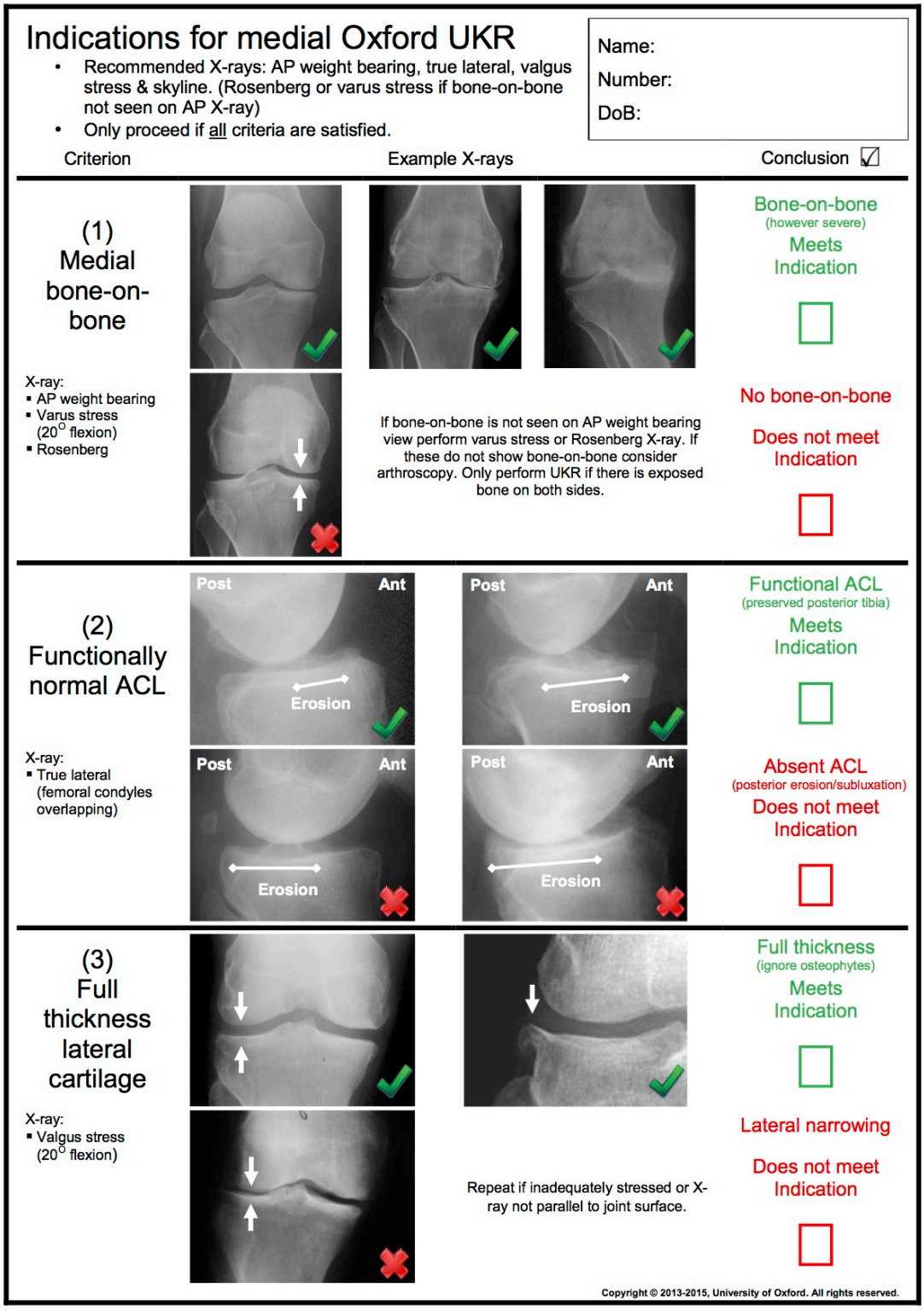
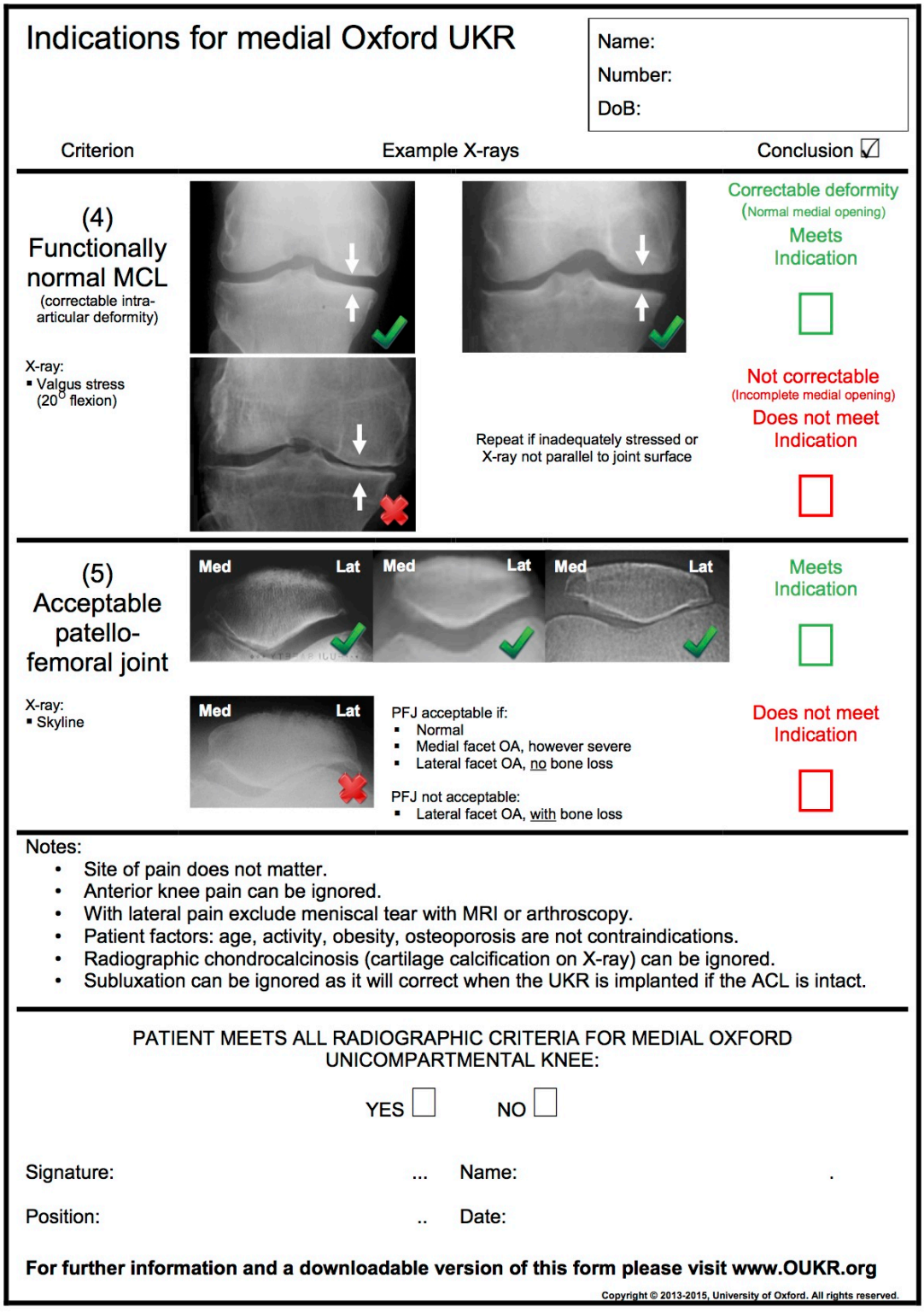


Figure 1-4 Radiographic decision aid for medial Oxford PKR (first page, reproduced from Hamilton et al[47] with permission)



Indications for medial Oxford UKR

Name:
Number:
DoB:

Criterion | Example X-rays | Conclusion ☑

(4) Functionally normal MCL
(correctable intra-articular deformity)

X-ray:
- Valgus stress (20° flexion)

Repeat if inadequately stressed or X-ray not parallel to joint surface

Correctable deformity
(Normal medial opening)
Meets Indication

Not correctable
(Incomplete medial opening)
Does not meet Indication

(5) Acceptable patello-femoral joint

Med Lat

X-ray:
- Skyline

PFJ acceptable if:
- Normal
- Medial facet OA, however severe
- Lateral facet OA, no bone loss

PFJ not acceptable:
- Lateral facet OA, with bone loss

Meets Indication

Does not meet Indication

Notes:
- Site of pain does not matter.
- Anterior knee pain can be ignored.
- With lateral pain exclude meniscal tear with MRI or arthroscopy.
- Patient factors: age, activity, obesity, osteoporosis are not contraindications.
- Radiographic chondrocalcinosis (cartilage calcification on X-ray) can be ignored.
- Subluxation can be ignored as it will correct when the UKR is implanted if the ACL is intact.

PATIENT MEETS ALL RADIOGRAPHIC CRITERIA FOR MEDIAL OXFORD UNICOMPARTMENTAL KNEE:

YES ☐ NO ☐

Signature: ... Name: .

Position: .. Date:

For further information and a downloadable version of this form please visit www.OUKR.org

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Figure 1-5 Radiographic decision aid for medial Oxford PKR (second page, reproduced from Hamilton et al[47] with permission)

Various philosophies exist regarding the use of partial knee replacement, and these interact with the severity of arthritis (Table 1-2 & Figure 1-6). Those that use UKR as an alternative to TKR tend to implant PKR in knees with severe ('bone-on-bone') osteoarthritis. In contrast, some surgeons have suggested partial knee replacement should be used in early arthritis[48, 49], and in doing so delay total replacement (Table 1-2). Partial knee replacement is consequently reserved for patients with symptomatic early arthritis in whom the surgeon is unwilling to perform a total replacement.

There is only one study that has attempted to look at the prevalence of use in early arthritis. This study looked at a sample of radiographs from the National Joint Registry of England, Wales, Northern Ireland and the Isle of Man, and found that almost a third (29%) of PKR implanted between 2006 and 2010 had been implanted in those with early arthritis[50].

Table 1-2 'Bone-on-bone' TKR alternative vs 'early arthritis' Pre-TKR philosophy for PKR

Philosophy	**TKR alternative**	**Pre-TKR[48, 49]**
Usage	Definitive implant	'*Supplement to future TKA'*
Arthritis severity	Medial bone-on-bone arthritis Full thickness lateral cartilage	Mild to marked joint space narrowing (Ahlback* 2 and 3 most commonly, can be considered in Ahlback 4)
Clinical findings	Symptoms of severity to warrant joint replacement Range of motion >100 degrees	Patient 'inconvenienced' rather than disabled by their arthritis. Age > 45 Range of motion at least 10 to 100 degrees.
Contraindications	Inflammatory arthritis Anterior cruciate or medial collateral ligament deficiency Bone loss in lateral facet of patellofemoral joint	Inflammatory arthritis Significant patellofemoral symptoms Sclerosis with loss of lateral joint space on Merchant radiograph
*Ahlback[51] Grade 1 is joint space narrowing (joint space < 3mm), Grade 2 is 'bone-on-bone', Grade 3 is <5mm of bone loss, Grade 4 is 5-10mm of bone loss. However, the Repicci paper has an example picture marked as Grade 2 showing preserved joint space. TKA total knee arthroplasty		

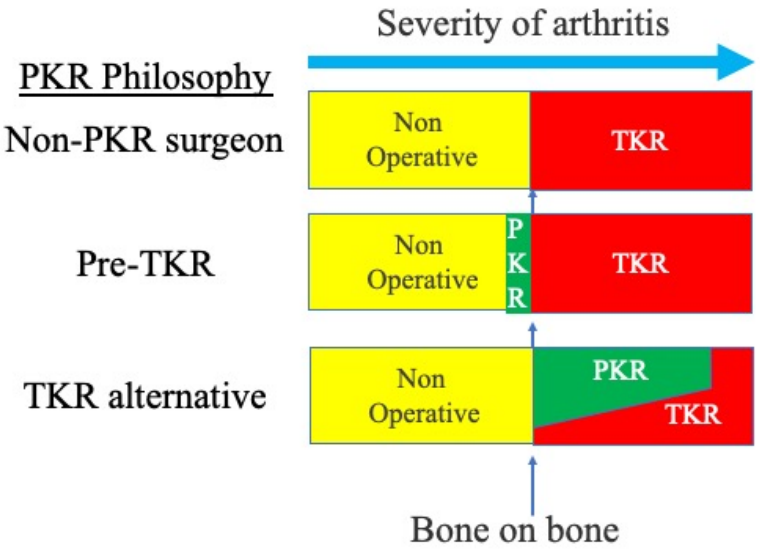


Figure 1-6 Different philosophies for PKR use
Many surgeons believe that partial replacement should be done before total replacement is considered. If the arthritis is severe and affects more than one compartment, then total replacement should be performed from the outset. Those that use PKR in severe osteoarthritis use PKR as an alternative to TKR and choose an appropriate prosthesis depending on underlying pathoanatomy.

PKR and TKR are two procedures that share indications in a subset of patients with knee osteoarthritis. When used for defined evidence based indications[52] as an alternative to TKR, where the arthritis is severe, all PKR could have TKR. However, not all TKR patients could have PKR. Where PKR is considered a 'pre-total' replacement, the two do not share overlapping indications. For the purpose of this thesis, the 'TKR alternative' indications are taken as the gold standard, and all patients receiving PKR could also receive TKR.

There are several studies that have attempted to identify the proportion of patients that may be eligible, or candidate, for partial replacement (Table 1-3). Those that have been

published represent essentially two schools of thought: three studies represent 'TKR alternative' indications, with the senior authors being Professor Cobb of Imperial College London (Willis-Owen et al[53]), Professor Murray of Oxford University (Hamilton et al[47]), and Professor Price of Oxford University (Wang et al[54]). The other two represent New York, with the senior authors being from New York University Langone Medical Centre (Arno et al[55]), and the Hospital for Special Surgery, New York (He et al[56]). This geographical distinction is represented in their estimates, the former estimating 49-56% could have medial PKR, with the latter estimating 18-21% (Table 1-3). None of the peer-reviewed literature has estimated eligibility in different age groups.

Differences in methodology reflect differences in beliefs surrounding replacement of the joint. The studies by Hamilton et al[47], Wang et al[54] and Willis-Owen et al[53] all made their assessment of PKR eligibility by using a combination of preoperative radiographs and clinical information. The indications were similar to those described in Table 1-2. Hamilton et al[47] reviewed 457 knees using a combination of standard weight-bearing anteroposterior and lateral radiograph, supplemented with stress radiographs where required. Wang et al[54] and Willis-Owen et al[53] determined eligibility based on anteroposterior and lateral radiographs alone.

Arno et al[55] used different methodology. They looked at 97 femoral and tibial resections from total knee replacements, and undertook a visual, histological and clinical analysis to determine whether indications were met for medial PKR. They graded their visual and histological findings. Via histology they determined that the osteoarthritic involvement of the lateral compartment was too severe in 25 cases (26%). Of these, only 11 were considered to be too severe on visual inspection. It is difficult to know how to approach

their findings, as most studies regarding PKR outcome have used radiographs to assess the lateral compartment. It is possible, and in fact is quite likely, that a normal joint space on radiograph has signs of osteoarthritis on more detailed investigation. This is a concept that is explored further in Chapter 4, but in one study using MRI 89% of patients with a normal radiograph were shown to have signs of osteoarthritis[57]. Further, in another study which used MRI, only one third of lesions involving the lateral tibial plateau had progressed over two years[58]. As a retrospective histological analysis is not possible to undertake prior to patient surgery, this method is somewhat impractical to implement. Further, it is unknown how many of these knees would have gone on to fail in the lateral compartment, and thus it is difficult to interpret the findings of this study.

He et al[56] looked at 300 knees and used a combination of preoperative radiographs and clinical findings to determine if they were candidate for medial PKR. They determined that only 54 (18%) were. However, they determined that 107 (36%) were ineligible due to varus deformity ≥10 degrees, and a further 119 (40%) were ineligible due to being unable to flex past 90 degrees. To contrast this, the findings from Arno et al were that all 97 knees (i.e. 100%) could flex past 90 degrees[55]. This finding of 40% being unable to flex past 90 degrees suggests a population with perhaps quite severe arthritis which may therefore not be generalisable. Further, an inability to flex past 90 degrees is not a contraindication provided the knee can flex past 90 when anaesthetised. Additionally, varus deformity is not considered a contraindication to Oxford PKR. As comparative information, a separate study established in a UK population that 8% undergoing medial PKR had varus deformity ≥10 degrees, and this group, when compared to other alignments actually had the best functional outcome following surgery[59]. Given these exclusions it is thus difficult to interpret the findings of this study

Table 1-3 Studies examining eligibility for partial knee replacement

Author	Senior author region	Patient region	Year	Number	Selection	Method	Medial	Lateral	PFJ	Mixed
Willis-Owen[60]	UK	UK	2009	200 knees	Patient undergoing any knee replacement	Pre-operative Radiographs	56.0%	12.6%	10.5%	20.8%
Arno[55]	USA	USA	2011	97 knees	'TKR with medial osteoarthritis'	Clinical and post-operative histology	21%	Not assessed	Not assessed	79%
Hamilton[47]	UK	USA	2017	457 knees	Consecutive TKR and medial PKR	Pre-operative radiographs	49%	Not assessed	Not assessed	51%
He[56]	USA	China	2018	300 knees	Patients undergoing TKR	Clinical and radiographs	18%	Not assessed	Not assessed	82%
Wang[54]	UK	China	2018	155 patients 168 knees	Patients undergoing TKR in China	Pre-operative Radiographs	51.2%	6.5%	1.2%	45.9%
NR not reported; PKR partial knee replacement; TKR total knee replacement										

It may be suspected that if PKR is being used as a 'pre-total' replacement that younger patients would be more likely to receive it. In the United Kingdom, the number of partial and total replacements performed in total are reported in the NJR annual report[1], and are plotted in Figure 1-7. There is a clear association with age, with 23% of those younger than 55 at surgery receiving PKR, with only 4% of those older than 75 years at surgery receiving PKR. Whilst these estimates demonstrate a clear reduction in use with age, it remains unclear if this reflects the underlying pathoanatomy.

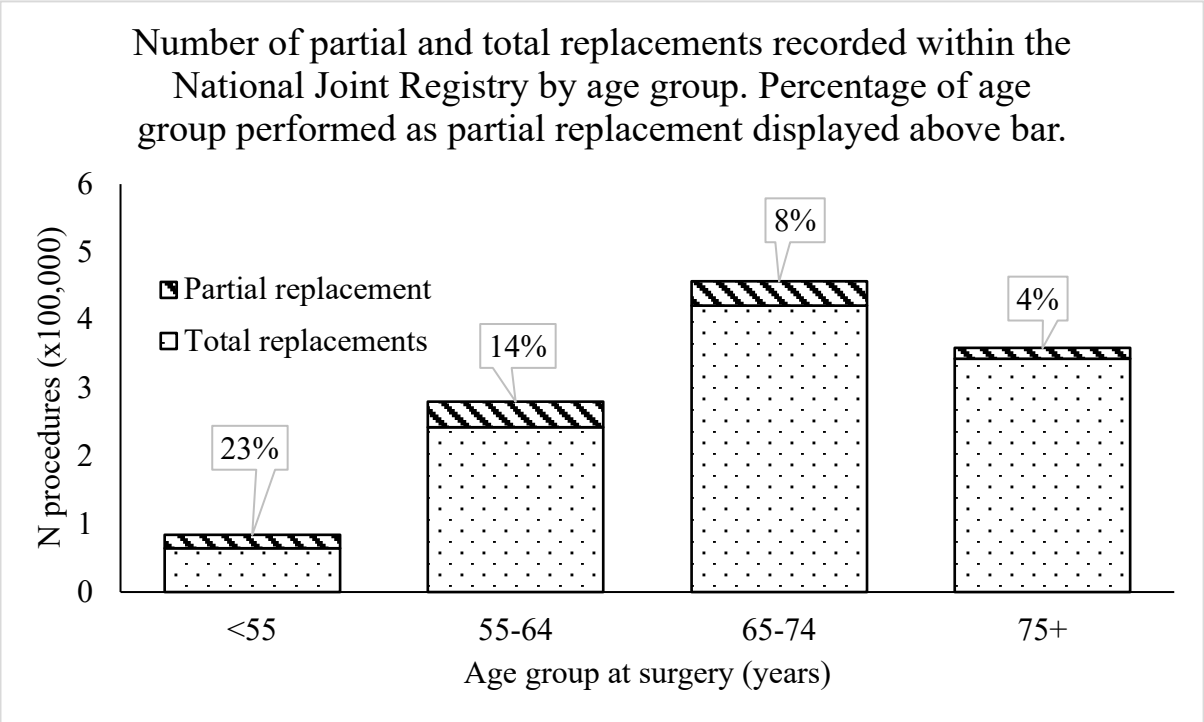


Figure 1-7 Recorded procedures (PKR or TKR) by age in the NJR

There are no peer-reviewed studies looking at the selection of patients for PKR or TKR by age. Looking at usage alone will not be able to identify or separate the indications for usage. It is important to understand the proportion of patients that may be eligible for

PKR given the need to weigh up potential risks and benefits in different age groups. Further, as discussed next in 1.4 Outcome, a key predictor of outcome is related to the number of PKR undertaken by a surgeon. Thus having an idea of the proportion of patients eligible for PKR will be useful for surgeons and healthcare providers.

1.4. Outcome

By replacing structurally abnormal ('diseased') knee parts with a prosthesis, the main aim of knee replacement is to restore function and alleviate pain. These goals are common to both PKR and TKR. Several domains of outcome are important: function, pain, further surgery (including revision), morbidity and mortality, and cost-effectiveness (specific scoring systems are presented in the Appendix). Despite the breadth of these domains, there is wide variability in the reporting of adverse events related to knee replacement (Table 1-5), particularly with regards to joint registries which predominantly report on revision surgery alone.

Table 1-4 Brief overview of outcome scores used in this thesis

Oxford Knee Score[61, 62]	PROM around knee pain and function
Tegner Activity Score[63]	PROM around activity level
EQ-5D[64]	PROM regarding quality of life, often used in health economic analyses
American Knee Society Score Objective component[65]	Clinician completed report regarding alignment and range of motion of knee
American Knee Society Score Function component[65]	PROM regarding pain, walking distance and requirement for walking aids
PROM patient reported outcome measure	

Table 1-5 Commonly and sometimes reported adverse events in knee replacement

Commonly reported:	Revision
Sometimes reported:	Morbidity and mortality Failure to improve in pain or function Significant ongoing disability of any cause attributable to the operation

The most rigorous data to date comes from the Total or Partial Knee Arthroplasty Trial[66] (TOPKAT), a prospective, pragmatic, randomised controlled trial of 528 patients from 68 UK surgeons across 27 sites. The five-year results were published in The Lancet in 2019. It found a non-significant one point difference in the primary outcome of Oxford Knee Score (favouring PKR), but did find a significantly higher EQ-5D in those with PKR. There was no difference in complication rates or revision rates, which is in contrast to registry reports. However, some authors have criticised the trial design[67], arguing that the requirement that surgeons perform ten procedures per year with either prosthesis was unfair. They argue that the expertise required to perform ten PKR per year is much higher than the expertise to perform ten TKR per year.

Before TOPKAT, most comparisons had been matched, observational studies. These are all at risk of confounding by indication, where the prostheses are used for different indications (see 1.3 Selection for a discussion on PKR indications). Despite this, many variables were matched to attempt to balance the two groups. Further, as some outcomes are rare (e.g., mortality, perioperative morbidity such as stroke or heart attack) a randomised trial is impractical, and observational datasets represent the only feasible way of obtaining this important information.

The largest study identifying function is of 14,076 patients matched between PKR and TKR on multiple variables from a combined, linked dataset of NJR and Hospital Episode Statistics (a database containing patient level information with regards to comorbidities and readmissions)[68]. This study found benefits with PKR across multiple outcomes, including six-month OKS being two points higher, EQ-5D being higher (0.772 vs 0.751), a higher satisfaction (odds ratio 1.27), and complications being less likely to be reported.

Given the expense of randomised controlled trials is it not feasible to power a trial for rare events. In this case the best way to identify rare complications are observational studies. Liddle et al performed a matched observational study utilising registry data and hospital episode statistics, matched 101,330 patients (25,334 PKR, 75,996 TKR) and found that morbidity and mortality was lower with PKR[3] (Figure 1-8). Mortality was a rare event: 90-day mortality for TKR was about 1 in 200 patients, and for PKR was about 1 in 500 patients. Overall they found that if 400 patients were treated with PKR instead of TKR, one life would be saved within 90 days. Furthermore, serious adverse events that do not lead to mortality were also significantly lower with PKR, these include stroke (odds ratio 0.37, p=0.02), heart attack (odds ratio 0.53, p=0.02), and thromboembolism (odds ratio 0.49, p<0.001; Figure 1-8). Whilst confounding by indication may exist in this study, once the patients have been matched on comorbidities, age and other variables there is little biological plausibility to support that the arthritic severity within the knee would lead to a higher level of comorbidity or mortality. As such, these results are likely to be true, and the study was published in The Lancet. These findings have been supported by other hospital studies[69, 70].

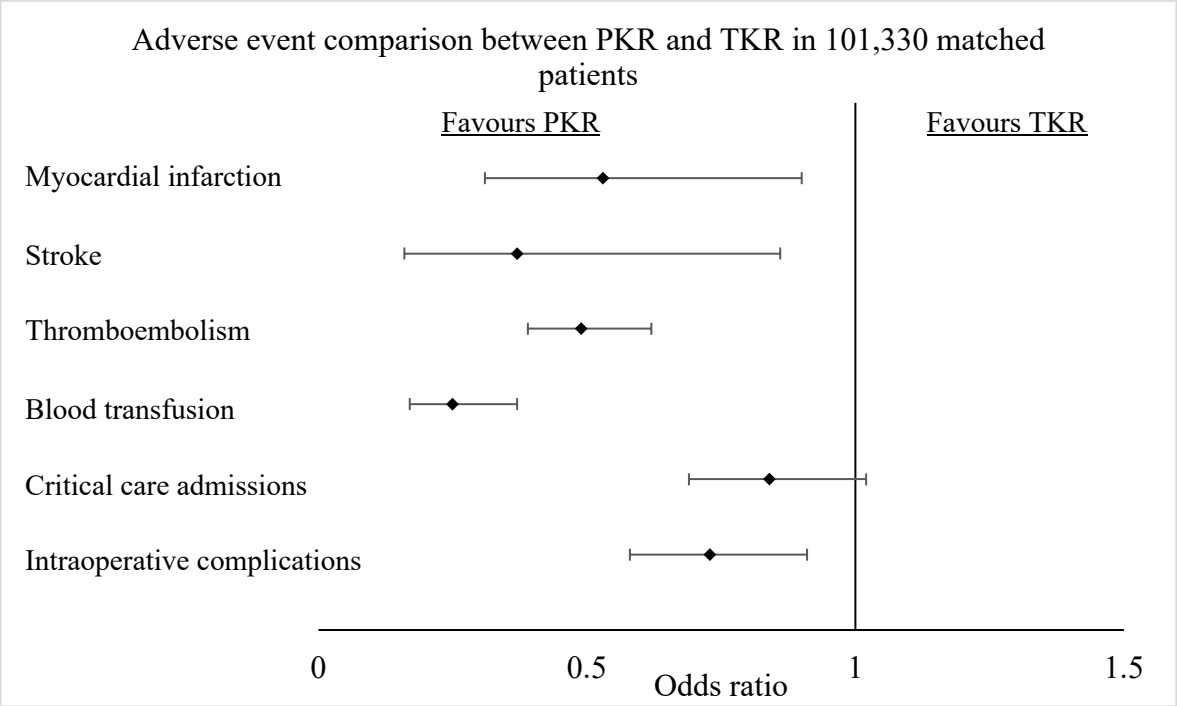


Figure 1-8 Adverse events between PKR and TKR
Adapted from Liddle et al[3]. The displayed adverse events are substantially reduced when PKR is received.

In nearly all analyses, TKR has been shown to have lower rates of revision than PKR, particularly in results from joint registries (Figure 1-9). However, multiple large cohort studies, and now TOPKAT, have published long term revision rates much lower than that reported in the registries. One explanation for the discrepancy is the 'threshold to revision'. If, for example, a knee replacement has a problem and requires further surgery, and there are two choices, one is an extensive operation with substantial morbidity, and one is a more straight forward operation which is performed frequently, a surgeon and patient will probably choose the smaller and less morbid procedure. In this context, a revision of a PKR to a simple, straight-forward TKR is more likely to be offered than a complex revision of a TKR involving added constraint for bone and ligament losses. This

is reflected in data from the New Zealand Joint Registry, who report that 60% of PKR with a poor functional outcome are revised, compared to 10% of TKR[38].

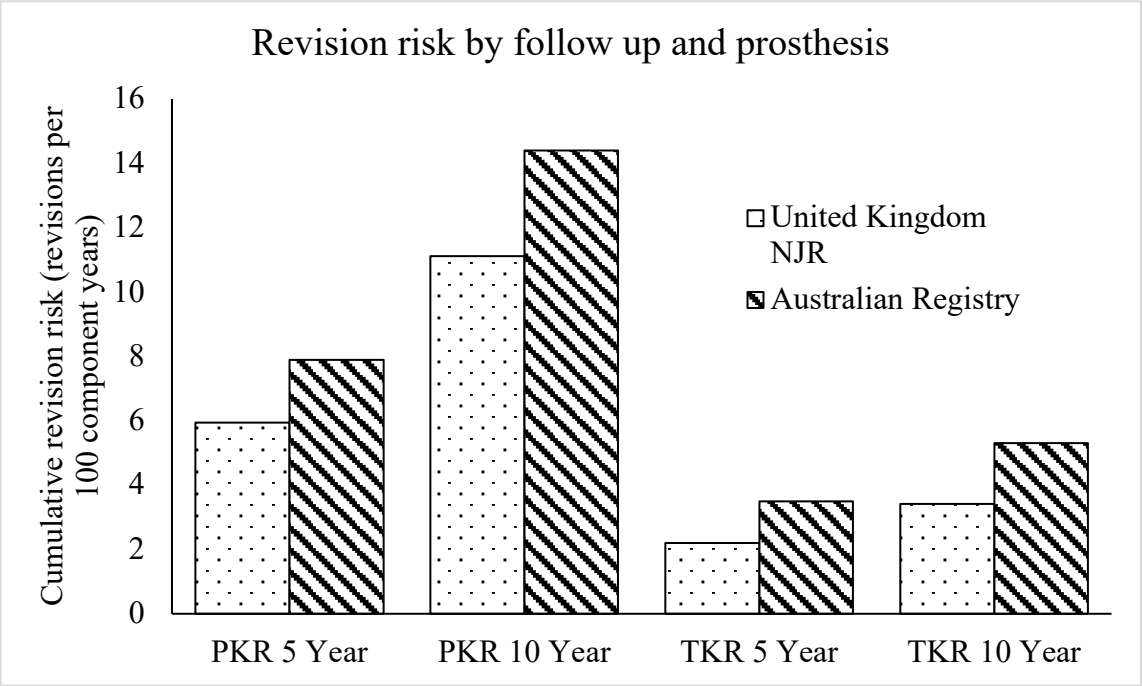


Figure 1-9 Revision risk by prosthesis and follow up in the Australian and UK registries
The revision rate of PKR is significantly higher than that observed in TKR. PKR partial knee replacement; TKR total knee replacement.

Surgeon usage, defined as the proportion of the surgeons' knee replacement practice that is performed as PKR, has been demonstrated to be associated with subsequent revision rates[71-73]. It is an extension of the idea of caseload, which is the annual number of procedures undertaken by a surgeon. It stands to reason that higher caseloads will lead to greater expertise in the procedure, specifically in patient selection and technique, which in turn will lead to better outcomes. For both PKR and TKR an effect of caseload has been demonstrated, though the effect is greater with PKR: Liddle et al[72] in a study based

on the NJR, demonstrated that the most commonly performed number of PKR per surgeon per year in the UK is one. Further there was a non-linear effect with caseload for PKR. There was a significant reduction in revisions per 100 component-years, a surgeon performing 5 cases per year would have 3 revisions per 100 component-years, those performing 10 cases per year would have about 2 revisions, and those performing over 30 cases per year would have about 1 revision per 100 component-years. For TKR the relationship was linear but less: those performing 5 cases per year would have about 0.7 revisions per 100 component-years, in those performing 50 cases per year there would be about 0.5 revision per 100 component-years.

Despite this strong effect of caseload, there were some reports of surgeons having a high revision rate despite performing what was considered an acceptable caseload. In one report[74], 22 procedures were performed per year, representing 7% of the surgeons usage. They reported a 5-year survival of 86.5% (95% CI 78-95), and following their report discontinued the use of the intervention.

An increasing recognition of the different philosophies of PKR was emerging, as discussed in Chapter 1.3 Selection, where some surgeons use PKR in patients they are unwilling to perform TKR in (those with early arthritis), whilst others perform at as a definitive intervention. Further, the size of a surgeon's knee replacement practice is often beyond their control, and many surgeons would be unable to increase the size of their practice. Thus the concept of usage emerged.

Usage introduces the surgeon's philosophy to the outcome measurement. A study based on 42,000 patients from the NJR showed that usage was also related very closely with

revision rates[73]. Those performing less than 5% of their practice as PKR had the highest revision rates. Optimal results were found with a usage of 40-60%. Hamilton et al undertook a systematic review and meta-analysis, and showed that usage was more important than caseload in determining outcome[71]. Performing greater than 24 PKR per year led to a revision rate of 0.88% per year (95% CI 0.63 to 1.61), whilst a usage of more than 30% was associated with a revision rate of 0.69% per year (95% CI 0.50 to 0.90). Further, a high usage >20% was associated with lower revision rates whether the caseload was high or low.

This thesis compares mobile bearing Oxford PKR with TKR, however fixed bearings are an alternative PKR option in many patients. Historically fixed bearings had a higher rate of linear polyethylene wear[75-77] but couldn't dislocate, and mobile bearings had a lower rate of linear polyethylene wear, but could dislocate. Debate continues regarding what constitutes troublesome wear[78-80] but the introduction of ultra-high molecular weight polyethylene bearings, which are highly cross linked thus preventing wear, has seen the longevity of the fixed bearing increase[81]. Whilst differences remain in the modes of failure[82, 83], systematic reviews of comparative studies[82-86] and registries [1, 87-89] now demonstrate equivalence in overall implant survival. Therefore consideration should be given to implantation of fixed bearing devices, particularly in patients where there is a preference to avoid dislocation, for example in the elderly [90].

The type of revision procedure undertaken has also not been particularly well studied. It is known that revisions of PKR are less complex than revisions of TKR[91]. Complex revision procedures will lead to greater functional disability. Further, a bearing exchange for a dislocated bearing in mobile-bearing PKR is different to a two-stage, complex

revision for infection; yet both are counted as a ‘revision’. This is a concept explored further in Chapter 7 with terminology introduced of ‘simple’ and ‘complex’ revisions. Revisions exist on a spectrum; at the lesser end is a simple bearing exchanged for a bearing fracture or dislocation. For many PKR, where minimal bone is resected from the condyles, if the fixation is lost it can be revised to another PKR component, or often to a primary TKR. However, as a primary TKR takes more bone than a primary UKR, it will require greater reconstruction when revision procedures are undertaken. Therefore by the nature of the primary surgery TKR revisions are more likely than PKR revisions to be considered complex, requiring more stems, wedges and stabilisation.

A major limitation of registries is that the indications for the revisions are not reported in detail. Infection is arguably the most serious consequence following knee replacement and is a much rarer occurrence after PKR. In one study, around one in four TKR revisions were for infection, whilst one in 33 were PKR revised for infection[92]. They then went on to exclude these patients prior to their comparative analysis of ‘aseptic’ revisions, demonstrating a philosophy that the indication for revision is important in the minds of surgeons and authors. However, there is limited data available regarding the long term outcome of revision by indication.

1.5. Generalisability: Designer centre bias?

In making treatment decisions, doctors and patients must take into account relevant evidence. Relevance depends on generalisability, also known as external validity. That

is, whether the results can be reasonably applied to a definable group of patients in a particular clinical setting in routine practice[93].

The measurement of outcome is a fundamentally important exercise in order to determine the best treatment for patients. The ability, resources and motivation to follow up large numbers of patients is often possessed by designing centres. With regards to Oxford PKR, this has led to a preponderance of designer centre studies, in one review accounting for one half of all published studies[94] reporting outcomes of the prosthesis. The designer centre results were found to publish revision rates that were four times better than those reported in national registers[94]. Further studies have found that designing centres tend to publish results that are superior to that observed in registers[95].

National registers were established, in part, to overcome publication bias and report on the outcome of all implanted prostheses, and widely hail themselves as providing the most generalisable results. There certainly are advantages to registries. They provide early identification of poorly performing implants, and revision rates are updated yearly[96].

Which, then, provides the true results? Which should patients and surgeons believe? Simple questions, but no simple answer. The true results depend on which question is being asked. If the question is, what is the revision rate for all the prostheses implanted in the country, then the register provides the true answer. If the question relates to what expert surgeons can achieve, then perhaps it is the designer centre results that should be believed, in the absence of individual surgeon level data.

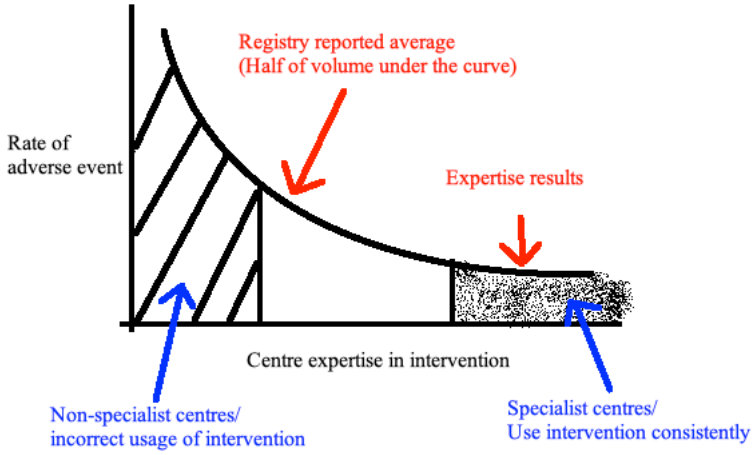


Figure 1-10 Expected results against intervention expertise
Schematic showing difference between generalised averages and specialist centre results. Figure created for this thesis.

To complicate matters further, one can take a health service perspective. From this perspective it can be asked how outcomes can be improved for a population. As part of this, well performing units and surgeons can be identified and lessons learned for the health system. One of the questions this thesis aims to address, is whether the designer centre results can be replicated in other centres, therefore providing some evidence towards generalisability under specific circumstances.

Multiple centres were chosen to inform this thesis, all using the Oxford medial PKR. The Oxford medial PKR has a long history of use, and there are several series of patients that have moderate to long term outcome data. All of these centres tend to be high volume users, as these centres have the inclination and funding to undertake follow up of large numbers of patients. One is the designer centre. One is a high volume surgeon outside of the designer centre based in the United States. This surgeon is knowledgeable with use

of the device and has contributed to the design of several instruments related to implantation. Centres in Japan, New Zealand, and Australia all had surgeons who had undertaken fellowships in Oxford.

1.6. Aims, scope and structure of thesis

The aims of this thesis are to, **with a focus on age**:

1. Explore patient selection for partial and total knee replacement;
2. Describe, compare and predict outcomes of partial and total knee replacement; and
3. Explore generalisability between designer and non-designer cohorts.

This thesis is structured into three Sections. **Section I** addressing the concept of selection for PKR and TKR by describing the proportion of knees that may be eligible for PKR. **Chapter 2** analyses the type of knee replacement (partial, PKR, or total, TKR) performed at the Nuffield Orthopaedic Centre, Oxford (the designer centre) by all knee surgeons, and categorises them into different age groups to describe differences in the proportion being performed. **Chapter 3** externally validates the proportion of knees being performed as PKR at an external specialist centre in the USA. However, the results may have been influenced by referral bias, and thus the accuracy of radiographs was determined in identifying candidates for PKR. This information was then employed in **Chapter 4**, where a centre that isn't at risk of PKR referral bias was analysed in Australia using a

radiographic review. This chapter provides generalisable estimates of PKR eligibility in different age groups.

Having established an estimate of how many patients may be eligible for PKR, **Section II** addresses the outcome of PKR in different age groups. **Chapter 5** looks at the long term outcomes of a prospectively followed cohort of knees from the Nuffield Orthopaedic Centre. It aimed to look at the functional outcome, implant survival, indication for revision, and type of revision procedure undertaken in each age group. To gather evidence regarding generalisability of findings from the designer centre, **Chapter 6** examines data acquired from three other centres to compare the implant survival, indication for revision, and type of revision undertaken.

Finally, **Section III** aims to compare results between PKR and TKR in different age groups. **Chapter 7** matches knees from the designer centre with a prospectively followed cohort of TKR. Attempts were made to exclude those TKR that would ineligible for medial PKR based on intraoperative data. Function, implant survival, and type of revision are examined in different age groups. Finally, an outcome that has recently become popular is the concept of lifetime revision risk, which is important for patients of different ages. **Chapters 8 and 9** contain modelling of lifetime revision risk for PKR and TKR respectively in different age groups.

Each section contains a section introduction, section discussion, and section summary to orient the reader, and provide detailed discussion. It has been structured this way to consolidate relevant parts of the introduction to the section, avoid repetition within each chapter, and allow the reader to have an overview of the thesis from the thesis

introduction, whilst providing further detail within the section introduction. In addition, a section discussion and summary are provided at the end of the final chapter within each section.

This thesis consists predominantly of statistical analysis of datasets. In the first section I acquired, cleaned, verified and tallied the data sources from Oxford and from Melbourne. The data from America had been compiled and cleaned for another purpose. My analysis was therefore a secondary analysis using different endpoints.

In the second section all the cohorts had been prospectively followed. However, the New Zealand and Japanese data required cleaning prior to statistical analysis. All statistical analyses were decided upon and undertaken by me.

In the third section, the Knee Arthroplasty data had been collected prospectively but required cleaning. The propensity models and statistical analyses were developed by me. The lifetime revision risk models had not previously been used in this context, and were developed from a theoretical basis.

Through the completion of this thesis I learned many statistical models and analyses, how to use statistical programs including R (R Core Team, Vienna, Austria) and Stata (StataCorp, Texas, USA), and was introduced to computational programming in the form of MATLAB (Mathworks, Massachusetts, USA).

Section I: Selection and age

2. Age-stratified PKR usage at the designer centre: the Nuffield Orthopaedic Centre, United Kingdom

2.1. Selection for knee replacement: Section Introduction

Provision of knee replacement is increasing [9], and is most rapid in those historically considered too young (<60 years of age)[10, 97]. The National Joint Registry for England, Wales, Northern Ireland and the Isle of Man (NJR) shows that young patients are more likely to receive partial knee replacement (PKR) than their elderly peers [98]. However, registries do not contain information on patient selection and therefore do not reflect true candidacy: it is likely that some of patients receiving PKR were not indicated for PKR, whilst others undergoing total knee replacement (TKR) could have had PKR. It thus remains unknown how age affects eligibility for PKR.

Goals of surgery in young patients differ to those in older patients; generally speaking, younger patients require a higher functioning knee, and will wish to avoid major revisions given their longer life expectancy, contrarily older patients will ideally undergo a procedure with a rapid recovery and minimal risk of medical complications that restores appropriate function. Both PKR and TKR can be used for anteromedial osteoarthritis of the knee. PKR provides shorter hospital stays, better function, fewer deep infections, lower mortality, and fewer perioperative complications such as venous thromboembolic and major cardiac events[99-102]. The main criticism of PKR is its higher revision rate, with registries showing a higher revision rate for PKR than TKR[88, 103].

The designer centre in Oxford uses PKR whenever a patient is appropriate for it. Thus the usage from this centre will reflect the candidacy at this hospital. Whilst it functions mainly as a primary referral centre, there are a few referrals from outside the region from surgeons who think patients are appropriate for PKR. Therefore there is a chance estimates from this centre may lack external validity, and may be inflated due to referral bias.

The indications for PKR can be identified radiographically, but often requires specialist imaging, such as stress radiographs, which are not routinely available in non-specialist centres. The accuracy of these radiographs when compared to surgeon usage has not previously be identified. However, radiographic estimates from specialist centres may also be subject to referral bias a generalisable estimate cannot be made. It will consequently be important to identify the accuracy of radiographs without stress views, in identifying eligibility for PKR.

It will be of interest to patients, surgeons and health providers to have an idea about how candidacy for medial PKR might change with age. No previous studies have looked at the proportion of patients in different age groups who are eligible for medial PKR.

The aims of this section are to:

1. Determine the proportion of patients in each age group eligible for PKR at the designer centre
2. Determine the proportion of patients in each age group eligible for PKR at a non-designer centre
3. Determine the accuracy of limited radiographs on determining PKR eligibility

4. Determine the proportion of patients in each age group eligible for PKR at a non-designer, non-specialist centre

2.2. Chapter introduction

The designer centre is the Nuffield Orthopaedic Centre, Oxford, UK and surgeons are all familiar with partial knee replacement. The philosophy of implantation is that if a knee needs replacing it should receive a partial knee replacement unless there is a reason that total replacement is required. Therefore usage estimates from this centre should accurately reflect the proportion of patients eligible within the centre.

The primary aim of this chapter is to investigate the proportion of knees appropriate for partial knee replacement in different age groups.

2.3. Methods

A retrospective cross-sectional study of consecutive primary knee replacements was studied to determine the effect of age on candidacy for PKR. Between November 2017 and October 2019 1,424 consecutive primary knee replacements were undertaken. The pragmatic study design identified all consecutive primary knee replacements by nine consultant surgeons and those under their supervision. These included all primary TKR and PKR. Patellofemoral replacements and revision surgeries were excluded. The PKR undertaken were Oxford medial PKRs (Oxford Microplasty PKR, Zimmer Biomet, Warsaw, Indiana), Oxford domed lateral PKRs (Zimmer Biomet, Warsaw, Indiana), and fixed lateral Oxfords (FLO, Zimmer Biomet, Warsaw, Indiana).

As a designer centre all surgeons have extensive experience with PKR. The type of surgery undertaken is decided based on the pathoanatomy and the wishes of the patient. Indications are bone-on-bone tibiofemoral arthritis, preservation of the remaining compartment, intact anterior cruciate and collateral ligaments, and an acceptable patellofemoral joint (see Introduction, 1.3 Selection, page 7). Contraindications to PKR include inflammatory arthritis, ligament deficiency, and patient preference. The Nuffield Orthopaedic Centre is a primary referral centre from the community for joint evaluation, and whilst it also serves as a tertiary referral centre for complex joint pathology the majority of its work is elective primary replacement. The patients were identified through physiotherapy records. Ethical approval was not necessary under NHS research governance as the data was anonymised observations from routine patient care.

The main variable of interest was the type of knee replacement undertaken. This was categorised as partial if a medial or lateral partial knee replacement was undertaken, or as total if a total knee replacement had been undertaken. Age was categorised as per joint registries into <55, 55-<65, 65-<75, and 75+.

Statistical analysis: Counts were tallied, and frequencies calculated. Significance was tested using a chi-squared test. For each age group, the number of partial or total knee replacements performed during the study period were calculated. Student's t-test was used to determine significance between normally distributed variables. Wilcoxon's rank sum test was used for two group non-parametric data, and a Kruskal-Wallis test used for multiple groups. A $p < 0.05$ was considered statistically significant. R (R Core Team, Vienna, Austria) was used for statistical analyses.

2.4. Results

During the study period 1,424 primary knee replacements were undertaken. The mean age at surgery was 69.5 years (SD 10, range 17 to 95). The mean age of the partial knee replacement group was slightly lower than that of the total knee group (PKR mean 68.5 years, SD 10; TKR mean 70.9, SD 11, difference 2.4 years, $p<0.001$).

Eight-hundred and twenty three were PKR (58%). In all age groups, more PKR were performed than TKR (Figure 2-1). The relative proportion of patients receiving PKR reduced with increasing age, and was 63%, 64%, 57% and 53% ($p=0.01$) in those <55, 55 to <65, 65 to <75 and 75+ respectively.

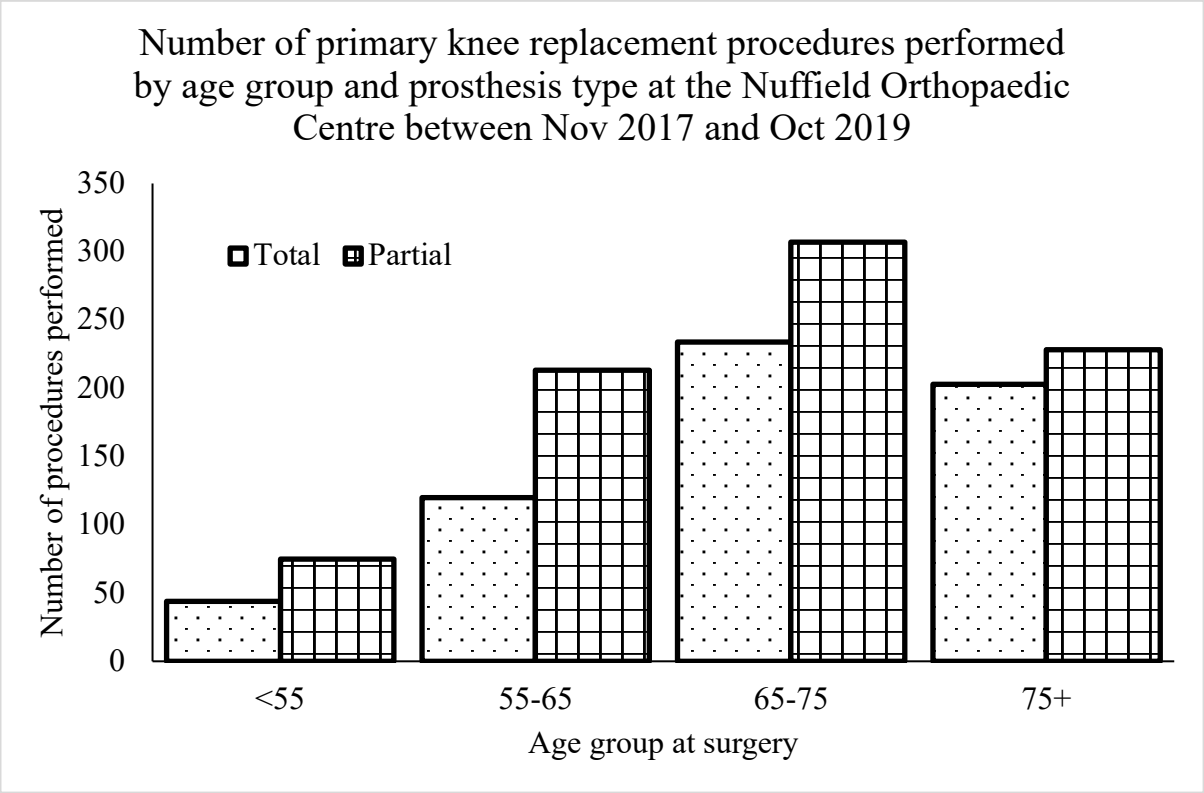


Figure 2-1 Type of knee replacements in Oxford by age

2.5. Discussion

In all age groups partial knee replacement was performed more frequently than total knee replacement. The relative candidacy was 63%, 64%, 57%, and 53% in those <55, 55-65, 65-75, and 75+ respectively. The association with age was significant, with reduced numbers of elderly patients (those older than 75 at surgery) receiving PKR, but this percentage was still 53%. The length of stay was also significantly lower with PKR than TKR in all age groups.

As the designer centre this study will be open to allegations of designer centre bias, including inappropriate usage and referral bias. However, appropriate usage is defined against post-operative outcomes, and in the designer centre cohorts that have been followed and published in peer reviewed journals the outcomes have been excellent[104, 105]. A referral bias may exist in younger patient groupings, as these patients tend to be motivated to research their options and the prospect of a higher functioning knee may lead them to seek out partial knee replacement. Further, non-specialist surgeons will be less likely to undertake knee replacement in these patients and will likely refer them on for specialist treatment. Where this will happen in younger patients, it is unlikely that the same surgeons would refer on more elderly patients, where all surgeons performing knee replacement would be comfortable to perform a TKR. The estimates in the older patients are therefore the most robust.

In conclusion, PKR was undertaken in over 50% of all age groups at the Nuffield Orthopaedic Centre during the time studied and was significantly associated with age (63% of those <55, 53% of those 75+, p=0.01).

3. Age-stratified PKR eligibility assessed through usage and radiographs at a non-designer, but specialist centre in the USA[1]

3.1. Introduction

Having examined the usage of partial knee replacement at the designer centre, it is important to see if the finding can be replicated. This chapter looks at the eligibility for partial replacement in the practice of a surgeon from the USA, who is a specialist hip and knee replacement surgeon who performs many partial knee replacements, to address the question of whether similar findings to the designer centre can be replicated externally.

The radiographic indications have been discussed in the Introduction (1.3 Selection, page 7). In order to undertake a complete evaluation, these indications require stress radiographs. Many centres do not possess the resources to undertake stress radiographs, and those that do tend to be specialist centres; opening them to accusations of referral bias. Thus a secondary aim of this chapter was to address the link between usage (as used in the designer study) and radiographic eligibility, with and without stress views.

The questions addressed in this chapter are: 1) what is the association of age and candidacy for medial PKR, and 2) how does the candidacy determined by actual usage, radiographs including stress views, and radiographs excluding stress views compare?

[1] This chapter has been accepted for publication: Kennedy JA, Mellon SJ, Lombardi AV, Berend KR, Hamilton TW, Murray DW. Candidacy for medial unicompartmental replacement declines with age. Orthop Traumatol Surg Res [accepted 5th Nov, 2019].

3.2. Methods

A retrospective cross-sectional study of a consecutive series of knee replacement patients (PKR and TKR) was studied to determine the effect of age on candidacy for Oxford medial PKR.

Between 01 January 2008 and 31 December 2008, 457 consecutive knees with complete preoperative imaging underwent primary TKR or primary medial Oxford mobile-bearing PKR (Oxford Phase 3 PKR, Zimmer Biomet, Warsaw, Indiana). All procedures were performed by an experienced joint replacement surgeon (KRB). All patients signed an institutional review board approved general research consent allowing for retrospective review. Details of this cohort has been reported[47], this study is a secondary analysis focussing on age.

Candidacy for medial PKR was determined in three ways. The first was based on the senior surgeon's actual implantation of PKR. This decision was based on a full history (including patient preference), examination findings, review of radiographs and intraoperative confirmation. The criteria used by the surgeon are medial compartment bone-on-bone osteoarthritis, no cartilage defects in the weight-bearing portion of the lateral compartment, and functionally intact anterior cruciate and medial collateral ligaments. Cartilage defects in the patellofemoral joint were accepted as long as there was no bone loss on the lateral facet. The second method used two blinded reviewers to identify candidacy on radiographs. To satisfy the decision for medial PKR, a weight-bearing anteroposterior radiograph, a valgus stress radiographs, a lateral radiograph and

a patella skyline radiograph were required to demonstrate the above patho-anatomy. In addition, if medial bone-on-bone was not seen, a Rosenberg and/or a varus stress view was required. The final method also used radiographs, but did not include stress radiographs. The decision aid used in identification is displayed in Figure 1-4 & Figure 1-5.

Demographic variables of age, body mass index (BMI), and patient sex were recorded. The primary outcome was the percentage of patients who were a candidate for medial PKR in different age groups. This was determined by the different methods described above, including usage, and radiographic candidacy.

Statistical analysis: Intra and interobserver agreement was calculated with Cohen's kappa. To estimate the effect of age on candidacy, the percentage of knees receiving PKR was calculated against age using pre-defined age groups of <50, 50 to <60, 60 to <70, 70 to <80, and 80 years or older at surgery, and 95% confidence intervals were determined with Clopper-Pearson confidence intervals. Significance was tested with univariate logistic regression with age as a continuous variable. Standardised likelihood by age group was determined by dividing age-stratified candidacy estimates by the total candidacy estimate of PKR performed in this study and those reported in the registry. To assess test accuracy sensitivity, specificity, and accuracy were calculated. For continuous secondary outcomes (functional scores) the mean score was determined, and tested for significance with univariate and multivariate linear regression models.

STATA version 14 (STATA corp, Texas, USA) and R (R Core Team, Vienna, Austria) were used for statistical analyses. A p-value of <0.05 was considered significant.

3.3. Results

There were significant differences in baseline characteristics with regards to age, with younger patients having higher BMI, pre-operative AKSS-F and pre-operative LEAS (Table 3-1). Younger patients had worse AKSS-O, but there were no significant differences in the percentage of females, or pre-operative flexion. For radiograph review, there was excellent intra- (Cohen's kappa 0.90) and inter-observer (Cohen's kappa 0.85) agreement.

Table 3-1 Pre-operative demographics

	Age group					**P value**
	<50	50-60	60-70	70-80	80+	
Number	31	130	157	97	42	N/A
Mean age in years (range)	45.6 (39-50)	56.0 (50-60)	65.1 (60-70)	74.2 (70-80)	83.8 (80-93)	N/A
Mean body mass index (SD)	37.0 (8)	34.2 (7)	33.6 (7)	29.3 (6)	26.9 (5)	<0.001
Number females (%)	16 (52%)	72 (55%)	105 (67%)	59 (61%)	24 (57%)	0.25
Preop range of movement in degrees (SD)	112 (10)	112 (11)	112 (12)	114 (10)	111 (10)	0.31
Preop Knee Society Score Objective (SD)	35.1 (13)	39.6 (17)	39.4 (15)	42.7 (18)	34.4 (17)	0.04
Preop Knee Society Score Functional (SD)	59.8 (16)	57.0 (15)	55.6 (18)	54.6 (17)	41.2 (21)	<0.001
Preop Lower Extremity Activity Scale Score (SD)	9.3 (3)	10.0 (3)	9.3 (3)	8.7 (3)	8.2 (3)	0.02
N/A not applicable, SD standard deviation						

Overall candidacy, estimated from patients receiving PKR was 46% (CI 41 to 51, n=210/457). Candidacy estimated using radiographs including stress views was 49% (CI 44 to 53, n=223/457). There was a negative association between candidacy in those receiving PKR and age (Odds Ratio 0.98, 95% CI 0.96 to 0.99, p=0.008). The percentage of knees receiving PKR progressively increased with younger age grouping; from oldest to youngest estimates were 36% (CI 22 to 52, n=15/42), 41% (CI 31 to 52, n=40/97), 43% (CI 35 to 51, n=68/157), 52% (CI 43 to 61, n=68/130), and 61% (95% CI 42 to 78, n=19/31). Candidacy from radiographs revealed similar trends (Figure 2-1). Lateral compartment wear was the most common reason for not being appropriate for medial PKR (Table 3-2).

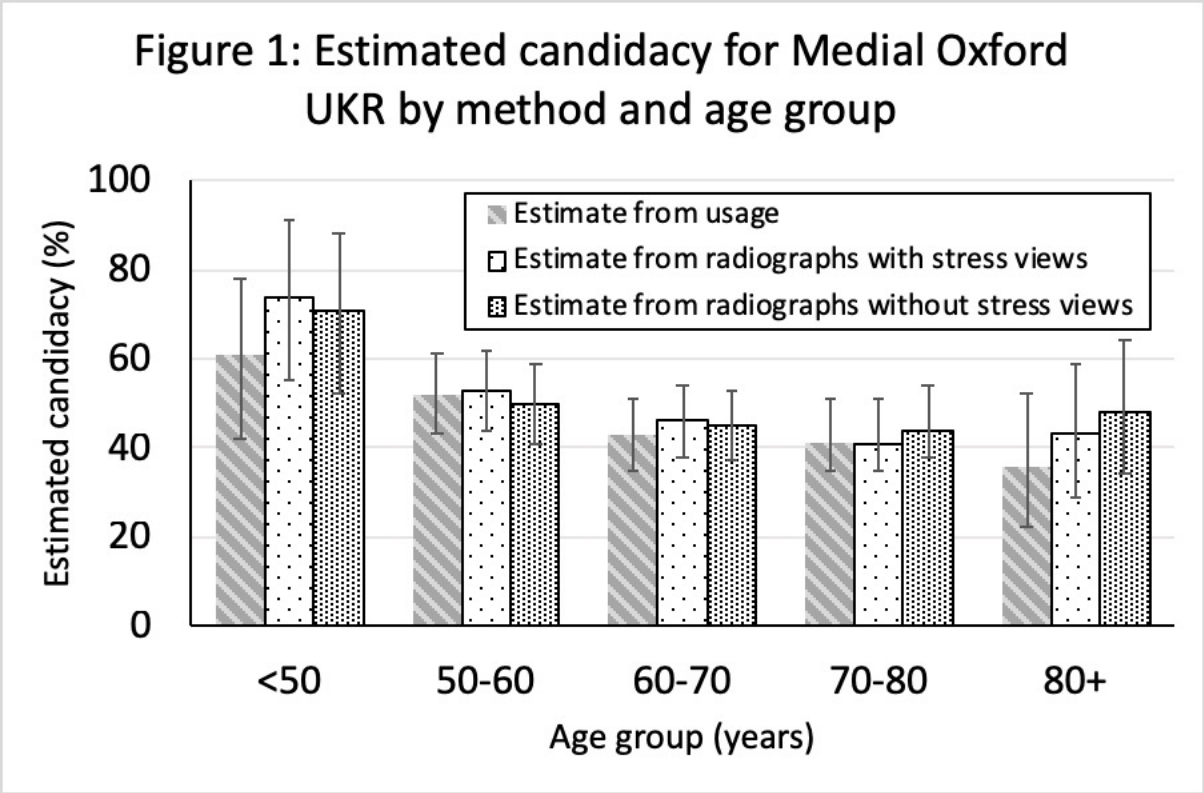


Figure 3-1 Candidacy for PKR by method and age

Table 3-2 Radiographic contraindications to PKR by age group

Age group	N	Contraindication prevalence (%)				
		Lateral wear	Medial PTCL	ACL deficiency	MCL deficiency	Bone-on-bone lateral facet patella arthritis
<50	31	22.6	9.7	3.2	4.0	6.5
50 to <60	130	27.7	28.5	17.2	9.5	9.4
60 to <70	157	34.4	20.4	25.6	7.8	9.6
70 to <80	97	41.2	28.9	26.8	13.5	7.2
80+	42	47.6	19.1	34.2	9.5	7.1
P value	N/A	<0.01	0.97	<0.01	0.44	0.50

Each knee can have more than one contraindication. Findings from varus and valgus stress radiographs included.
ACL Anterior Cruciate Ligament; MCL Medial Collateral Ligament; N Number; N/A Not Applicable; PTCL Partial Thickness Cartilage Loss (not bone-on-bone); PKR Partial Knee Replacement

Candidacy estimated with an AP, lateral and skyline radiograph was 48% (CI, n=220/457). The accuracy of this method compared to usage was 87% (95% CI 84-90). Test sensitivity was 89% and specificity was 86%. When assessed against the decision made using all available radiographs (including stress views), accuracy was 94% (95% CI 91-96), with sensitivity of 93% and specificity of 94%. There was no difference between candidacy estimated by usage, and by all radiographs (p=0.74), or using AP, lateral and patella skyline radiographs alone (p=0.89).

3.4. Discussion

This study shows that PKR candidacy is strongly associated with age, with decreasing candidacy in older age groups identified from usage and from radiographic evaluation.

Candidacy decreased with age and was 61% for those <50, 52% for those 50-60, 43% for those 60-70, 41% for those 70-80 and 36% for those 80+. The NJR[98] suggests that overall 8% of primary knee replacements are PKR and that usage of PKR decreases with increasing age being 18% in those <60 years, 9% in those 60-70, 5% in those 70-80, and 3% in those 80+. Overall candidacy of this cohort of knee replacement patients from the United States of America (USA) was about 50%. This is identical to radiographic candidacy assessed in an independent centre in the United Kingdom [53], and is similar to usage of surgeons from centres around the world who achieve good results with PKR [104, 106-112].

Arguably, elderly patients benefit most from PKR due to lower morbidity and mortality associated with the procedure [3]. Due to limited life expectancy revision is unlikely and was not seen in this study. A simple analysis suggests that a cohort of elderly patients undergoing PKR by an experienced surgeon might have 1-2% more revisions over their lifetime relative to TKR [98], however there would be half the number of strokes and myocardial infarctions [3]. Furthermore, a health-economic study based on NJR data[113] showed in this group of patients, over their life time, that PKR provides better quality of life and is less costly than TKR.

It would seem many surgeons preferentially use PKR for young patients (Figure 3-2). This may be because PKR provides better function[17, 114]; or it may be surgeons feel that in the elderly TKR is better as it is definitive surgery, whereas in the young PKR is a pre-knee replacement and an easier revision[115]. If surgeons reserve PKR for younger patients, they will only perform a limited number of procedures[73]. Recent evidence suggests that surgeon usage of PKR (number of PKR as a percentage of their knee replacement practice) is more important than caseload in determining revision rate, and to achieve low revision rates surgeons should use PKR for at least 20% of their knee replacements [106] (discussed further in 1.4

Outcome). Therefore, to achieve acceptable usage and optimise patient outcomes, surgeons should use PKR for all age groups, not just the young [73].

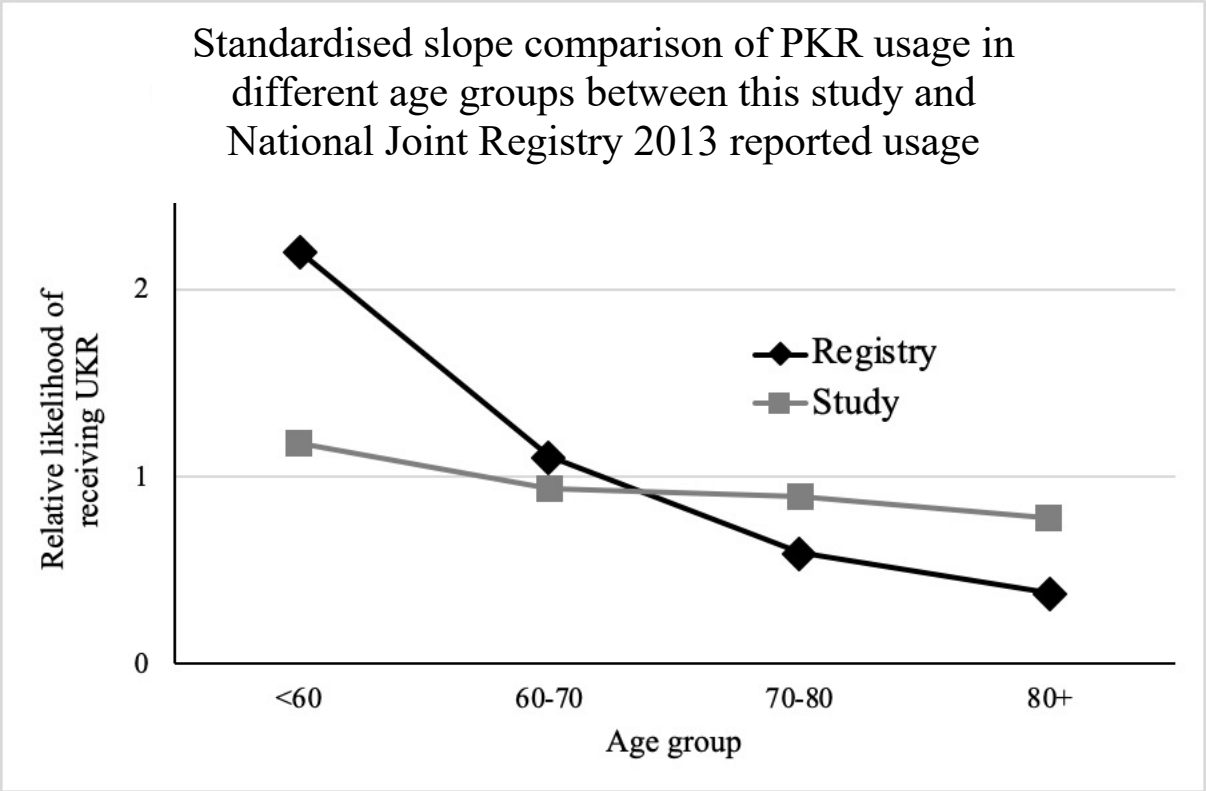


Figure 3-2 Differences in age provision: Study centre vs UK registry
Standardised slope comparison of PKR usage in different age groups between this study and National Joint Registry 2013 reported usage. A comparison of the relative likelihood of PKR implantation in different age groups. The slope suggests that surgeons within the registry are not performing PKR on elderly patients and are selectively choosing younger patients, when compared to the trends of candidacy seen in this study. However, candidacy estimates from this chapter also show that many more patients in each age group could receive PKR than currently receive it.

Many centres do not undertake stress radiographs for knee replacement, and undertake weight-bearing anteroposterior, lateral and patella skyline radiographs only. Using these alone, which were well aligned in this series, accuracy was high, with about nine out of ten patients being correctly identified as a candidate or not. Furthermore, they overestimated actual implantation by only 2%. Therefore, these X-rays are satisfactory for estimating candidacy in a series, but due to false positives and false negatives are not ideal for determining if an individual patient is appropriate for PKR. In each age group,

the most common reason why patients were not appropriate for PKR was the presence of radiographic evidence of lateral compartment osteoarthritis. It is thus important to assess the lateral compartment with radiographs in the preoperative work up, and intra-operatively. In all groups, valgus stress radiographs identified narrowing in about 10% of cases that were not identified on standard radiographs. It is therefore sensible, at least for inexperienced surgeons, to use the full set of radiographs.

The main limitation of the study was that the population was selected from a high volume joint replacement surgeon with an interest in PKR. This may increase candidacy owing to the possibility of local referral patterns, whereby patients who were PKR candidates may have been referred. For this reason, the likelihood was compared between age groups, as this reflects willingness to perform PKR in different age groups and is independent of the actual number candidate (Figure 3-2). A strength of this study is that, as a high volume joint replacement centre, complete imaging and work up for PKR allowed estimation for the utility of weight bearing AP, lateral and skyline radiographs to help inform future studies. This work is important as there are no previous estimates looking at the effect of age on candidacy, nor is there validated accuracy for estimation using radiographs without stress views.

In conclusion, PKR candidacy is strongly associated with age, with candidacy decreasing with increasing age and about two thirds of very young patients (<50) and one third of very old patients (>80) being appropriate. This was similar to that found in Chapter 2 and confirmed replicability at an external centre. However due to the limitation of possible referral bias, a further study was required for generalisability. Radiographs without stress

views were found to have an accuracy of over 90%, which will allow further studies to be performed.

4. Age-stratified radiographic PKR eligibility at a representative, non-designer, non-specialist centre in Australia

4.1. Introduction:

A generalisable knee replacement practice that does not advertise as specialist PKR centre was chosen for the final study in this section. The previous study validated the accuracy of anteroposterior and lateral radiographs against usage and found the accuracy to be greater than 90% in each age group. Taking this information forward a generalisable practice in Melbourne, Australia, was chosen.

There are three compartments in the knee (medial, lateral and patellofemoral) and all can be involved in the osteoarthritic process. Current knee replacement technology can replace each individual compartment, or in combination, depending on the location of the arthritis. The arthritis can be assessed indirectly with plain radiographs, computed tomography and magnetic resonance imaging, and with direct visualisation through arthroscopy or arthrotomy. An important predictor for a good outcome in knee replacement is the presence of bone-on-bone arthritis[12, 116-124] (often referred to as Kellgren-Lawrence, KL, Grade 4[125], or Ahlback Grade 2[51]). Previous studies examining patterns of knee arthritis have not used this as an endpoint[126-128], or have been limited by possible selection bias[47], non-validated assessment methodology[60], or in patients presenting late in the disease process compared to Western populations[54].

The aim of this chapter is (1) to describe the patterns of severe osteoarthritis in a population from a generalisable knee replacement practice in Melbourne, Australia, (2)

to determine the proportion of knees undergoing replacement by indications other than severe arthritis on radiograph, and (3) to examine the effects of age on the arthritic patterns.

4.2. Methods:

A retrospective cross sectional study was designed to assess the location of bone-on-bone arthritis in the knee, and to determine if the anterior cruciate ligament (ACL) is intact. Consecutive patients undergoing knee replacement (partial or total knee replacement, PKR or TKR) by two surgeons (AS, JB) were retrospectively identified from practice billing codes at a private Orthopaedic practice in Melbourne, Australia. The severity of arthritis and the functional integrity of the ACL was graded in a similar fashion to that described in an evidence-based radiographic decision aid for PKR[47]. The study outline is provided in Figure 4-1.

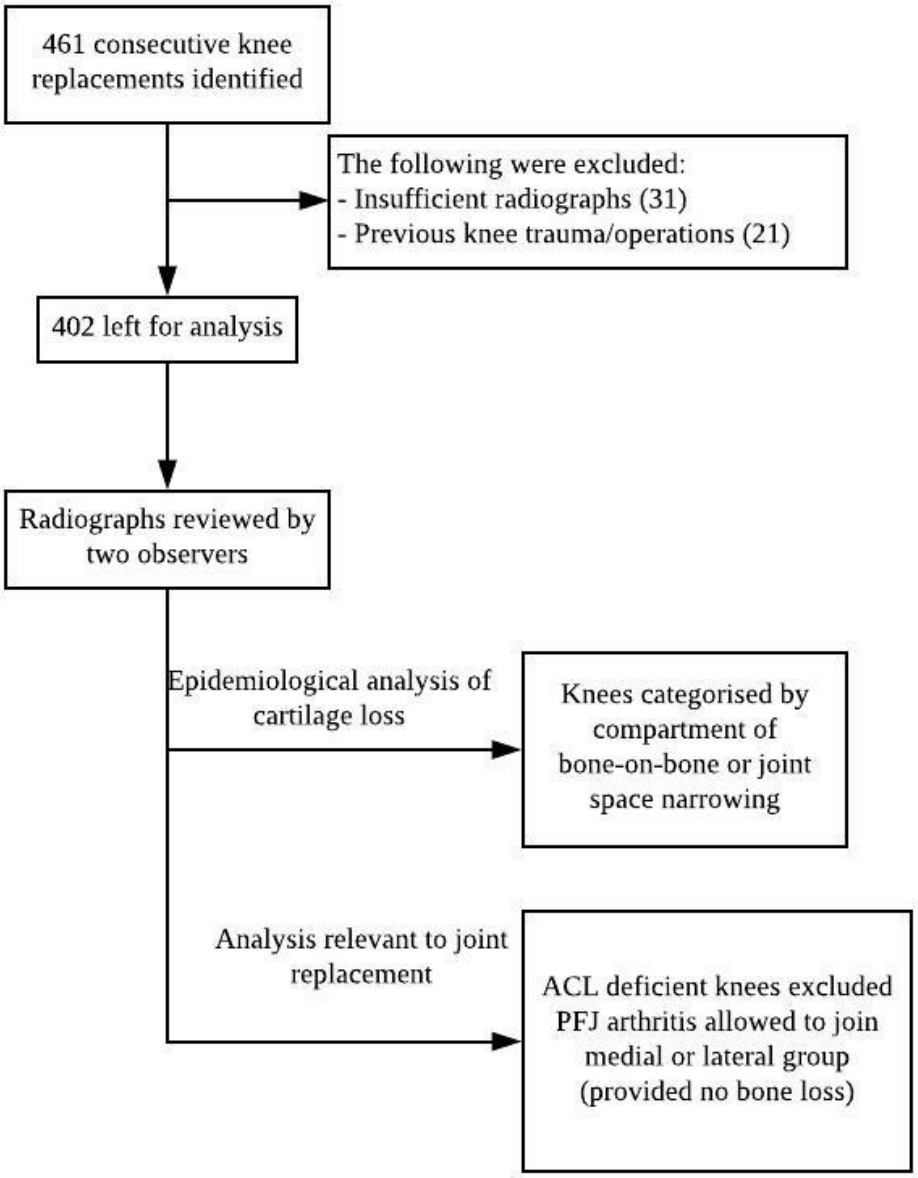


Figure 4-1 Study flow diagram

Consecutive knees that had undergone total or partial knee replacement (TKR and PKR respectively) between October 2016 and January 2019 were identified. Both surgeons are independent from PKR design, and do not advertise as PKR surgeons. Inclusion criteria included a joint replacement for primary knee osteoarthritis, age older than 18, and the

presence of weight-bearing anteroposterior and lateral radiographs. Patients were excluded if they had previous reconstructive or traumatic knee surgery on the affected knee, or did not have both weight-bearing anteroposterior and lateral radiographs available for analysis.

The primary outcome was to determine the percentage of patients that demonstrated bone-on-bone arthritis in different compartments of the knee. The presence of osteophytes was ignored as these do not correlate to structural progression[129] or indicate likelihood of compartment deterioration following joint replacement[130]. To increase the utility of this finding with regard to PKR, the status of the ACL was also recorded. As some designs of PKR allow some arthritis in the patellofemoral joint, a second analysis was undertaken describing tibiofemoral bone-on-bone, only excluding those with bone loss in the patellofemoral joint. Further, as bone-on-bone arthritis is not an absolute indication for knee replacement, further imaging and investigation used in those patients who did not demonstrate bone-on-bone on their preoperative radiograph was identified. Finally, the effect of covariates such as age and body mass index on the location of severe arthritis were examined.

To assist with identification of arthritis severity, a radiographic decision aid was used. This decision aid provides five binary criteria based on plain preoperative radiographs regarding the location of arthritis, and the integrity of the ligaments. It is provided in Figure 1-4 & Figure 1-5. Following a period of training on the decision aid, radiographs from immediately prior to operation were retrieved and reviewed by two Orthopaedic registrars (JK and AP). For each compartment the location and severity of arthritis was recorded, with bone-on-bone of a compartment identified as complete loss of joint space

or bone erosion. Further, the status of the ACL was determined via the extent of medial bone loss, with bone defects extending to the posterior half of the medial tibial plateau considered to be ACL deficient[131, 132].

Demographic details including age at X-ray, BMI, American Society of Anaesthetists (ASA) grade, ethnicity, sex and side were collected. The average age was additionally determined for those selected for PKR and TKR to allow comparison to the Australian joint registry.

Statistical analysis: The first forty radiographs (~10% of the total) were marked by both reviewers for assessment of interobserver reliability. These were assessed again two weeks later for intra-observer reliability. Interobserver and intraobserver reliability was assessed using percentage agreement and Cohen's kappa. Counts and percentages were calculated for PKR candidacy. Binomial Clopper-Pearson exact 95% confidence intervals were constructed. Association between covariates and pattern was done using logistic regression for each pattern independently.

Power: It was assumed that 50% of patients would be eligible for PKR based on previous research[47, 54, 60]. With a precision of 5% and an infinite population size, the estimated sample size using a Binomial Exact Confidence Interval was 385 knees.

4.3. Results:

461 knees in 427 patients were identified. 31 knees were excluded as their immediate preoperative radiographs did not include both weightbearing anteroposterior and lateral views, and a further 21 knees (5%) were excluded due to previous knee trauma or operations including ACL reconstructions, high tibial osteotomies, tibial plateau fracture, or patellofemoral realignment procedures (figure 1). This left 405 knees for analysis. The mean age was 68 years (range 42 to 92) and mean BMI 30 (range 21 to 57; Table 1). The mean age for those who underwent PKR was 65.4 (SD 8, range 48 to 82), and for TKR was 68.9 (SD 8, range 42 to 92). Intraobserver and Interobserver agreement was excellent (mean Cohen's kappa 0.88 and 0.86 respectively).

Table 4-1 Study demographics

Study demographics		
Age (years)	Mean 68 (SD 8 range 42 to 92)	
Body mass index (kg/square metre)	Mean 30 (SD 6 range 21 to 57)	
Number of females (%)	213 (53%)	
Region of birth	Australia/New Zealand	295 (73%)
	Europe	63 (16%)
	Asia	15 (4%)
	Other	4 (1%)
	Missing	25 (6%)
American Society of Anaesthetists score	1	43 (11%)
	2	196 (48%)
	3	139 (34%)
	4	3 (1%)
	Missing	20 (5%)

Overall, 70% of knees (281 knees, 95% confidence interval 65 to 75) demonstrated bone-on-bone osteoarthritis (Figure 2). The majority of this was in the medial compartment alone (150 knees, 37%), followed by combined medial and patellofemoral disease (40 knees, 10%), and then lateral compartment alone (33 knees, 8%).

Excluding knees with an absent ACL (n=44), and allowing those with patellofemoral arthritis to fall into the medial and lateral tib-fem groups, provided there was no patellofemoral bone loss, resulted in a 149 knees with medial compartment arthritis (37%), followed by 35 knees with lateral compartment arthritis (9%), and 18 with medial and lateral tibiofemoral arthritis (4%, Figure 2). If the sample is restricted to only those demonstrating bone-on-bone, the relative proportions relevant to the most frequent joint replacements were: medial compartment arthritis 49%, multiple compartment arthritis or ACL deficient 32%, lateral compartment arthritis 11%, and patellofemoral arthritis in 2%.

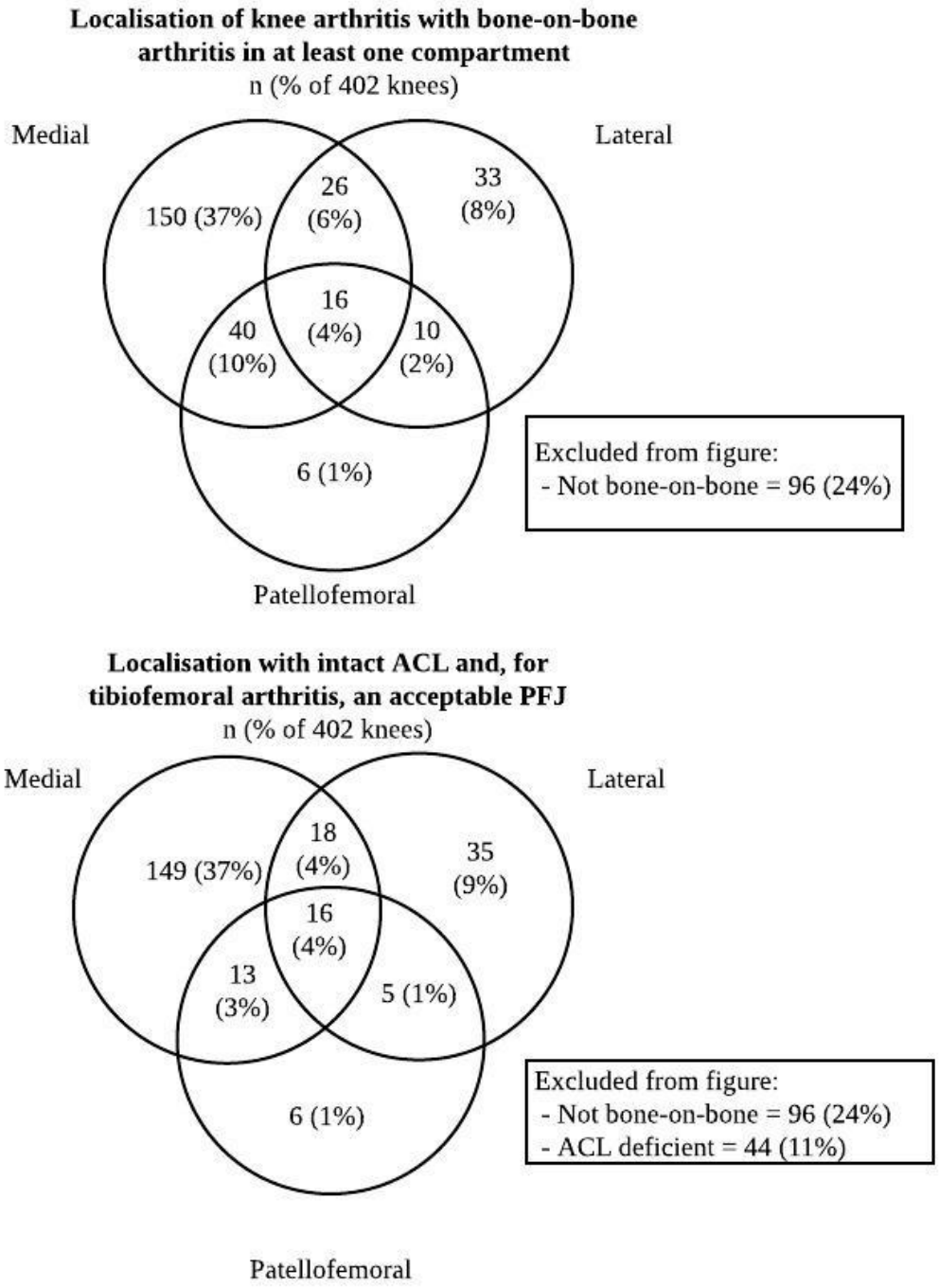


Figure 4-2 Venn diagram of arthritic patterns in the knee

Bone-on-bone arthritis was not identified in 95 knees (24%). In these MRI had been used as part of the decision making process in 48 knees, arthroscopy in 15 knees, a combination of MRI and arthroscopy in in eight knees, and a computed tomography arthrogram in two knees. One MRI confirmed osteonecrosis, otherwise all these investigations described various MRI biomarkers of osteoarthritis often taken to indicate severe arthritis. The remaining 22 knees without bone-on-bone had significant disability attributed to their knee arthritis and only had plain radiographs.

Increasing age was associated with multiple compartment arthritis, and reduced chance of having isolated medial arthritis (Table 2). No effect was seen for patellofemoral or lateral arthritis.

Table 4-2 Age stratified compartment involvement in those with bone-on-bone arthritis

Age group	Number	Medial	Medial + PFJ	PFJ	PFJ + Lateral	Lateral	Lateral + Medial	Tricompartmental or ACL deficient
<60	50	24 (48%)	4 (8%)	1 (2%)	1 (2%)	7 (14%)	1 (2%)	4 (8%)
60-75	175	95 (54%)	6 (3%)	3 (2%)	2 (1%)	18 (10%)	15 (9%)	30 (17%)
75+	66	28 (42%)	3 (5%)	2 (3%)	2 (3%)	9 (14%)	2 (3%)	19 (29%)
P value		0.03	0.82	0.44	0.37	0.88	0.95	0.03

4.4. Chapter discussion:

This chapter has identified different patterns of knee arthritis in this generalisable, consecutive series of joint replacement patients. With regards to important patterns for joint replacement, isolated bone-on-bone arthritis in the medial compartment was found in 37% of knees, in the lateral compartment in 9%, in the patellofemoral compartment in 1%, and in multiple compartments in 24%. The remaining 24% of knees did not demonstrate bone-on-bone arthritis on plain radiograph. These patterns of arthritis are important as they reflect important practice patterns with regards to the type of knee replacement that could be undertaken.

This is the first study to describe the location of knee arthritis as important to joint replacement by age. Its strengths lie in the use of a validated method with known sensitivity and specificity for the identification of medial compartment arthritis severity (the predominant pattern), and that it covers all possible knee arthritis patterns. It also represents a generalisable practice of knee replacement in Australia, and has similar demographics to that reported by the registries of Australia, New Zealand and the United Kingdom (Table 3). The main limitations are that not all patients identified from these radiographs would be eligible for PKR as clinical and intraoperative findings, and varus and valgus stress radiograph were not available. However, the absence of this extra information has been reported to affect overall estimates by less than 5%, and thus the findings should broadly be correct[133]. Despite validation of these criteria in the selection of medial PKR patients[47], there is large variation in surgeons opinion of who is eligible for PKR[134-136] and not all will be convinced by these findings. Further, there was not

sufficient information about the postoperative function of the knees to be able to explore differences between early arthritis and bone-on-bone arthritis.

Table 4-3 Comparison of study population to joint registries

Partial knee replacement				
	Study	Australian registry*	NZ registry	UK registry**
Mean Age (SD)	65.8 (8)	65.3 (10)	66.1 (10)	63.7 (10)
% Female	36.7%	46.8%	46.1%	46.9%
Mean BMI % BMI 18.5-30	50.0%	42.5%	29.9 (5)	**
% ASA 1-2	73.3%	62.9%	83%	84%
Total knee replacement				
Mean Age (SD)	68.6 (8)	68.5 (9)	68.3 (9)	69.7 (9)
% Female	55.8%	56.7%	52%	57.7%
Mean BMI % BMI 18.5-30	52.9%	42.5%	31.3 (6)	**
% ASA 1-2	57.0%	62.9%	75%	84%
*Aus registry reports BMI and ASA for PKR and TKR, but age and gender separately. ** UK registry does not report BMI				

Patterns of osteoarthritis were first described in the early 1990's on anatomical specimens from the 18th and 19th centuries[126] (Table 4-4). Later studies classified osteoarthritis on

the presence of any joint space narrowing, but did not address what the clinically important distinctive entity of 'bone-on-bone'[127, 128]. More recent studies have classified the patterns of arthritis identified on radiographs that might be acceptable for PKR[54, 60]. This study builds upon these by analysing more knee replacements, and in a population more generalisable to Western populations.

Table 4-4 Other studies examining arthritis patterns in the knee

Lead author	Year	Number	Selection	Method	OA identification	Medial alone	Lateral alone	PFJ alone	Mixed
Waldron[126]	1991	22 knees	Skeletal examination	Paeloanthropological examination	Eburnation or osteophytosis + bone defect	Left: 6.3 Right: 0	Left: 25.0 Right: 28.6	Left: 31.3 Right: 52.5	Left:37.5 Right: 19.0
McAlindon[127]	1992	418 knees	Community: symptomatic knees	Radiographs	Definite joint space narrowing	Males: 21.2 (14-29) Females: 12.3 (9-16)	Males: 1.7 (2-6) Females: 2.7 (1-5)	Males: 11.0 (5-17) Females: 24.3 (20-30)	Males: 9.3 (NR) Females: 10 (NR)
Ledingham[128]	1993	252 patients	Patients referred to hospital and with definite joint space narrowing	Radiographs	Definite joint space narrowing	10%	1%	24%	64%
Willis-Owen[60]	2009	200 knees	Patient undergoing any knee replacement	Pre-operative Radiographs	Joint space narrowing to <3 mm	56.0%	12.6%	10.5%	20.8%
Wang[54]	2018	155 patients 168 TKR	Patients undergoing TKR	Pre-operative Radiographs	Bone-on-bone arthritis	51.2%	6.5%	1.2%	45.9%
NR not reported; TKR total knee replacement									

Bone-on-bone arthritis is associated with better functional and survival outcomes in TKR[12, 116-121, 137-140] and PKR[122, 123, 141]. The outcomes of knee replacement are influenced by many factors, but a consistent finding of risk is the presence of 'early arthritis'. With the exception of one paper that uses intraoperative findings of bone exposed[122], all use radiographs to determine the extent of arthritis with early arthritis variably defined somewhere between KL grades or joint space width measured in millimetres. In TKR, Riis et al[118] found that in those with KL Grade 4 (bone-on-bone) 8% had moderate or severe pain at one year, compared to 26% for those KL Grade ≤ 3 (marked narrowing or less). In a separate comparative study of painful TKR, Polkowski et al[116] found early arthritis (defined as ≤ KL Grade 2, definite joints space narrowing) in almost 50% of 49 persistently painful TKR, compared to only 5% in a group of 100 consecutive TKR performed in the same year, and 6% in a cohort of 80 asymptomatic TKR. In a study of PKR, upwards of 70% underwent further surgery due to persistent problems over a mean 63 months when the joint space was preserved[123], compared to the overall reoperation rate in the study of 19%. Finally, a fifth of patients undergoing PKR without intraoperative 'bone-on-bone' identified failed to improve by the minimal clinically important difference in the Oxford Knee Score[122]. It is clear that radiographic severity of arthritis is associated with post-operative function and survival of knee replacement.

Arthritis associated with ACL deficiency or multiple compartment arthritis was found in 24% of patients. In this scenario patients can be offered TKR. TKR replaces the entire joint, excising all articulating surfaces and menisci in the knee. It is currently used in the majority of patients undergoing knee replacement (>90%)[1, 142]. There is no consensus on structural indications however, and it can and probably is used no matter the pattern of arthritis in the knee. It is an extremely successful procedure with low requirements for

revision surgery (<5% over 10 years), and significant improvements in joint function[114, 143]. However, around one in five patients are unsure or dissatisfied with their outcome following knee replacement[4, 15]. In an attempt to address this, other types of knee replacement are offered to address specific patterns of arthritis.

In this study about 40% of knee arthritis was confined to the medial compartment. When this is the case medial PKR can be offered. PKR replaces only the damaged part of the joint, leaving the other compartments intact. As PKR replaces less of the joint, it has been associated with significantly less perioperative morbidity and mortality when compared to TKR[3]. Further, it provides better joint function measured by patient reported outcomes[68, 99]. Historically the higher revision rate of PKR has been of great concern, however, this is highly dependent on the surgeon undertaking the procedure[71, 144], and a recent controlled trial has shown equal revision rates between PKR and TKR[66] for surgeons who are performing more than 10 per year. The median number of PKR performed per year in the UK is 6, compared to 37 TKR[114]. On the basis of these results, around four in every 10 knees should be suitable for medial PKR. As a consequence, a surgeon performing 30 knee replacements per year (>50% of UK surgeons) should be able to meet this threshold, with subsequent benefits to patient and health care system.

Other knee replacement options include lateral PKR for lateral compartment arthritis, patellofemoral replacement for patellofemoral arthritis, or bicompartmental replacement, where a tibiofemoral compartment is replaced at the same time as the patellofemoral compartment. As these patterns of arthritis are relatively rare, only high volume centres have reported results. Patellofemoral arthritis tends to present as a different phenotype from tibiofemoral osteoarthritis, with patients often younger and with a long standing

history of patella problems. Joint registries suggest that these operations are not performed commonly.

Around one in four patients (24%) did not have bone-on-bone demonstrated on radiograph. The majority of these patients had been investigated with magnetic resonance imaging in addition to their weight-bearing radiograph, and, with the exception of one case of osteonecrosis, all showed varying severities of cartilage loss and other changes associated with osteoarthritis. It remains unclear how MRI findings affect patient function or implant survival following joint replacement. In a cohort study of 710 knees with normal radiographs, 631 (89%) showed MRI evidence of osteoarthritis[57]. Further, the natural history of MRI defined osteoarthritic lesions is not straight forward, with varying amounts of progression, stabilisation and resolution seen. For example, over a two year period one quarter of tibial cartilage defects identified in the lateral compartment had improved, just under a half had stabilised, whilst only one third had progressed and enlarged[58], with similar findings in other studies[145-147]. There are no studies that have attempted to provide a prognosis for knee replacement on the basis of MRI findings and, given the increasing popularity of MRI in diagnostic work up, this is an urgent area for future research. It is likely that many of these patients may have demonstrated bone on bone arthritis if stress radiographs or arthroscopy had been performed.

In conclusion, this chapter has identified a representative sample of patients and shown about one in every two patients undergoing knee replacement may be eligible for PKR. Most commonly this will be medial PKR and doctors and patients should be familiar with the procedure. Further research is urgently needed to define the role of MRI in the identification of candidates for joint replacement surgery.

4.5. Selection for knee replacement: Section Discussion

These studies have consistently found that about half of knee replacements could be eligible for partial knee replacement. In Chapter 2 it was found that at the designer centre that over half of all primary knee replacements were partial knees, and that there was a significant association with age (63-64% in those <65, 53% in those 75+). Chapter 3 examined a high volume centre at risk of referral bias, but expanded upon this demonstrating that between 60-65% of those <50 were candidate, falling to about 40% in those 80+. This study validated the accuracy of radiographs without stress views to identify partial knee candidates. Finally, the work in Chapter 4 undertaken at a generalisable centre that does not undertake stress views, confirmed that about half of knees were eligible for partial knee replacement. Once again there was an association with age with about 64% eligible for partial replacement in those under 60 years of age, and 59% of those over 75 being eligible for partial replacement (p=0.03).

Each study used different methods to attempt to address identified shortcomings in the other studies. Chapter 2 used actual usage rates at the designer centre, under the assumption that all candidates eligible for PKR receive it. However, other surgeons may not use the prosthesis in all candidates, or may use slightly different criteria to determine candidacy. Chapter 3 aimed to bridge the gap between usage and radiographic candidacy and showed small differences between methods. Radiographs tended to overestimate candidacy compared to actual usage, especially in older age groups. However, the

difference was no more than a few percentage points. With this knowledge, a generalisable study could be performed at a centre completely independent to referral bias for partial knee replacement. This again confirmed that a large proportion of knees would be eligible, based on their radiographs, for partial knee replacement.

There was a statistically significant effect of age in each cohort, with more younger patients being candidate than older patients. The estimates from usage and radiographs were similar, except in the oldest age group (80+) where the radiographic analyses had an apparent increase in candidacy (Figure 4-3). The indications used for surgery between the cohorts were consistent: there must be bone-on-bone arthritis in the affected compartment, full thickness cartilage/joint space in the retained compartment, a functionally intact medial collateral and anterior cruciate ligament, and an acceptable patellofemoral joint. As age increased, there was a significant association with increasing ACL deficiency, and retained compartment arthritis.

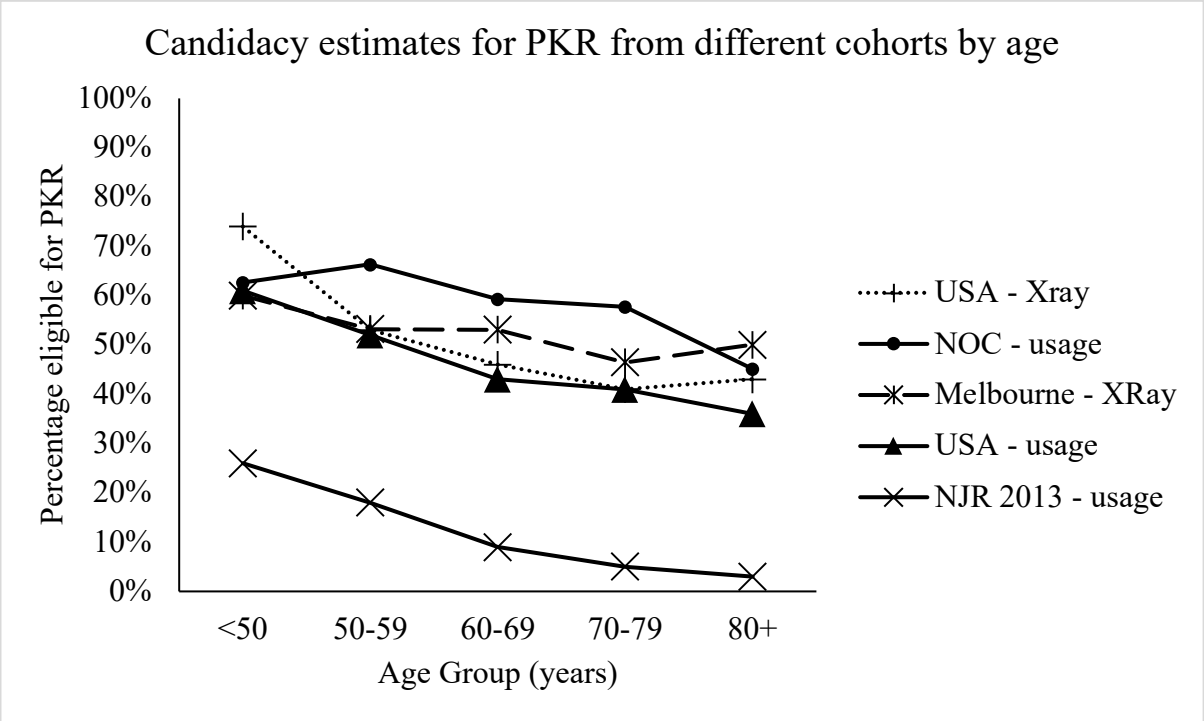


Figure 4-3 Candidacy estimates for PKR from different cohorts by age
The series name denotes whether the estimate was from XRay (radiographic analysis), or usage (actual implantation rates).

Whilst increasing age led to a decrease in candidacy, the lowest estimates in the older age group were still above 40%, and at the Nuffield Orthopaedic Centre was 45%. The estimated usage of PKR, taken from the 10th National Joint Registry annual report 2013[98] (the last report to provide detailed age break down in these categories), found that only about 3% of all knee replacements in those older than 80 years were PKR. Therefore, the eligibility for PKR in this age group is about 15 times higher than those currently receiving it.

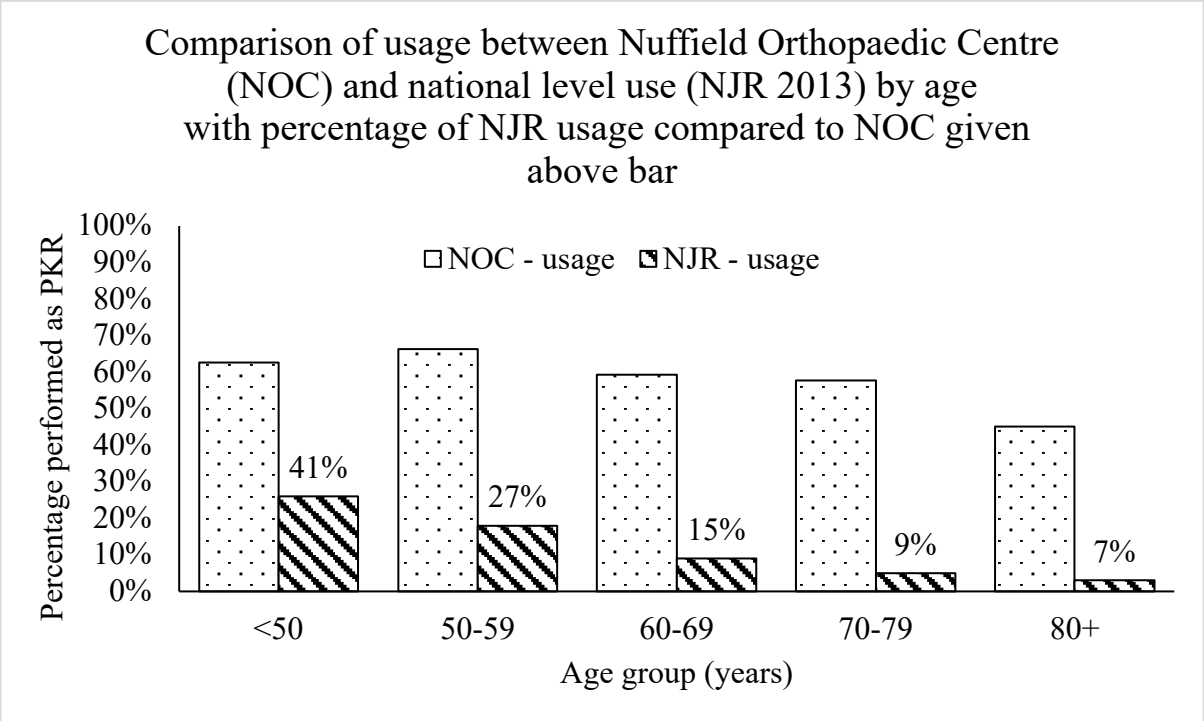


Figure 4-4 Comparison of NOC usage compared to NJR

In the youngest age group, the Nuffield Orthopaedic Centre used PKR in 63% of knees, whilst in the NJR it was used in 26%. A difference of only 2 times. However, it is highly likely that many patients in the NJR did not have bone-on-bone arthritis, and it may therefore be an unfair comparison[50]. This is highlighted by the difference in usage between the oldest and youngest groups (Figure 4-5): as a proportion of all knee replacements, at the NOC 1.39 times more patients under 50 received PKR compared to those over 80, whilst in the NJR it was 8.67 times higher.

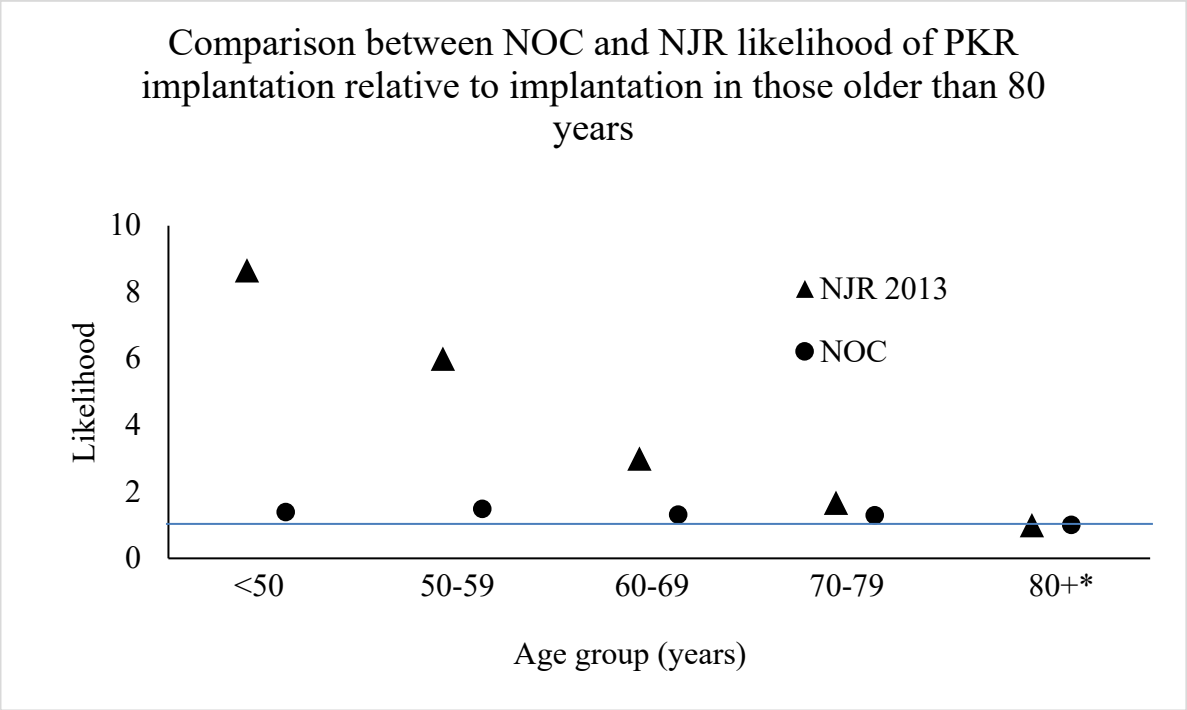


Figure 4-5 Relative implantation by age - NJR and NOC
*The 80+ age group was the reference age group and is thus equal to 1 (reference line). NOC Nuffield Orthopaedic Centre; NJR National Joint Registry.

The volume of knee replacements being performed each year in the UK is now over 100,000 per year[1]. In 2013, the last year where detailed age data was provided in the NJR annual report, the number performed was about 80,000[148]. Those aged 60-80 receive the greatest number of knee replacements (Figure 4-6). In 2013, about 8% (n = 6625/80626) of knee replacements were PKR[148]. In contrast, based on the usage at the Nuffield Orthopaedic Centre, about 57% could be performed as PKR. Based on the rate of knee replacement being performed today, that would equate to 57,000 knees being eligible, compared to the current rate of implantation, of about 10,000. Under this assumption, that means 47,000 patients are receiving total knee replacement, who may be eligible for partial replacement. With these sort of numbers, small differences in outcome are important. Based on matched mortality data, the number needed to treat to save a life at

90 days was 400, so in 47,000 patients there would be a reduction in 90 day mortality of 118 patients. Conversely, based on the unmatched registry revision rate, which is about three times higher (2.7x), there would be an extra 1767 revisions by five years. This estimate of revision needs to be interpreted with caution however, as the disproportionate number of PKR performed in young patients suggests use in early arthritis, which is known to lead to poor outcomes, and will increase the revision rate. And, in fact, the data from TOPKAT suggests an equivalent revision rate over five years (Revision rate PKR 4.08%, revision rate TKR 3.72%, difference 0.36%, projected extra revisions with PKR 171; reoperation rate PKR 8.98%, reoperation rate TKR 10.41%, difference -1.43%, projected fewer reoperations with PKR 672).

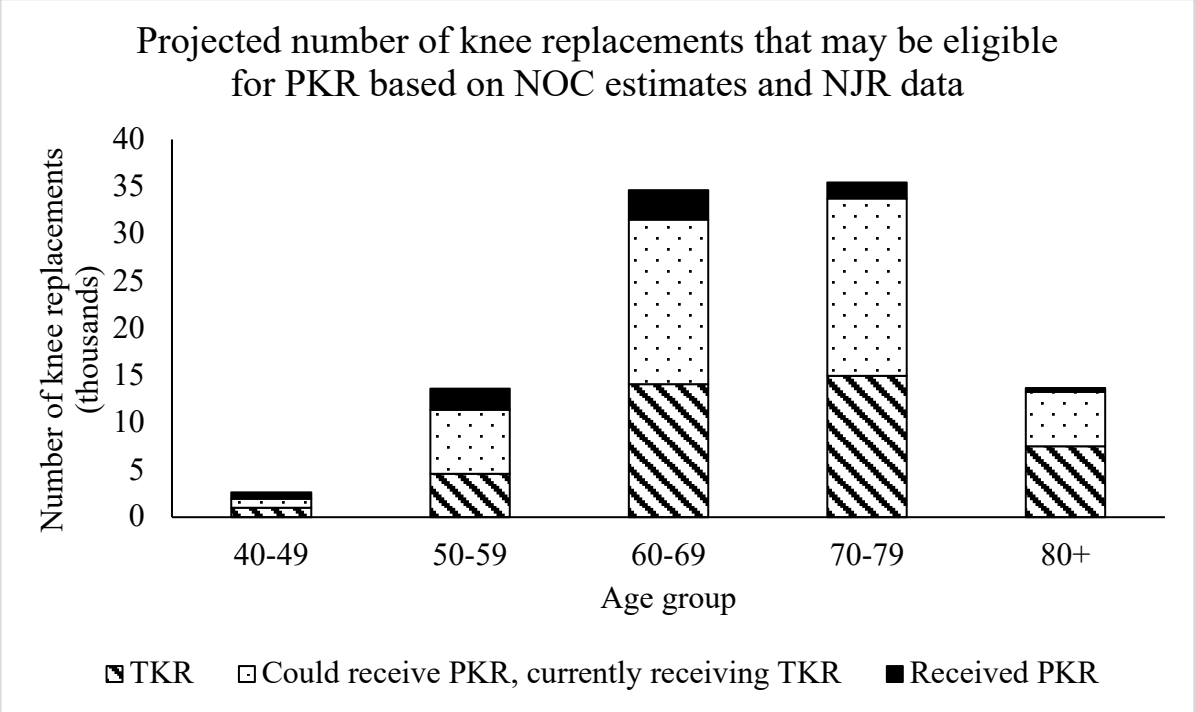


Figure 4-6 Potential eligibility for different types of knee replacement by age

Two other studies have provided estimates that are similar[53, 54], with overall PKR eligibility stated as 58-69% for medial or lateral PKR. One study was based on the same patients as included in this section[47]. Finally, two other studies use different criteria for their medial PKR, and thus have come up with lower estimates than those found here[55, 56], being 18-21% eligible for medial PKR alone. None of these studies provided information on age stratification. Details of these studies have been provided in the introduction (Table 1-3).

The major limitation to this section is that this section has not examined any outcome data. As eligibility/indications/candidacy for a procedure should be based on expected outcome, this is an important shortcoming that is addressed in the next section. Further, the main comparisons between the Nuffield Orthopaedic Centre and the NJR may not be fair. The NOC had, on average, the highest estimates of PKR eligibility. However, its estimates were not dissimilar to estimates from other centres and it is a like for like population with the NJR. Further the NJR usage is likely to include a particularly large number with early arthritis[50], and thus it is almost certain that they weren't used for bone-on-bone arthritis which limits the comparisons. In addition, the NOC estimates included both medial and lateral PKR, whilst the USA data included only medial PKR, meaning that the USA data would have underestimated overall candidacy. Further the validation of radiographs was performed only for the medial side. The strengths are that it has built upon limitations in previous studies to provide consistent estimates for eligibility that should be generalisable to the joint replacement population. It has examined only those with severe bone-on-bone arthritis, and as such these findings should not be extrapolated to those with early arthritis.

In conclusion, about half of all patients at three centres around the world (United Kingdom, United States, Australia) are eligible for partial knee replacement. There is an association with age. About 6 in 10 patients younger than 60-65 years could receive partial knee replacement, this number falling to 4-5 in 10 patients older than 75-80 years. This is much higher than current usage.

4.6. Selection for knee replacement: Section summary

This section examines the percentage of patients that might be eligible for partial knee replacement in a population with arthritis severe enough to warrant joint replacement. It addresses limitations of using a single methodology to determine eligibility, and has developed evidence to expand eligibility estimates on the basis of radiographs without stress views.

In the first study a cohort of over 1000 knees from the designer centre were analysed dependent on the implantation of partial or total knee replacement. This revealed that over half of all knee replacements were partial, and there was a mild, but significant, effect with age: increasing age reduced the number of patients receiving PKR. But in those over 75, it was still 53%.

The second study looked at a cohort of 457 knees from a high volume referral centre in the United States of America that had data about prosthesis implantation, and full sets of radiographs including stress radiographs. This allowed us to link radiographic findings

to actual implantation rates. Whilst also at risk of referral bias, about half of knees were eligible for partial knee replacement, with a moderate (and still significant) effect with age.

The third study was a private Orthopaedic Practice from Australia (>70% of knee replacements undertaken privately, >50% of population has private health insurance). This practice does not advertise as a partial knee replacement centre. 402 knees were identified. Estimates were once again that about half of knees could have partial knee replacement, with a mild, but significant, effect of age.

In summary, this section has provided age stratified eligibility estimates from three centres. It has addressed issues of referral bias and linked implantation to radiographs. It has not looked at outcomes of partial knee replacement however, and this is considered in the next section.

Section II: Outcome and age

5. Age-stratified function and implant survival at the designer centre: the Nuffield Orthopaedic Centre, United Kingdom[2]

5.1. Outcome and Age: Section introduction

The previous section has established that about half of all patients receiving knee replacement in all examined age groups could receive partial knee replacement. However, no outcomes were examined in these studies to determine if these were appropriate.

Partial and total knee replacement (PKR and TKR) are treatment options for medial compartment osteoarthritis and avascular necrosis of the knee [149]. When used for appropriate indications PKR provides better function [17, 53, 150, 151], faster recovery[69, 143] and lower morbidity and mortality[3, 70, 152] compared to TKR. However, this is at the expense of a higher revision rate. National joint registries consistently report increasing revision rates with decreasing patient age for both TKR and PKR [153-156]. They also report very high PKR revision rates in the young, being about 20% at ten years in patients under 55 [153-155]. Due to the high revision rate of PKR in the young, youth has long been considered to be a contra-indication to PKR[157].

The increased failure rate in younger patients is generally considered to be due to higher levels of activity. This results in more frequent and greater mechanical loads being

[2] This chapter has been published: Kennedy JA, Matharu GS, Hamilton TW, Mellon SJ, Murray DW (2018) Age and outcomes of medial meniscal-bearing unicompartmental knee arthroplasty. The Journal of Arthroplasty 33:3153-3159

applied to the prosthesis and the bone-prosthesis interface. Mobile-bearing Oxford PKR has theoretical advantages that may decrease the revision rate in this situation. The fully congruent bearing has low contact stresses so should minimise wear[158, 159], and transmits predominately compressive forces to the bone-implant interfaces so should minimise loosening[160]. It is therefore possible that Oxford mobile-bearing PKR, if used for appropriate indications, may not have a marked increase in revision rate in young patients.

Previous studies exploring the effect of age on PKR outcomes have been limited by small numbers[161, 162], short-term follow-up[163-165], lack of comparator groups[166-169], or binary analyses[170-174] (i.e. outcomes in those younger or older than 60 years of age). Taken together they suggest that short-term functional outcomes are good in young patients. There are no long-term studies of PKR patients which compare age and patient reported outcome measures (PROMs). Furthermore, the relationship between age and implant survival is variable.

The outcomes of partial knee replacements in different age groups when used for severe osteoarthritis has not been examined. The aim of this section is to describe the functional and implant survival outcomes of patients undergoing partial knee replacement for severe osteoarthritis, and compare the results of the designer centre with non-designer centres using the implant for similar indications.

5.2. Chapter Introduction

This chapter assesses the effect of patient age on functional outcomes and revision rates following medial mobile-bearing PKR in a large non-registry cohort. The cohort was selected for PKR using the recommended indications with age not considered to be a contra-indication.

5.3. Methods

A prognostic cohort study was performed using a prospectively followed consecutive cohort of cemented medial mobile-bearing PKR to assess the influence of age on PROMs and implant survival.

Between June 1998 and March 2009, 1000 consecutive cemented medial mobile-bearing (Oxford) Phase 3 PKR (Zimmer Biomet, Bridgend, United Kingdom) were implanted through a minimally invasive approach in 818 patients by two designer surgeons (CAFD, DWM) for the recommended indications as described by Goodfellow et al[175]. The pathological diagnosis was anteromedial osteoarthritis (AMOA) in 977 knees and spontaneous osteonecrosis of the knee in 23. Patients were followed up for a mean of 10 years (range 5 to 17). Details of this cohort have been reported in detail[52, 104, 176]; the present study was designed to specifically explore the effect of age on outcomes.

Patients were followed up by research physiotherapists independent of surgical and clinical teams. Functional outcomes were assessed using the Oxford Knee Score (OKS; 0 to 48 with 48 the best outcome)[177], and the Tegner Activity Score (0 to 10 with 10 being

participation as an elite athlete)[178]. Patients were assessed pre-operatively and at one, five, ten, and 15 years post-operatively. Data were extracted from a prospectively maintained database on 1 September 2014. All patients had been contacted in the previous 18 months prior to data extraction to ascertain the current functional status of their knee and to identify any re-operations/revisions. If a patient had died, information about their knee status and any further operation was obtained from primary and secondary care records, and from the patient's relatives where appropriate. At the time of follow up, 118 patients (141 knees; 14%) had died without requiring a revision.

Age and weight at surgery were normally distributed. Pre-operative OKS was normally distributed, whilst post-operative scores were left skewed. Tegner activity score was normally distributed pre- and post-operatively.

Age was grouped into four *a priori* to allow direct comparison with the reporting styles of the National Joint Registry of England, Wales, Northern Ireland and the Isle of Man (NJR) [153], and the Australian [155] and New Zealand [154] joint registries. These groups were patients younger than 55 years, 55 to <65, 65 to <75, and 75 years or older (75+) at surgery.

Statistical analysis: Mean (standard deviation) and median (interquartile range) are presented. Differences between groups were tested with Kruskal-Wallis tests, whilst differences over time within a group were assessed with Wilcoxon's signed rank tests. The percentage of knees at each time point achieving an OKS of 34 or greater (considered a good or excellent outcome) was calculated. Differences in Tegner activity score

between age groups were assessed with ANOVA with Bonferroni correction, while differences over time were assessed with a paired t-test.

Implant failure was defined as revision surgery, with revision defined, as per the NJR, as component removal, exchange or addition. It therefore included insertion of a new bearing, addition of a lateral PKR or conversion to a total knee replacement (TKR). Ten-year Kaplan-Meier survival estimates are reported, and component-time incidence rates for overall and individual failure modes were calculated. Significance was tested with a log-rank test. Association between age group and type of revision components used was tested with ordered logistic regression, and the lowest p value for each comparison is reported.

Age at surgery was present for all knees, however, four knees (three patients) could not be traced for follow-up so their final revision status remains unknown. Missing values were present for OKS and Tegner Activity Score, and were excluded for individual analyses, but not from the dataset as a whole. When explored with logistic regression there was no association between missing values and age.

Statistical analyses were performed in Stata Version 14 (STATA corp, Texas, USA) and R (R Core Team 2016, Vienna, Austria). Statistical significance was defined as a p value of <0.05.

5.4. Results

Baseline characteristics: The mean age at surgery was 66.6 years (SD 9.6, range 33 to 88). Preoperatively, older patients were significantly lighter than younger patients (Table 5-1). There was no significant difference in the distribution of sex or preoperative OKS between groups.

Table 5-1 Descriptive characteristics of designer PKR cohort by age

Group	N knees	N patients	Age in years	Weight in kg	Proportion female
<55	116	98	49.6 (4.5)	86.8 (17)	.54
55 to <65	304	243	60.3 (2.9)	86.7 (18)	.45
65 to <75	374	310	69.9 (2.9)	80.4 (15)	.48
75+	206	173	79.3 (3.2)	71.8 (13)	.52
Entire cohort	1000	818	66.6 (9.6)	81.3 (17)	.49
p value	NA	NA	NA	<0.001	0.2
N: number; kg kilograms; NA: not applicable; Age, weight, and preop OKS reported as mean (standard deviation);					

Post-operative PROMS: There was significant improvement in post-operative OKS from pre-operative OKS at one, five and ten years for all age groups ($p<0.001$). There were no significant differences between groups at one or five year follow-up (Table 5-2). At five years in all groups the median OKS was 44 (Figure 5-1). At ten years there was a significant difference between scores ($p<0.01$) with the median OKS of those 75+ at surgery dropping to 38.5, and the others not changing significantly.

Table 5-2 Patient reported outcomes by age group

Age group (years)	Score	Pre op	Y1	Y5	Y10
<55	OKS Mean (SD)	23.1 (9.1)	**39.6 (7.5)**	**41.3 (7.6)**	39.1 (9.8)
	OKS Median (IQR)	23 (14)	**41 (7)**	**44 (8)**	43.5 (13.5)
	OKS % good/excellent	NA	83%	86%	75%
	Tegner Activity Score mean (SD)	2.71 (1.4)	**3.18 (1.3)**	**3.50 (1.5)**	3.15 (1.2)
55 to <65	OKS Mean (SD)	24.4 (8.5)	**40.3 (8.2)**	**41.2 (8.2)**	**41.5 (7.7)**
	OKS Median (IQR)	25 (11)	**43 (8)**	**44 (8)**	45 (10)
	OKS % good/excellent	NA	84%	87%	87%
	Tegner Activity Score mean (SD)	2.44 (1.2)	**3.02 (1.0)**	**3.03 (1.1)**	2.96 (1.2)
65 to <75	OKS Mean (SD)	24.5 (9.0)	**41.4 (7.1)**	**41.8 (6.6)**	**39.3 (8.9)**
	OKS Median (IQR)	24 (13)	**44 (7)**	**44 (7.5)**	**42 (12)**
	OKS % good/excellent	NA	87%	87%	76%
	Tegner Activity Score mean (SD)	2.34 (1.1)	**2.83 (0.9)**	**2.80 (1.0)**	**2.25 (1.0)**
75+	OKS Mean (SD)	26.2 (8.6)	**40.8 (7.5)**	**40.4 (8.2)**	37.1 (9.4)
	OKS Median (IQR)	26.5 (12)	**43 (8)**	**43.5 (9)**	**38.5 (13.5)**
	OKS % good/excellent	NA	86%	83%	79%
	Tegner Activity Score mean (SD)	1.96 (0.8)	**2.51 (0.7)**	**2.09 (0.9)**	**1.73 (0.8)**
Difference between age groups for OKS (Kruskal-Wallis)		0.08	0.05	0.55	<0.01
Difference between age groups for Tegner Activity Score (ANOVA)		<0.01	<0.01	<0.01	<0.01
Bold typeface indicates significant difference compared to prior score. Paired t-test for means, Wilcoxon's signed rank test for medians.					

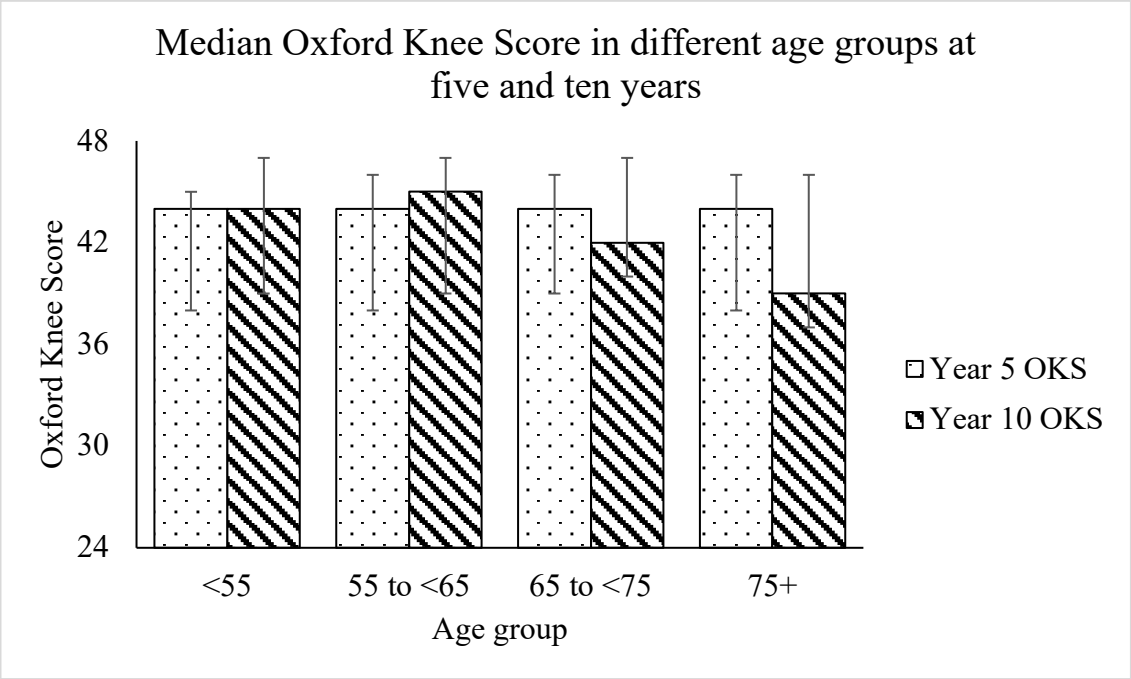


Figure 5-1 Median Oxford Knee Score in different age groups from the designer centre at five and ten years. Bars represent interquartile range.

The Tegner score improved in all age groups with surgery ($p<0.02$; Table 5-2). Younger patients had higher activity levels at each time point. There was varied response over time amongst age groups: those less than 55 showed continued improvement at one and five years post-surgery ($p<0.05$), 55-65 year olds plateaued from their one-year scores ($p>0.05$), and those 65+ declined from their one-year score ($p<0.05$).

Implant revision risk: There were 52 revisions. Those under 55 years had the lowest revision risk, compared with the other three age groups, though this was not significant ($p=0.6$). The cumulative ten year PKR survival rate for those younger than 55 was 97.2% (95% CI 92 to 99, at risk=46), between 55 and <65 was 93.7% (CI 90 to 96, at risk=137), between 65 and <75 was 94.3% (CI 91 to 97, at risk=159), and for those 75+ was 93.0% (CI 86 to 96, at risk=54). The revision rate per 100 component years was also lowest in

those under the age of 55 although, again, the difference was not statically significant (Table 3, p=0.74). There were no statistical differences between age groups for any specific revision indication.

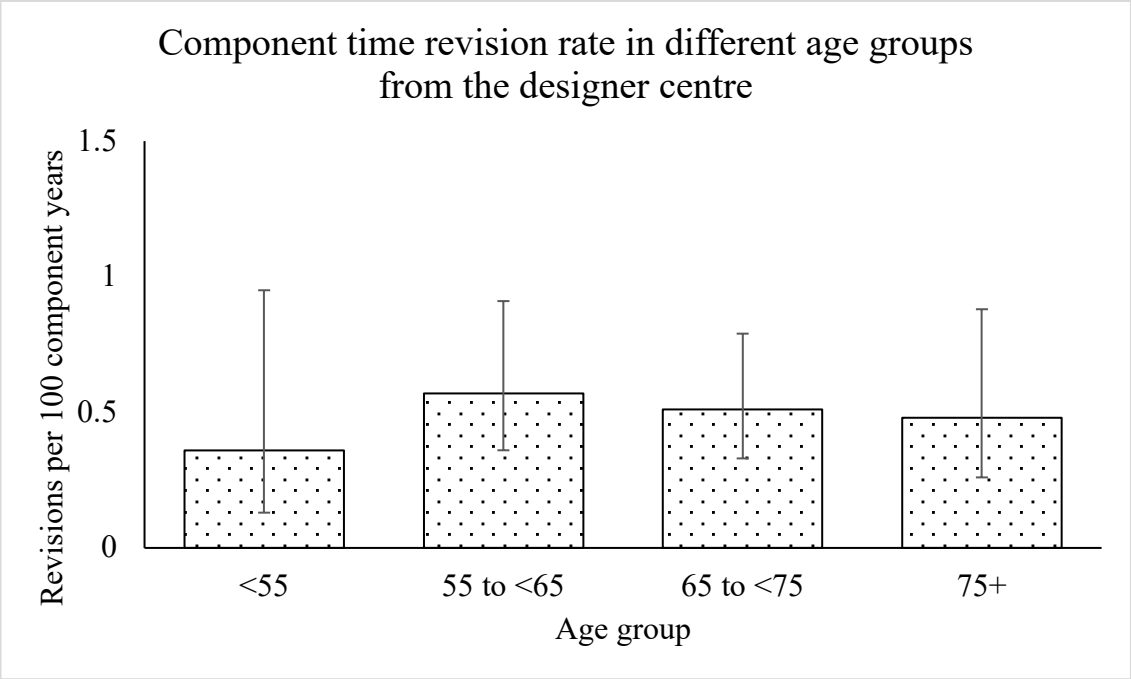


Figure 5-2 Component time revision rate in different age groups from the designer centre. Bars represent 95% confidence interval.

Table 5-3 Comparison of revision indications by age group presented as component time incidence rate per 100 years (95% confidence interval)

Age group	Overall	Lateral OA progression	Bearing dislocation	Pain	Infection	Instability	Aseptic Loosening	Other
<55	0.36 (0.13 to 0.95)	0.09 (0.01 to 0.63)	0.09 (0.01 to 0.63)	0.09 (0.01 to 0.63)	0	0	0	0.09 (0.01 to 0.63)
55-64	0.57 (0.36 to 0.91)	0.22 (0.11 to 0.47)	0.10 (0.03 to 0.30)	0.13 (0.05 to 0.34)	0.03 (0.00 to 0.23)	0.03 (0.00 to 0.23)	0.03 (0.00 to 0.23)	0.03 (0.00 to 0.23)
65-74	0.51 (0.33 to 0.79)	0.28 (0.15 to 0.50)	0.08 (0.02 to 0.24)	0.03 (0.00 to 0.18)	0.08 (0.02 to 0.24)	0	0	0.05 (0.01 to 0.20)
75+	0.48 (0.26 to 0.88)	0.29 (0.13 to 0.64)	0	0.05 (0.01 to 0.34)	0.10 (0.02 to 0.38)	0	0.05 (0.01 to 0.34)	0
P value	0.74	0.35	0.15	0.16	0.23	0.43	0.71	0.26

Most revisions (62%) were managed with conversion to primary TKR (Table 4). Two (4%) required revision TKR components, two (4%) had PKR components exchanged, and the remainder had lateral PKR (19%) added for disease progression or bearing dislocations with insertion of a new bearing (12%). There was no association between age group at surgery and revision with TKR ($p>0.68$), lateral PKR ($p>0.26$), or bearing exchange ($p>0.47$).

Table 5-4 Revision type overall and by age group

Age group	Revision	N	% of group
Overall	Primary TKR	27	52%
	Two stage primary TKR	5	10%
	Lateral PKR	10	19%
	Bearing exchange	6	12%
	Revision TKR components	2	4%
	PKR component revision	2	4%
<55	Primary TKR	2	50%
	Lateral PKR	1	25%
	Bearing exchange	1	25%
55 to <65	Primary TKR	11	61%
	Two stage primary TKR+	1	6%
	Revision TKR*	1	6%
	Lateral PKR	1	6%
	Bearing exchange	2	11%
	Tibial component revision^	1	6%
	Femoral component and bearing exchange$	1	6%
65 to <75	Primary TKR	9	45%
	Two stage primary TKR#	3	15%
	Lateral PKR	5	25%
	Bearing exchange	3	15%
75+	Primary TKR	5	50%
	Two stage primary TKR#	1	10%
	Two stage Revision TKR# (stemmed tibia)	1	10%
	Lateral PKR	3	30%

+Infection following ACL reconstruction leading to lateral compartment destruction
*Revised to hinged TKR due to medial compartment opening
^Revised due to tibial overhang
$Femoral component loosened whilst retrieving bearing. Bearing and femoral component revised
#All due to infection

5.5. Discussion

The most important finding of this chapter is that the revision rate of medial Oxford PKR did not increase with decreasing age. This observation was contrary to registry data [153-155, 179]. It is generally accepted that the revision rate of all joint replacements increases

with decreasing age. This difference may relate to the implant or to the indications for which it is used. In all age groups there were very good functional outcomes, and these were maintained in the long term except in elderly patients (75+) who had some deterioration at ten years. Younger patients also had higher activity levels at each time point.

It is widely perceived that younger patients will have higher revision rates due to high activity leading to mechanical failure of the implant or its fixation. In this study, as expected, it was found that younger patients are more active than older patients, with significantly higher Tegner scores. It has been observed that increasing activity is not associated with an increasing revision rate with the mobile-bearing PKR, but is actually associated with a decreasing revision rate[166, 169, 180]. The mobile-bearing Oxford has fully congruent contact and thus low contact stresses[158], so failure due to wear is theoretically very low[181]. As the bearing is mobile the loads transmitted to the bone implant interfaces are predominantly compressive so there is a very low theoretical risk of aseptic loosening[160]. In contrast with TKR, after there is some wear, shear may be transmitted to the interfaces, which increase the risk of wear and loosening[182, 183]. Furthermore, the instrumentation aims to accurately restore ligament tension and function[160], thereby restoring normal knee kinematics[184, 185]. These features should minimise the risk of failure in active patients, but would not make the revision rate progressively decrease with increasing activity. The youngest patients had the highest activity scores, and yet the lowest risk of revision due to disease progression. Although this may seem counterintuitive, it suggests that more active and younger patients have better quality cartilage and bone and are therefore less likely to fail from lateral osteoarthritis or aseptic loosening, which represent the two main modes of PKR failure.

National joint registries all demonstrate increased risk of revision in younger patients after both PKR and TKR (Figure 5-3). In the NJR [183] the revision rate for mobile-bearing PKR is 2.9 (95% CI 2.1 to 4.2) times higher in those <55 years of age compared with those 75+. As the majority of mobile-bearing PKR in the NJR are Oxford mobile-bearing PKR, it is likely that the revision rate for the Oxford PKR is about three times higher in those <55 compared with those 75+. In contrast, in this series the revision rate for the Oxford PKR was similar in those <55 compared with those 75+. As these results were achieved by the same implant the differences are likely to be related to the indications.

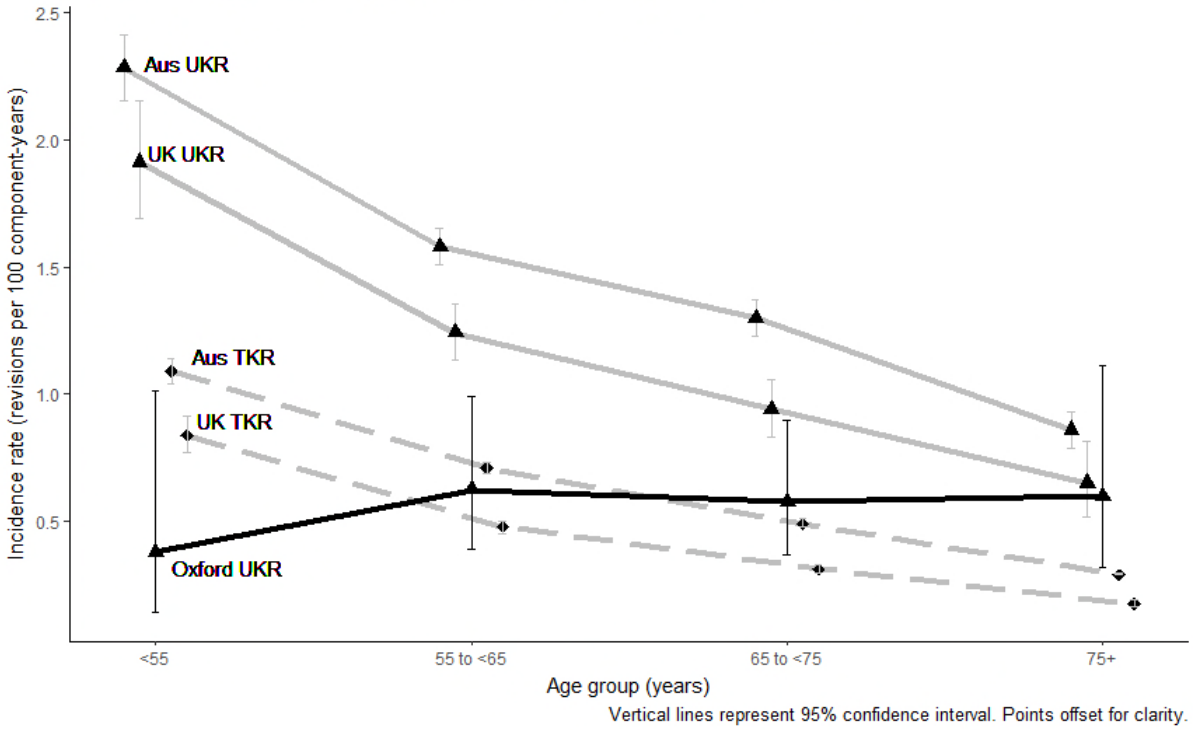


Figure 5-3 Revision rate comparison: Study centre vs registries

The indications for Oxford mobile-bearing PKR are based on disease patho-anatomy. In Oxford, patients are not excluded on the basis of age, weight, or activity[52, 172]. The primary indication is AMOA. There should be bone-on-bone arthritis medially, full-thickness cartilage laterally and functionally intact anterior cruciate and medial collateral ligaments. These are best identified radiographically[47]. If bone-on-bone is not identified medially on radiograph, then arthroscopic assessment prior to surgery can be useful[47]. The indications are satisfied in up to half of patients needing knee replacements[47, 53]. In the NJR, a substantial proportion of surgeons use PKR for a small proportion of knee replacements. It tends to be used in younger patients and has a high revision rate [73]. This suggests that these surgeons are using PKR for patients with early disease, possibly with partial-thickness cartilage loss, in patients on whom the surgeon is reluctant to perform TKR. Indeed, there is a widespread view that PKR should be used predominantly in this situation. However, patients with partial-thickness cartilage loss do not do well following PKR, with ongoing pain and higher revision rates[141, 186, 187]. If surgeons only implanted PKR in patients with bone-on-bone arthritis (i.e. using the recommended indications) the high revision rate of the mobile-bearing PKR in young patients would probably be avoided.

It is possible that the reason an increase in revision rate with decreasing age was not seen was a type II error due to the small number of revisions. As can been seen from the confidence intervals in Figure 5-3 it is unlikely that this accounts for the differences in trends between this data and registry data. There have also been a few previous studies, like this, that have looked at the influence of age on revision rate for mobile-bearing PKR but their conclusions were not consistent[161, 163-165, 170, 172-174] (Table 5-5). Most of these studies only compared patients over and under 60 years old. Of the five non-designer

centre studies, two reported an increased risk of revision in the young, and three did not. This supports these findings, and confirms that the revision rate of the mobile-bearing PKR does not necessarily increase with decreasing age.

Table 5-5 Comparison of other studies reporting age

Author	Region	Analysis type	Follow up in years (mean)	Age bracket	Number of knees (N at risk at follow up)	Outcome Survival (95% CI) or N revisions [percentage of cohort revised]
Young not at increased risk						
2012 Kristensen [173]	Denmark	Kaplan-Meier	10.7 (4.8)	<60 60+	248 (NR) 447 (NR)	86.5% (79 to 92) 82.4% (69 to 91)
2007 Kort* [163, 164]	Netherlands	N of failures in cohort	2-6 (NR)	<60 60+	46 (NR) 154 (NR)	2 revisions [4.3%] 17 revisions [11.0%]
2012 Matharu [165]	Birmingham	Cox regression	(4.4)	NA	459 total Not reported by age	Not significant
Pandit# [172]	Oxford	Kaplan-Meier	10 (5.6)	<60 60+	245 (NR) 755 (NR)	97.3% (91 to 100) 95.1% (91 to 99)
Young at increased risk						
2005 Price [170]	Oxford and Sweden	Kaplan-Meier	10 (NR)	<60 60+	52 (19) 512 (157)	91% (12.4) 96% (3.2)
2013 Ingale [161]	Scotland	Life table	6 (4)	<60 60-69 70-79 80+	110 (23) 164 (40) 145 (50) 51 (19)	84% (NR) 91% (NR) 94% (NR) 95% (NR)
2009 Kuipers [174]	Netherlands	Kaplan Meier	5 (median 2.6)	<60 60+	437 total Not reported by age	**77.2% (68-87)** **89.4% (85-94)**

*Results for <60 and 60+ from different series over same time frame; #Includes same patients as in current series; Bold typeface indicates significant difference; NR not reported; N Number

All age groups had substantial improvement following PKR in terms of pain and function. The OKSs were high (median 44) at five years and there were no differences between age groups. It was only at ten years that a significant difference occurred between the age groups, with the oldest group (75+) starting to deteriorate. This is not surprising as this group is now a minimum of 85 years old, and OKS is known to decline with age[188]. In the other groups the OKS did not show an appreciable decline at 10 years. In all groups the Tegner score improved substantially. The score was higher in younger patients, and these patients continued to improve with time. There are no other papers that have studied the influence of age on the OKS and/or Tegner score after PKR.

If the indications for Oxford mobile-bearing PKR are satisfied then, by definition, the ligaments are functionally normal. During the surgical technique ligaments are never released and the instrumentation allows the surgeon to accurately restore normal ligament tension and balance by removing bone[45]. Therefore not only are normal kinematics restored but also leg alignment is restored to what it was before the patient developed arthritis[160]. In keeping with observed knee alignment in the general population[189], this frequently results in varus knee alignment (~25%)[190]. The combination of normal leg alignment and normal kinematics is probably the reason why patients report high functional scores, particularly if they are young[190].

When considering whether to implant PKR or TKR their relative merits must be compared. Advantages of PKR include faster recovery[69, 143], lower morbidity and mortality[3, 70, 152] and better functional outcomes and patient satisfaction[17, 53, 150, 151]. The disadvantage is that PKR has a variable, but often higher revision rate, which may be attributed to use in early arthritis, low surgeon experience, and a lower threshold for

performing revision[191]. This study suggests that the relative merits are affected by age. All age groups had good OKS. In the elderly, the patient's life expectancy is relatively shorter, and the chance of a revision being required in their lifetime will be low, so there is little advantage in doing a TKR. In contrast, there are major advantages of PKR, particularly the faster recovery, and lower morbidity and mortality. The evidence would therefore suggest use of PKR whenever possible in elderly patients. In the young the revision rate of Oxford mobile-bearing PKR is surprisingly low. If the recommended indications are adhered to, it is probably similar to, or lower than, that of primary TKR (Figure 5-3). Furthermore, if a revision is required it is likely to be a simpler procedure than a revision TKR (Table 5-4)[92, 115, 192]. Therefore, in young patients if the indications are satisfied, and in particular if there is bone-on-bone arthritis, PKR is recommended.

The strengths of this study are long term follow-up (mean of 10 years), very low patient loss to follow-up (0.4%) and the large cohort – this is the largest non-registry PKR cohort to analyse the effect of age on outcomes. Limitations include the number of revisions being small which could influence findings regarding revision risk. There is no radiographic or clinical examination, however, the primary outcome is revision, to which these do not contribute. It is also a single centre series from designer surgeons. However, previous reviews of the published 10-year data of the Phase 3 PKR suggest that if surgeons use the recommended indications, and use PKR in greater than 20% of their knee replacement practice they can expect to get similar results[47, 107, 193, 194].

In conclusion, following medial Oxford mobile-bearing PKR good functional outcomes can be achieved in all age groups. Contrary to registry observations, the revision rate for PKR in this study was not influenced by age and was low in all age groups. Therefore,

with correct indications patient age should not be considered to be a contraindication to medial Oxford mobile-bearing PKR, and in all age groups PKR has advantages over TKR.

6. Age-stratified implant survival in designer and non-designer centres for the Oxford medial PKR: a multicentre study

6.1. Introduction

The number of knee replacements performed continues to increase annually[21]. The most rapid increase in relative provision for joint replacement is in those historically considered too young for replacement[10]. This is despite all joint registries suggesting that this group is at highest risk of revision surgery, and that they tend to have the poorest functional outcomes relative to other age groups[1, 89, 154, 195]. It is perhaps for this reason that many more surgeons consider undertaking a partial knee replacement, as evidenced by the higher rate of PKR implantation in younger patients in the registries[21, 195]. The registries also report a very high revision rate for PKR in young patients [21, 195]. In Chapter 5, the results from the designer centre were reported, and it was surprising to see that the revision risk was no higher in the youngest patients grouping when compared to the other age groups.

Reasons for the low rate of revision, relative to the joint registry, are likely to relate to indications for primary surgery. All of the patients in the Oxford cohort had severe bone-on-bone arthritis of the medial compartment, with complete joint space loss demonstrated on radiograph or joint inspection[104, 176]. They had an intact lateral compartment, as assessed by radiograph, and intact ligaments. Factors such as high activity level, radiographic malalignment, and residual varus alignment have been shown not to affect the risk of revision in medial Oxford PKR, and were ignored[59, 172, 180, 196].

There is inherent risk in attempting to generalise results from specialist surgeons. Unmeasured factors around patient selection, and operative technique and ability are not inherent to an implant device. This is typified by the discrepancy noted between joint registries and cohorts from specialist centres[94-96]. In determining the reasons for these differences, difficulties arise in that stringent follow up and measurement of cohorts is only rarely undertaken outside designer or specialist centres, which leads many to look at registry data for so-called generalisable data. However, factors such as surgeon usage, and the indications for primary or revision surgery are not well described in the registry which makes validation analyses within the registry impossible[38].

Further, it will be of interest to policy makers if a finding from a designer centre can be demonstrated to exist in other specialist centres. Other surgeons were therefore identified around the world who perform Oxford PKR for the correct indications, and who have follow up for their patients to undertake external validation.

This chapter describes the implant survival and revision rate of patients in different age groups from various surgeons around the world. Secondary outcomes were a qualitative description of the revision procedure undertaken, and a comparison between the demographic variables of the Oxford cohort and these other cohorts to try and identify any relevant differences in patient characteristics.

6.2. Methods:

A multicentre cohort study was undertaken identifying patients (and their knees) who had undergone a medial Oxford PKR and determining the number of knees that underwent subsequent revision. Centres with prospectively followed cohorts in Japan, New Zealand, and the USA were identified.

The New Zealand cohort consisted of 759 consecutive partial knee replacements undertaken by five surgeons across three hospitals in Christchurch, New Zealand between 2005 and 2011. These patients were followed prospectively. Thirty-nine passed away with their knee in-situ, 28 withdrew from follow up without problems with their knee at time of withdrawal, 23 had moved abroad, and 26 were lost to follow up. This left 655 knees available for analysis.

The USA cohort consisted of 194 consecutive medial PKR performed by a single surgeon in 2008 at Joint Implant Surgeons, Ohio. These had been followed prospectively. Age at surgery, body mass index, patient sex, and revision status with follow up were all recorded. The procedure performed in the revision was not well documented and a worst case interpretation was taken and recorded these as revised to TKR.

The Japanese cohort consisted of 1362 consecutive knees undertaken between 1996 and 2018. One hundred and twenty-four had been entered with missing data and were excluded, while a further 419 had less than one year follow up; these were also excluded. This left 819 knees available for analysis. The Japanese cohort did not have body mass

index recorded, and further, the recording of revisions was unclear. Therefore, the revision data from this cohort was not combined for the comparative analyses.

Two designer centre cohorts from Oxford were used. Both are prospectively followed. The first consisted of 1000 cemented PKR, undertaken between 1997 and 2006. During the follow up 118 patients died (142 knees), 36 patients (42 knees) withdrew because of poor health, and three patients (four knees) were lost to follow up. The second cohort consisted of 1059 cementless PKR undertaken between 2004 and 2017. There were 33 withdrawals during the follow up of this cohort; 22 knees from poor health, four from patients going abroad, and seven from patient requests to withdraw. At the time of withdrawal none of the knees had been revised. Both cohorts consist of knees undertaken by the two designer surgeons, and were undertaken at within the National Health Service at the Nuffield Orthopaedic Centre, and privately at The Manor Hospital, in Oxford, United Kingdom.

Statistical analysis: For normally distributed continuous variables the mean and standard deviation was calculated, otherwise median and interquartile range. Categorical data is presented as number and percentages. Demographics were compared with one-way analysis of variance and corrected with Tukey multiple comparison test, or a chi-squared test. Component time incidence rates for revision per 100 observed component years (CTIR) was determined, and 95% confidence intervals based on the Poisson distribution was calculated. Differences in survival between categorical variables were tested with a log-rank test.

6.3. Results:

The mean age was slightly younger in the cohort from the USA than from the other centres, whilst the oldest mean age was in Japan (Table 6-1, Figure 6-1). There were no significant differences between the cemented and cementless Oxford cohorts. The New Zealand cohort showed the most similarities to the designer centre cohorts in terms of the distribution of age, and the percentage of female patients. The BMI was significantly different from the cemented cohort (p=0.02) but not the cementless (p=0.65). BMI was greatest in the USA cohort. The USA cohort had a higher proportion of PKR practice being performed in the youngest age group (21%), compared to New Zealand (14%), and the Oxford cohorts (12% and 15%). The Japanese cohort demonstrated a large preponderance towards female patients (81%), which was higher than that seen in the other cohorts (about 50%). The Oxford cemented cohort had the longest mean follow up (10.1 years), whilst the USA cohort had the shortest (3.9 years). Overall the data from New Zealand and Oxford were similar, whilst the demographics of the Japanese and USA data were significantly different. Given the large difference in the demographics of the Japanese cohort, combined with the uncertainty around what constituted a revision from their data, it was decided to exclude them from the combined analyses.

Table 6-1 Demographics of the different cohorts

	New Zealand	Japan	USA	Oxford Cemented	Oxford Cementless	P value
N knees	655	819	194	1000	1059	NA
Mean age (SD)	66.1 (9)	71.1 (7)	63.3 (10)	66.6 (10)	66.2 (10)	<0.001
N <55 N 55 – 65 N 65 – 75 N 75+	89 (14%) 212 (32%) 228 (35%) 126 (19%)	21 (3%) 138 (17%) 410 (50%) 250 (31%)	40 (21%) 68 (35%) 58 (30%) 28 (14%)	116 (12%) 304 (30%) 374 (37%) 206 (21%)	157 (15%) 322 (30%) 369 (35%) 211 (20%)	NA
Mean body mass index (SD)	29.5 (5)	Not available	32.1 (8)	28.5 (5)	29.1 (5)	<0.001
N female (%)	293 (45%)	664 (81%)	115 (59%)	487 (49%)	491 (46%)	<0.001
Mean follow up (range)	6.9 (1-11)	5.7 (1-19)	3.9 (1-7)	10.1 (1-16)	5.2 (1-14)	<0.001
N number; SD standard deviation; NA not applicable; USA United States of America						

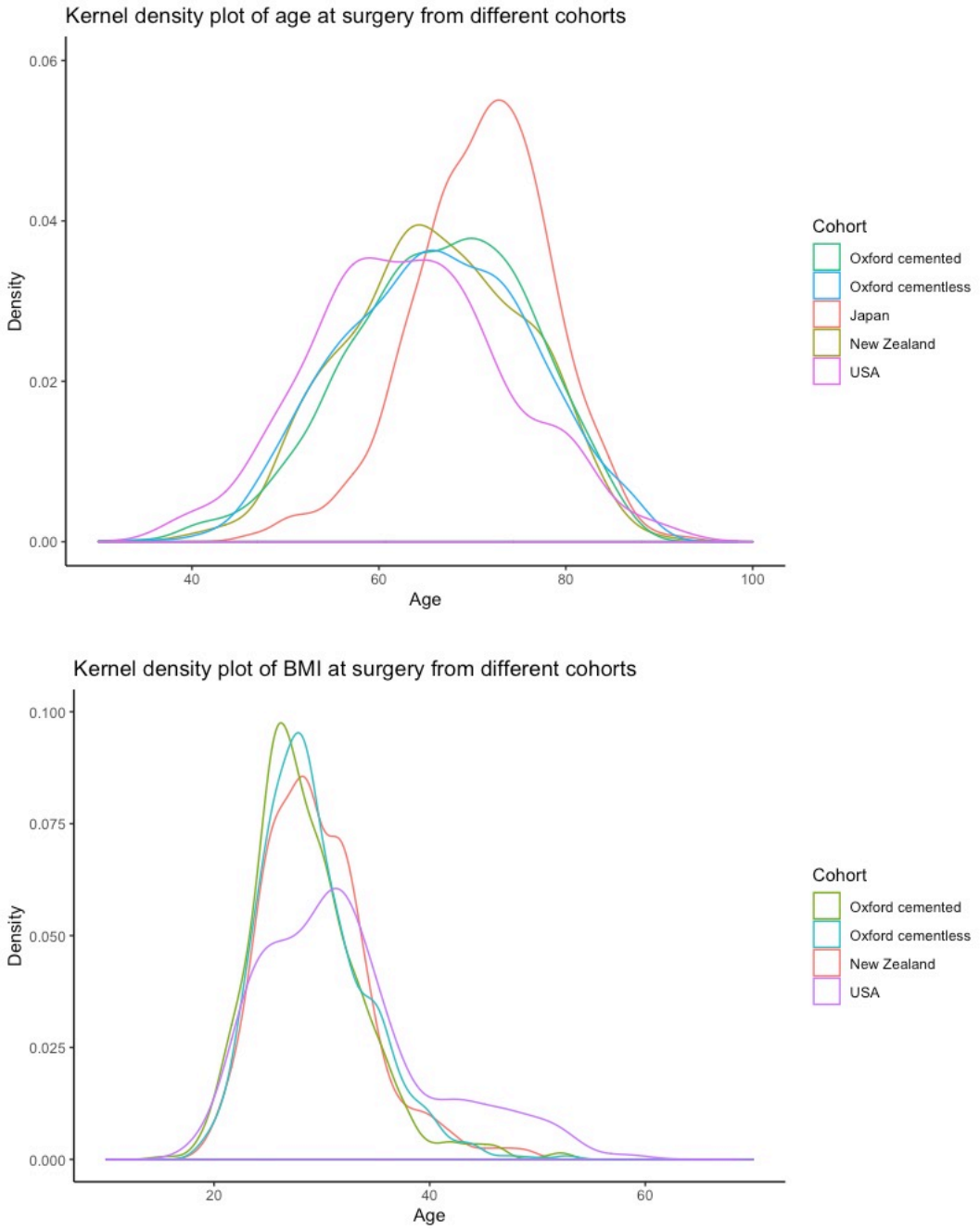


Figure 6-1 Comparison of provision by age and BMI between cohorts
Kernel density plots of age and BMI between the cohorts. The Japanese data did not have body mass index available and is therefore not plotted. There were minimal differences between the Oxford and New Zealand cohorts. BMI body mass index; USA United States of America.

The Oxford cemented cohort had the most revisions (52), giving an overall component time incidence rate (CTIR) of 0.57 (95% CI 0.42 to 0.75) per 100 component years (Table 6-2). This did not significantly vary with age categorisation (p=0.85). New Zealand had 22 revisions with a CTIR of 0.49 (95% CI 0.30 to 0.73), and again no significant difference nor trend seen between age groups (p=0.67). This trend was the similar for the other cohorts (Table 6-2). The cohort from the USA had an overall CTIR of 0.52 (95% CI 0.14 to 1.34)), with a non-significant, but higher risk in the youngest age group (1.94 revisions per 100 component years, compared to the overall risk 0.52, p=0.06). However, there were only four revisions in total.

Table 6-2 Number of revisions (N), person-time at risk (PT) and Component time incidence rates per 100 years (CTIR) by cohort and age group

	New Zealand			USA			Japan			Oxford: Cemented			Oxford: Cementless		
	N	PT	CTIR	N	PT	CTIR	N	PT	CTIR	N	PT	CTIR	N	PT	CTIR
Age < 55	4	646	0.62	3	154	1.94	0	103	0.00	4	1050	0.38	2	879	0.23
Age 55-65	8	1538	0.63	0	389	0.00	2	920	0.22	18	2883	0.62	3	1612	0.19
Age 65-75	5	1574	0.32	1	245	0.47	3	2501	0.12	20	3463	0.58	8	1815	0.44
Age 75+	5	774	0.65	0	119	0.00	4	1176	0.34	10	1673	0.60	5	985	0.51
Combined	22	4532	0.49	4	763	0.52	9	4700	0.19	52	9069	0.57	18	5291	0.34
CTIR component time incidence rate; N number															

Combining the data into non-designer centres (USA and NZ; Japan excluded due to demographic differences) and designer centre cohorts (Oxford cemented and cementless) found an equivalent rate of 0.49 revisions per 100 component years (Non Designer rate 0.49, 95% CI 0.32 to 0.72, Designer rate 0.49, 95% CI 0.38 to 0.62; rate ratio 1.01, 95% CI 0.62 to 1.60; Table 6-3; Figure 6-2). Reporting non-designer vs designer, in the youngest age group the rate was 0.88 vs 0.31, in those 55 to <65 it was 0.44 vs 0.47, in those 65 to <75 it was 0.34 vs 0.53, and in those 75+ it was 0.58 vs 0.56.

Table 6-3 Revision data by centre status (designer vs non-designer). Number of revisions (N), person time (PT), and component time incidence rates per 100 component years (CTIR)

Age group	Non-designer centres*			Designer centre			P value
	N	PT	CTIR	N	PT	CTIR	
< 55	7	800	0.88	6	1929	0.31	0.07
55-65	8	1839	0.44	21	4496	0.47	1
65-75	6	1787	0.34	28	5278	0.53	1
75+	5	869	0.58	15	2658	0.56	1
Total	26	5295	0.49	70	14361	0.49	1

CTIR Component time incidence rate; N number
*Japanese data excluded from analysis due to considerable differences in baseline characteristics of cohort and uncertainty around reliability of data.

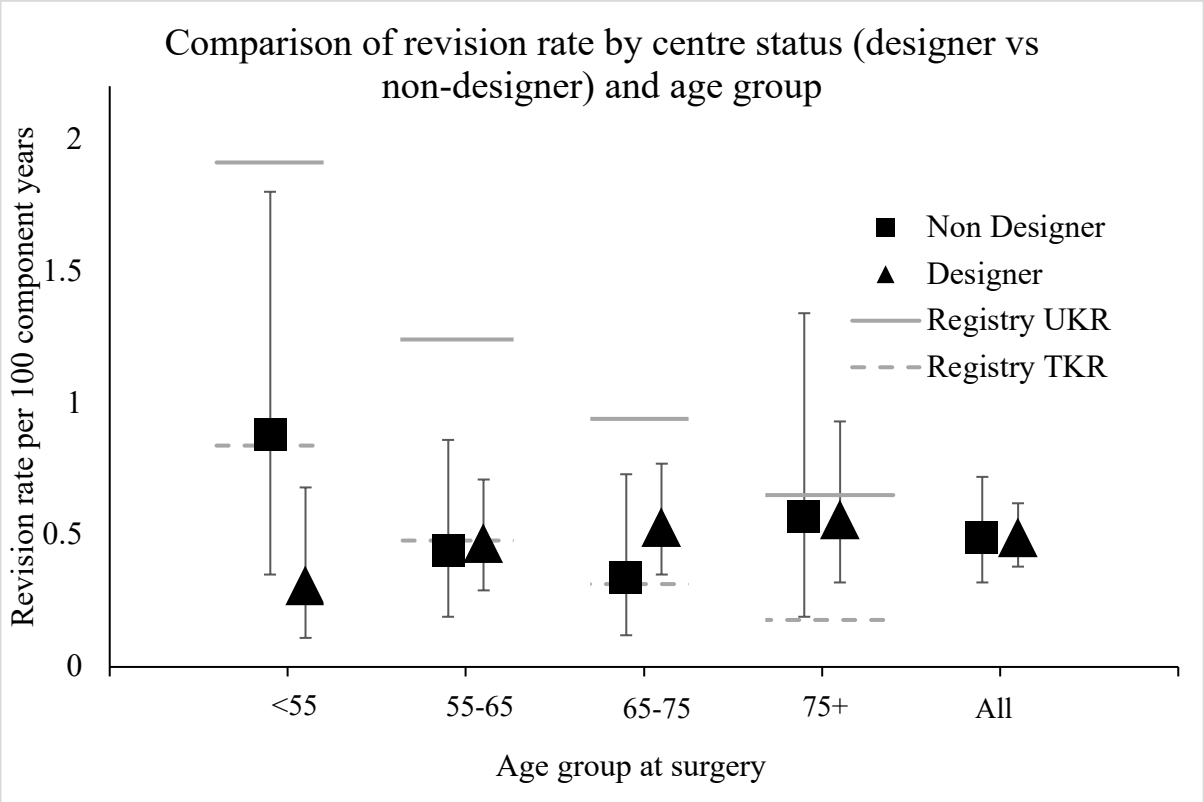


Figure 6-2 Comparison of revision rate by centre status and age group

Overall, about half of the revised knees went on to receive TKR (56%), followed by bearing exchange (24%), and the addition of a lateral PKR (16%). Following primary revision, 44% still had their PKR in situ. This did not vary significantly by age group with 55% of those undergoing revision retaining their PKR in those <55, reducing to 33% in those 75+ (Table 4). When considered against the total number of knees of medial PKR implanted, during the conduct of this study about 2% went on to be revised to TKR, and this was consistent across age groups.

Combining the estimates from all the centres gave an overall component time incidence rate of 0.49 (95% CI 0.40 to 0.60). For those younger than 55 at surgery the rate was 0.48 (0.25-0.82), for those 55 to <65 the rate was 0.46 (0.31-0.66), for those 65 to <75 the rate

was 0.48 (0.33-0.67), and for those 75 or older at surgery the rate was 0.57 (0.35-0.60). Considering TKR as the endpoint, the rate was 0.27 (0.20-0.35) revisions per 100 component years for all age groups combined, and was 0.18 (0.06-0.43), 0.28 (0.17-0.45), 0.25 (0.15-0.40) and 0.34 (0.18-0.59) for those aged younger than 55, 55 to <65, 65 to <75 and 75 or older respectively.

Table 6-4 Revision procedure undertaken in different age groups

Age group	Procedure	N (% of age group; % of all patients)
<55	Bearing exchange	5 (45%; 1%)
N=402	Lateral PKR	1 (9%; <1%)
	TKR	5 (45%; 1%)
55-65	Bearing exchange	4 (14%; <1%)
N=906	Lateral PKR	3 (10%; <1%)
	PKR to PKR*	4 (14%; <1%)
	TKR	18 (62%; 2%)
65-75	Bearing exchange	8 (24%; <1%)
N=1029	Lateral PKR	7 (21%; <1%)
	TKR	18 (55%; 2%)
75+	Bearing exchange	1 (6%; <1%)
N=571	Lateral PKR (+PFR+ACLR for 1)	5 (28%; <1%)
	TKR	12 (67%; 2%)

*Includes femoral component revision due to symptomatic femoral loosening, and tibial component revision for symptomatic overhang
N number; PKR partial knee replacement; TKR total knee replacement; ACLR anterior cruciate ligament reconstruction

6.4. Chapter Discussion

The work in this chapter found that there was no significant difference in the revision rate between non-designer centres and the designer centre, overall or for those in the youngest age group. Also found were differences in the practice patterns of PKR between some of the centres with regards to the percentage of patients that received PKR by age grouping, and in the body mass index of the patients being operated on.

All the surgeons are high volume PKR surgeons, who, in patients appropriate for knee replacement, tend to undertake PKR in those meeting the indications, and TKR in those that do not. The indications are now well defined and evidence-based for Oxford PKR, and consist of bone-on-bone medial osteoarthritis, intact lateral cartilage, and functionally intact anterior cruciate and medial collateral ligaments. All the surgeons contributing to the cohorts in this study undertake PKR in at least 50% of their practice, which is consistent with estimates of PKR candidacy from multiple regions around the world. Despite this, there were differences between the cohort demographics with regards to the body mass index and the age group distribution of the different surgeons. The USA cohort was heavier (BMI 32) than the other cohorts (about BMI 29), and also demonstrated a higher percentage of the surgeons PKR being performed in the youngest age group (21% vs about 13% for Oxford and NZ, and 2% for Japan). It is not possible from this data to demonstrate whether the patients' weight or body mass index may influence the proportion of patients who are eligible for PKR, but other data has shown that patient weight increases the risk of arthritis and joint replacement at an earlier age. The New Zealand cohort was very similar to the designer cohort in Oxford, whilst the

Japanese cohort demonstrated a great preponderance towards females and older patients undergoing joint replacement, which is in keeping with findings from other studies from Asia, in particular South Korea,[197, 198] Japan, [199-201] and China[202], with these studies also reporting that about 80% of knee replacements were performed in women. The component time incidence rates presented in Table 6-2 were low, which is in keeping with Yoshida's original case series[107] that reported a ten-year survival of 95%. However, marked differences have been noted in bone morphology between Asian and Western knees [203-207]. As a consequence they have a higher risk of periprosthetic fracture[203] and dislocation[208]. They also have a lower rate of disease progression[209]. As these variables could not be controlled or generalised, the Japanese data was not pooled with the Western series for the comparative analysis.

Proponents of joint registries have been continuing their debate regarding the generalisability of results, whilst in the United Kingdom national policy makers look to restrict the use of implants. The Getting It Right First Time[210] (GIRFT) campaign is a national level campaign that aims, among other things, to improve care by identifying underperforming implants. The primary aim of this chapter was to externally validate the earlier finding of a remarkably low rate of revision surgery in young patients. There were no significant differences between the designer and non-designer centre in those aged younger than 55 at time of primary surgery (p=0.07). Though there was a trend towards a higher rate in the non-designer centres, this was still substantially lower than that reported in the joint registry. However, the recommendation is not that young patients should receive a PKR from all surgeons, but rather, in surgeons who undertake PKR in a high proportion of their patients, PKR leads to significantly lower rates of revision than

that reported in the joint registry, and is in fact in line with that observed in total knee replacement (TKR) in the joint registry[21].

Ninety-six knees underwent a revision operation from a total cohort of 2908 knees. Of these, 41 (44%) still had PKR at the end of the revision procedure. In the younger age groups, who are traditionally considered to definitely require a revision procedure this is important, as conserving the original bone stock and ligament integrity is important for normal knee function in future years. Overall, less than 2% (52/2908) were converted to TKR over the duration of the study. In the elderly, this qualitative difference in revision severity becomes even more important due to their comorbid frailty. In this study the overall revision rate in those 75+ was higher than that seen for TKR in the registry, but a third were not converted to TKR – undergoing addition of further PKRs or bearing exchanges. In this age group, fewer than 4 in 100 (20/571=3.5%) required revision, and the remaining 96% will have benefited from the quicker recovery and significantly lower morbidity and mortality relative to TKR.

This chapter has compared specialist PKR surgeons with generalised results reported in the joint registry which is not a fair comparison. However, in young patients, the TKR tend to be performed by high volume TKR surgeons. Further the variability between surgeon usage and revision rate is not as marked with TKR, as it is in PKR[72]. This chapter raises several important questions for policy makers, the most important of which is should PKR be more widely adopted given the important advantages conferred by PKR?

In conclusion, two non-designer specialist centres have shown revision rates in different age groups that are equivalent to that seen in the designer centre. Particularly with regard

to young patients, these surgeons, who perform at least 50% of their knee replacement practice as PKR, achieve revision rates that are similar or lower than that seen with TKR in the NJR.

6.5. Outcome and Age: Section discussion

This section has described the outcomes of patients undergoing partial knee replacement from designer surgeons in the United Kingdom and found good functional in all age groups examined, and a strikingly low revision rate for partial knee replacement in the younger age groups which is in line with registry reports for total knee replacement revision rates. The revision rates from the designer centre were then compared to other centres in New Zealand and in the USA where no significant difference in revision rate was identified. This provides evidence that the designer centre surgeon results can be replicated at external centres.

Younger patients represent the group with the most rapid increase in provision for knee replacement; in total they represent about 20% of knee replacements. They often have difficulties with ongoing pain, and are widely recognised as having the highest revision rate for joint replacements, which is often attributed to their higher levels of activity. Due to their longer life expectancy, it is important that operations do not cause excessive bone loss, as later joint reconstruction will require adequate bone stock for implant fixation. This section has determined that the revision rate for partial knee replacement in this age group is about 0.48 revisions per 100 component years. This roughly equates to a ten-year survival of 95%. Identifying only revisions to total knee replacement, the component

time incidence rate was 0.18, equating to a ten-year survival of 98%. The joint registry revision rate for this age group is 92%[21], and a revision of a total knee replacement more often than not requires added constraint or augments[91, 92].

Older patients make up a larger proportion of those receiving knee replacement. This group is the most likely to receive total replacement. They tend to be less active than younger patients, and there is an age-related decline in functional scores noted. They had very similar function at one and five years post operatively (mean Oxford Knee Score about 40), which dropped at the ten-year mark (mean score 37), when they would be aged a minimum of 85 years. A component time incidence rate of 0.57 revisions per 100 component years was identified across designer and non-designer centres, falling to 0.34 with TKR as the endpoint. However, it is variables not measured in this thesis that are most important to this age group, that being lower morbidity and mortality around the procedure[3].

The majority of knee replacements are performed in the 65 to 75 years at surgery group. In this age group there are competing demands, and the pros and cons will need to be weighed up on an individual basis. Their functional outcome was found to be good to excellent with mean Oxford Knee Scores of about 40 (median score at ten years was 42). The revision rate between centres did not vary significantly, and was 0.48 revisions per 100 component years. With TKR as the endpoint, it was 0.25 revisions per 100 component years. This equates to about a 95% and 98% ten-year survival respectively.

Chapter 5 explored whether revision rates observed in the designer centre were reproducible at other centres and found that they were. There were no significant

differences in any age group. The demographics between the Oxford cohorts (cemented and cementless), and the New Zealand cohort were not significantly different. The cohort from USA was significantly heavier. However, analyses performed looking at weight have not found significant differences in revision risk with different weights[211, 212] and therefore no attempt was made to control for this in these analyses.

There are limitations to these studies. Primarily, these results do not provide evidence that all surgeons can achieve these rates, but rather that the designer centre results are replicable. However, factors such as surgeon usage of PKR have been found to be related to surgeon revision rates[71-73, 213], and as established in Section 1 about half of knees are eligible for PKR. No radiographic or clinical analysis was undertaken, but revision was the primary outcome. Further morbidity and mortality was not analysed, but as these are rare results a much larger dataset would be needed and this has been performed by Liddle et al on over 100,000 patients[3].

In conclusion, the results of PKR are good to excellent in the majority of patients in each age group. The revision rates in different age groups from independent centres were no different to the design centre.

6.6. Outcome and Age: Section summary

This section has examined outcomes following partial knee replacement in different age groups.

A designer centre cohort demonstrated that excellent functional outcomes are achieved with medial PKR, with low rates of further surgery, in all age groups. Surprisingly, it was found that, even in the presence of adequate time at risk, the revision rate in the youngest age group was no higher than that in the older age groups. A result in stark contrast to the revision rates reported in all joint registries.

To validate this finding externally, Chapter 6 compared the revision rate of two other centres, one in the USA and one in New Zealand. There were no statistically significant differences in the revision rate in any age group from the designer centre cohort. Further, it was shown that only about half of revision surgery, as defined by any further surgery adding, removing, or exchanging prosthetic components, was to total knee replacement. The other half retained their partial knee replacement.

In doing so, this section has shown that designer centre bias is not present in the results, and that in these centres, the revision rate in young patients is far lower than that reported in the registries, and is actually lower than the revision rate reported for total knee replacement in the registries.

Section III: Comparisons of partial and total replacement of the knee

7. An age-stratified, matched comparison of partial and total knee replacement reporting functional outcomes and implant survival

7.1. Comparisons of PKR and TKR: Section introduction

The previous sections have established that about half of patients undergoing knee replacement could undergo a partial replacement, and that the rate of further surgery (revision) is consistent between age groups, in the hands of the designer surgeons and selected independent surgeons. In the younger age groups (<55), this rate is possibly lower than that seen with total replacement.

Knee replacement rates are increasing worldwide, and the most rapid increase in provision is in those younger than 60 years of age[10]. About half of patients undergoing knee replacement are eligible for PKR [47, 60], and younger patients are more likely to receive PKR than their elderly peers[214]. Worldwide PKR is used for less than 10% of knee replacements, with the remainder being TKR[89, 195, 215, 216]. No matched studies comparing patient reported outcomes and revision rates of PKR and TKR in different age groups were identified.

In large age standardised comparisons between PKR and TKR, PKR has been shown to have better patient reported outcomes[17, 60, 217], faster recovery[218, 219] and reduced morbidity and mortality[3, 152, 220, 221]. However, PKR are reported in national registries as having a higher revision rate [222-225]. The revision rate is, however, variable and, for example, multiple long-term series published from those using mobile-bearing medial PKR for the recommended evidence-based indications report revision rates comparable

with TKR [104, 107, 226-229]. This has been confirmed in Section II. Additionally, in comparing age groups, all national joint registries report increased revision rates in younger patient groupings, with younger patients commonly defined as younger than 55 or 60 years of age at operation[89, 195, 215, 216]. This finding is typically attributed to increased activity levels which places greater stress on the prosthesis and bone prosthesis interface which leads to revision predominantly due to loosening or implant failure.

The main indication for medial PKR is anteromedial osteoarthritis, in which there is severe arthritis with bone-on-bone medially, full thickness cartilage laterally and functionally normal ligaments [44, 52]. Based on the recommended indications about half of patients requiring knee replacement can be treated with PKR (Section II), and surgeons achieving good results tend to use PKR for at least 20% and commonly 50% of their knee replacements[73]. In contrast, most surgeons contributing to the National Joint Registry (NJR) do small numbers of PKR (the commonest number is one per year) and use PKR for less than 10% of their knee replacements, often for early arthritis, which is associated with poor results. [72, 230] Therefore, to reflect what can be achieved with PKR the assessment of lifetime risk of revision should be based on surgeons adhering to the recommended indications.

The aims of this section are to compare the functional and implant survival of partial and total knee replacement in a matched cohort, and to project the lifetime revision risk for partial and total replacement.

7.2. Chapter Introduction:

As has been established in Section II, the outcomes of PKR in different age groups are good, and as established in Section I, it is estimated that about half of knees in each age group would be eligible to receive PKR. In the setting of severe arthritis warranting a joint replacement, the alternative treatment to PKR is a TKR (see 1.3 Selection, page 7).

No previous studies exist comparing PKR and TKR in different age groups. The TOPKAT trial[66], as discussed in 1.4 Outcome (page 19), did not report age-stratified results. It has about 500 patients in total, and has recently reported 5 year outcomes. This chapter sets out to compare the long term outcomes (10 year) using two large cohorts with sufficient follow up and large numbers of patients.

The aims of this chapter are to, in different age groups, compare the Oxford Knee Score and various measures of implant survival and treatment failure between PKR and TKR.

7.3. Methods

Included were two large, separate, prospective cohorts followed for a median of ten years with baseline demographics and outcome measures (Figure 7-1). One was a series of medial PKR implanted for the recommended indications. The other was a series of TKR in which intraoperative findings were recorded so that it was possible to deduce which should have been appropriate for PKR. Patients with PKR were propensity score matched to patients with TKR that could have had PKR. Oxford Knee Score, revision rates and

'failure', which was defined as a composite of revision or reoperation or no improvement in OKS, were analysed following matching.

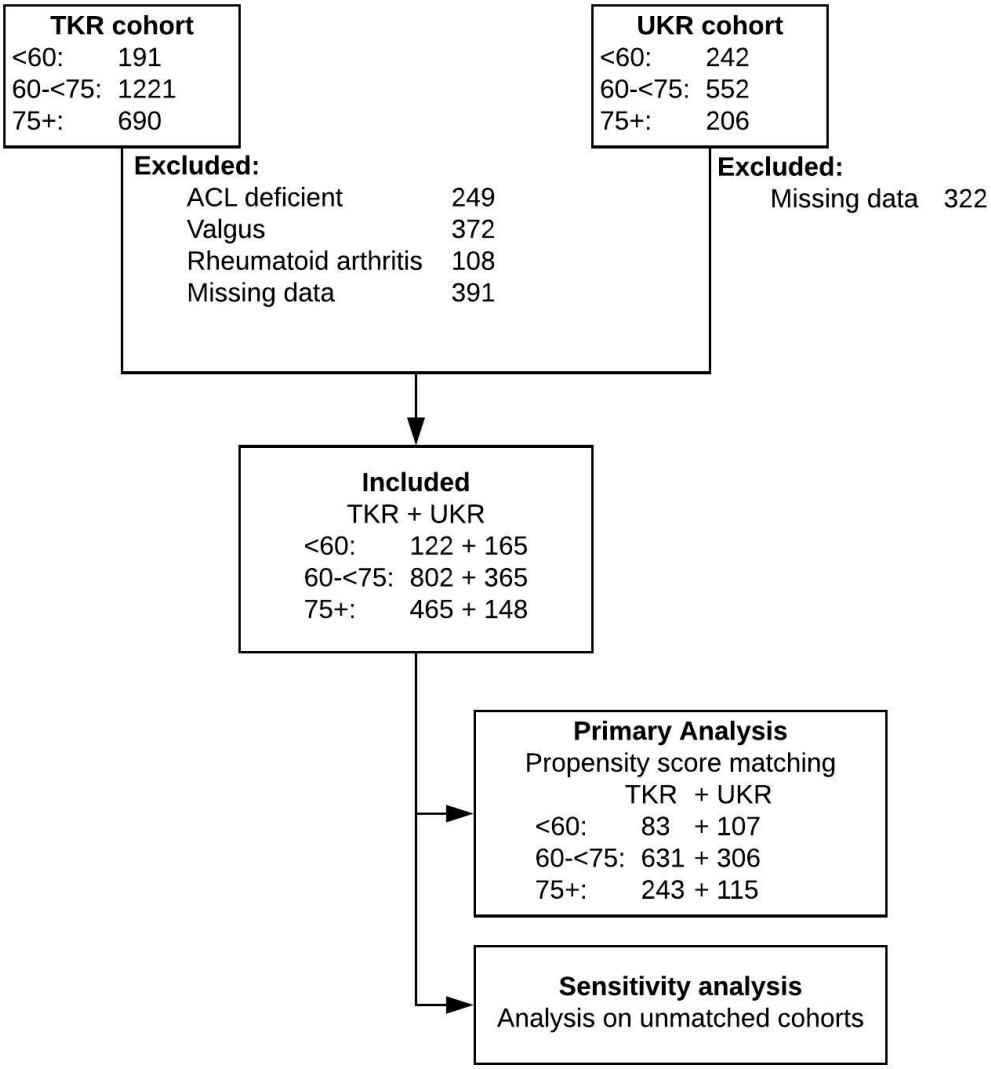


Figure 7-1 Study flow
Numbers indicate the number of knees within each age group. Missing data included any data required for matching or outcome; most commonly missing weight or preoperative Oxford Knee Score led to exclusion. TKR total knee replacement; UKR unicompartmental knee replacement.

One cohort was the Knee Arthroplasty Trial (KAT)[231]. KAT is a multicentre randomised controlled trial undertaken in the United Kingdom to prospectively evaluate different aspects of knee arthroplasty design. 2352 participants were recruited between July 1999 and January 2003. Patients received yearly postal questionnaires with the primary outcome measure being the OKS. Postal and telephone reminders were undertaken to complete data collection. Hospitals were contacted for details of readmissions. For this study, the randomisation was not taken into account, thus forming a prospective cohort. Knees with inflammatory arthritis, in valgus, or with a deficient anterior cruciate ligament were excluded so that those analysed should have been eligible for medial PKR.

The second cohort was a prospectively followed series of 1000 consecutive Phase 3 cemented Oxford medial mobile-bearing PKR (Zimmer Biomet, Warsaw, Indiana) implanted in 818 patients. Two designer surgeons performed all procedures using recommended indications, which are: anteromedial osteoarthritis[44], defined as medial compartment bone-on-bone arthritis, full thickness cartilage in the lateral compartment, and functionally intact anterior cruciate and medial collateral ligaments; and medial avascular necrosis. Patients were not excluded based on age, weight, sex, activity level, lateral compartment osteophytes, or the presence of patellofemoral cartilage loss. All knees were implanted between June 1998 and March 2009. The patients were assessed clinically at five and ten years and by postal questionnaires, with subsequent telephone follow up if required. This cohort has a median ten year follow up and the primary outcome measure was the OKS.

Knees were included providing they were eligible for medial PKR, had required variables for matching, and follow up data with information regarding revision status. Matching

was generated within age-strata by logistic regression based on patient age at surgery, patient sex, preoperative weight, preoperative OKS and length of follow up. Nearest neighbour matching without replacement was used, with a calliper of 0.2 standard deviations specified within which controls could be drawn[232]. Standardised mean differences were used to assess the success of matching (a standardised mean difference of <0.1 indicating satisfactory matching).

Mean and median OKS[177] (48 best) are the primary outcome for pain and function. The percentage of patients falling into OKS categories corresponding to excellent (>41 points), good (34 to 41), satisfactory (27 to 33) and poor (<27), the percentage not meeting minimum important change associated with the knee being "better" of nine points[233], and those with no improvement, whose final OKS was worse than their pre-op OKS, were also calculated. The percentage of possible change (POPC) in OKS was calculated by dividing the improvement by the total possible improvement[234].

Revision was defined similarly to the National Joint Registry of England, Wales, Northern Ireland and the Isle of Man[215], meaning that any component removal, addition or exchange were considered revisions. In addition amputation and periprosthetic fractures requiring open reduction and internal fixation were counted as revision. Furthermore, a major revision was defined as any further surgery requiring more than a single-stage operation with primary TKR components. A reoperation included any knee procedure requiring the administration of general or regional anaesthetic including manipulations and washouts.

Finally, a composite outcome measure was defined representing "failure of the knee replacement", which was defined as patients that had a revision or re-operation, or no improvement in OKS between pre-op and final score.

A sensitivity analysis was undertaken using all available data without matching to assess the impact of excluding patients with missing data.

Statistical analysis: Significance in OKS was tested between groups with Student's t tests and Mann-Whitney-U tests. Categorical variables were tested with a Chi-Squared test. Revision rates were determined per 100 component-years, and Kaplan-Meier implant survival estimates calculated. Significance was tested with a log-rank test. $P<0.05$ was considered statistically significant and $p<0.01$ highly statistically significant.

KAT received ethical approval from the Multicentre Research Ethics Committee for Scotland (ref: MREC/98/0/100). Ethical approval for the follow up of PKR patients was sought but deemed not required under NHS research governance arrangements.

R statistical programming software was utilised. Matching was performed with the MatchIt package.

7.4. Results:

Unmatched results:

There were differences in baseline characteristics in the unmatched data with the preoperative OKS being significantly higher in PKR, and small differences in age and weight (Table 7-1). There were substantial differences between the outcome of TKR and PKR within the different age groups (Table 7-2). PKR had significantly higher OKS scores at five and ten years in all age groups, with the biggest magnitude of difference in younger patients. At ten years the difference in median OKS, from youngest (<60) to eldest (75+), was 13, 7 and 2 (all highly significant), all in favour of PKR. Ten-year implant survival was not significantly different in the two older age groups, for those 60-75, TKR 96% and PKR 94% and in those 75+, 96% and 93%. However, in those <60 survival was significantly ($p<0.001$) better for PKR being 86% and 96% respectively (Table 7-3).

Table 7-1 Characteristics of unmatched and matched cohorts

	Unmatched				Matched		
<60	TKR	PKR	SMD		TKR	PKR	SMD
Number	122	165	NA		83	107	NA
Mean Age (SD)	55.8 (5)	54 (5)	-0.34		55.2 (4)	55.3 (3)	0.01
Mean Weight (SD)	87.2 (17)	88.2 (16)	0.06		85.6 (18)	87.3 (18)	0.09
N female (%)	53 (43%)	84 (51%)	0.15		56 (46%)	70 (43%)	-0.06
Mean preop OKS (SD)	16.4 (9)	24.1 (9)	0.82		18.5 (7)	18.6 (7)	0.01
Mean follow up (SD)	9.3 (3)	9.6 (4)	0.1		9.7 (3)	9.6 (4)	-0.02
60-<75	TKR	PKR	SMD		TKR	PKR	SMD
Number	802	365	NA		631	306	NA
Mean Age (SD)	68.3 (4)	67.5 (4)	-0.18		67.9 (4)	67.9 (4)	0.00
Mean Weight (SD)	84.4 (16)	82.7 (14)	-0.1		82.8 (15)	83.2 (16)	0.02
N female (%)	384 (48%)	200 (55%)	0.14		326 (52%)	164 (54%)	0.04
Mean Preop OKS (SD)	18.6 (7)	24.3 (9)	0.67		22.1 (7)	22.2 (8)	0.01
Mean Follow up (SD)	9.4 (3)	9.6 (3)	0.05		9.7 (3)	9.7 (3)	0.00
75+	TKR	PKR	SMD		TKR	PKR	SMD
Number	465	148	NA		243	115	NA
Mean Age (SD)	79.4 (3)	79.3 (3)	-0.06		79.2 (3)	79.4 (3)	0.06
Mean Weight (SD)	75.7 (15)	71.6 (13)	-0.32		72.9 (14)	72.6 (13)	-0.02
N female (%)	197 (42%)	67 (45%)	0.06		107 (44%)	52 (45%)	0.03
Mean Preop OKS (SD)	18.5 (7)	26.2 (8)	0.89		23.8 (7)	24 (8)	0.02
Mean Follow up (SD)	7.5 (3)	8.2 (2)	0.25		8.4 (3)	8.2 (3)	-0.06

SD standard deviation, OKS Oxford Knee Score, Preop Pre-operative, N number,
TKR total knee replacement, PKR partial knee replacement,
SMD standardised mean difference, NA not applicable

Table 7-2 Outcomes by age group and prosthesis unmatched data

	<60			60 to <75			75+		
	TKR	PKR	P value	TKR	PKR	P value	TKR	PKR	P value
Year 5 OKS									
Mean (SD)	32.9 (11)	40.7 (8)	<0.001	35.1 (10)	41.8 (7)	<0.001	33.8 (11)	40.4 (8)	<0.001
Median (IQR)	35 (25-42)	44 (37-47)	<0.001	38 (28-43)	44 (40-47)	<0.001	36 (26-43)	44 (37-46)	<0.001
POPC	51.3	69.4	<0.001	55.5	71.6	<0.001	49.9	62.4	<0.001
N Excellent OKS (%)	27 (27)	113 (63)	<0.001	213 (33)	282 (68)	<0.001	87 (32)	88 (63)	<0.001
Year 10 OKS									
Mean (SD)	31.0 (12)	40.9 (9)	<0.001	33.8 (10)	39.8 (9)	<0.001	31.6 (13)	37.1 (9)	0.002
Median (IQR)	32 (21-42)	45 (37-47)	<0.001	35 (27-43)	42 (36-47)	<0.001	36 (22-44)	38 (31-44)	0.007
POPC	44.1	70.1	<0.001	51.2	56.4	<0.001	41.5	58.3	0.05
N Excellent OKS (%)	22 (26)	76 (66)	<0.001	139 (30)	141 (54)	<0.001	33 (29)	25 (39)	0.16

Table 7-3 Revision outcomes from unmatched analysis

All revisions							
Age group	N revisions (% of cohort)		Component time incidence rate (95% confidence interval)		Ten year Kaplan-Meier survival (95% confidence interval)		
	TKR	PKR	TKR	PKR	TKR	PKR	P value
<60	18 (14%)	12 (5%)	1.52 (0.9-2.4)	0.53 (0.3-0.9)	85.5% (80-92)	95.7% (93-98)	<0.001
60-75	34 (4%)	30 (5%)	0.43 (0.3-0.6)	0.59 (0.4-0.8)	95.9% (94-97)	93.8% (91-96)	0.01
75+	16 (3%)	10 (5%)	0.44 (0.2-0.7)	0.60 (0.3-1.1)	95.9% (94-98)	93.0% (88-98)	0.30
For major revisions (defined as revision surgery requiring greater than a single stage primary TKR)							
<60	12 (9%)	0 (0%)	1.01 (0.5-1.8)	0.00 (0.0-0.2)	90.1% (85-96)	100.0% (100-100)	0.002
60-75	27 (3%)	5 (1%)	0.34 (0.2-0.5)	0.10 (0.0-0.2)	96.7% (95-98)	98.9% (98-100)	0.10
75+	10 (2%)	2 (1%)	0.27 (0.1-0.5)	0.12 (0.0-0.4)	97.3% (96-99)	99.0% (98-100)	0.40

Matched results:

One-thousand, four hundred and eighty-five patients were matched. Following matching there were no differences in baseline covariates (Table 7-1). There was significant improvement in OKS following surgery. In all age groups the OKS was better in PKR than TKR (Table 7-4, Figure 7-2): Reporting youngest group (<60) to eldest (75+); at

five years the difference in median OKS was 8, 4, and 4 (all highly significant), and at ten years it was 12, 5 and 2 (all highly significant except 75+).

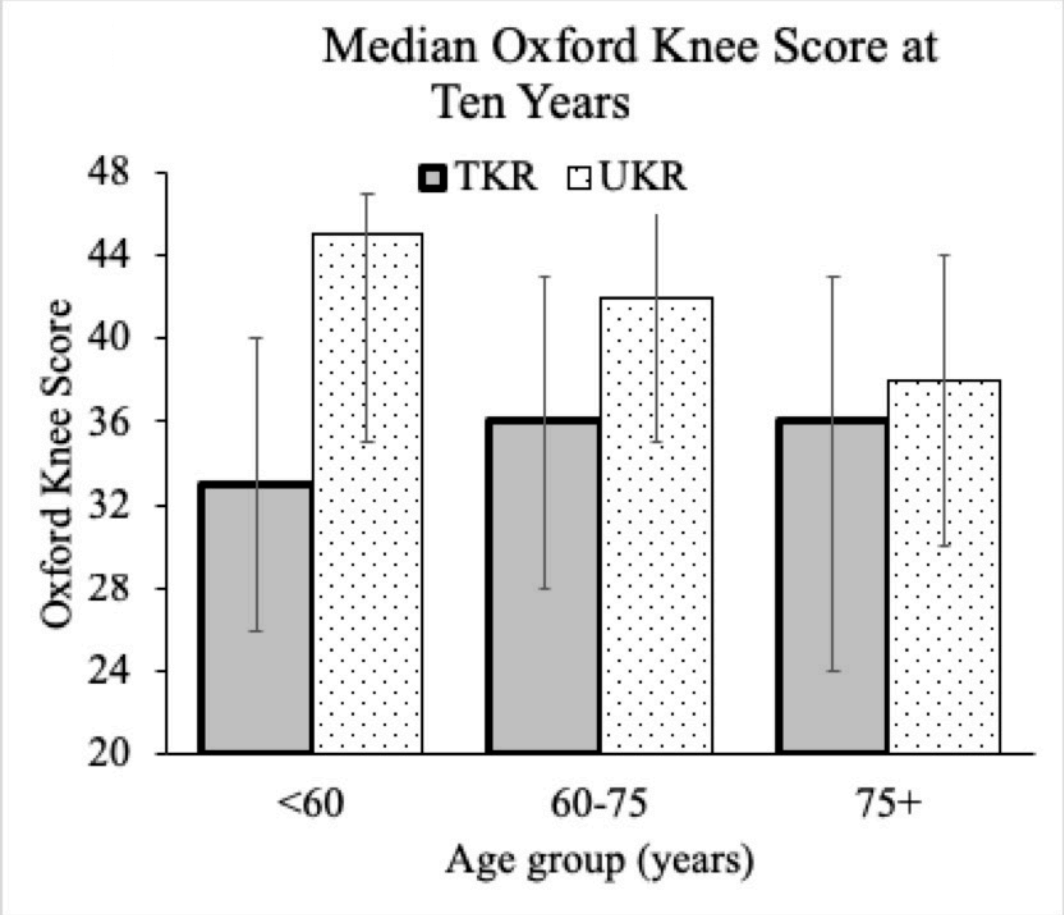


Figure 7-2 Oxford Knee Score by age and prosthesis
Median Oxford Knee Score and interquartile range at ten years by age group and prosthesis.

Table 7-4 Oxford Knee Score by age group and prosthesis

Table 2: Oxford Knee Score Outcomes by age group and prosthesis										
Age	<60				60-<75				75+	
	TKR	PKR	P value		TKR	PKR	P value		TKR	PKR	P value
Year 5 OKS										
Mean (SD)	34.8 (10)	39.8 (10)	<0.01		36.2 (10)	41.2 (7)	<0.001		35.4 (10)	39.6 (8)	<0.001
Median (IQR)	36 (29-42)	44 (36-47)	<0.001		39 (30-44)	43 (39-46)	<0.001		38 (28-44)	42 (35-46)	<0.01
POPC (IQR)	52.9% (39-79)	83.9% (62-94)	<0.001		65.8% (37-83)	81.8% (64-92)	<0.001		59.2% (27-86)	75.6% (50-91)	<0.01
N Excellent OKS (%)	19 (30%)	51 (63%)	<0.001		199 (38%)	159 (65%)	<0.001		70 (40%)	44 (54%)	0.04
Year 10 OKS										
Mean (SD)	32.4 (11)	39.6 (10)	<0.001		34.8 (10)	39.0 (9)	<0.001		32.9 (11)	35.5 (11)	0.25
Median (IQR)	33 (26-41)	45 (34-47)	<0.001		37 (28-43)	42 (35-46)	<0.001		36 (25-43)	38 (30-44)	0.24
POPC (IQR)	51.5% (27-75)	88.0% (62-96)	<0.001		59.5% (29-81)	75.4% (52-91)	<0.001		46.2% (16-77)	61.4% (28-86)	0.12
N Excellent OKS (%)	12 (21%)	37 (63%)	<0.001		127 (33%)	79 (52%)	<0.001		21 (27%)	11 (34%)	0.46
N number, OKS Oxford Knee Score, POPC Percentage of possible change of OKS, SD standard deviation, IQR interquartile range, TKR Total Knee Replacement, PKR Partial Knee Replacement											

Ten-year implant survival was lower with TKR than PKR for those <60 (89% v 94%) and higher in the two older age groups (60-<75 96% vs 95%, 75+ 96% vs 90%; none significant; Table 7-5, Table 7-6, Table 7-7, and Figure 7-3). Ten-year survival with major revision as the end-point (those requiring more than single stage operations with primary TKR components) was significantly lower with TKR than PKR in all age groups. Ten-year survival with revision/reoperation as the endpoint was lower with TKR in those <60 and 60-75, and higher in those 75+ (none significant).

Table 7-5 Revision outcome by age group

All revisions							
Age group	N revisions (% of cohort)		Component time incidence rate (95% confidence interval)		Ten year Kaplan-Meier survival (95% confidence interval)		
	TKR	PKR	TKR	PKR	TKR	PKR	P value
Reoperation (any knee procedure requiring general or regional anaesthetic)							
<60	15 (18%)	13 (12%)	2.02 (1.1-3.3)	1.30 (0.7-2.2)	81.7 (74-91)	89.5 (84-96)	0.25
60-75	58 (9%)	21 (7%)	1.00 (0.8-1.3)	0.72 (0.4-1.1)	90.6 (88-93)	92.5 (89-96)	0.19
75+	13 (5%)	9 (8%)	0.67 (0.4-1.1)	0.98 (0.4-1.9)	93.9 (91-97)	88.6 (81-97)	0.36
Revision (subset requiring implant addition, exchange, removal, amputation or ORIF of periprosthetic fracture)							
<60	9 (11%)	8 (7%)	1.12 (0.5-2.1)	0.77 (0.3-1.5)	88.9 (82-96)	92.7 (88-98)	0.54
60-75	29 (5%)	14 (5%)	0.48 (0.3-0.7)	0.47 (0.3-0.8)	95.3 (94-97)	94.8 (92-98)	0.95
75+	11 (5%)	7 (6%)	0.56 (0.3-1.0)	0.74 (0.3-1.5)	94.7 (92-98)	90.4 (83-98)	0.52
Major revision (subset requiring greater than a single stage primary TKR, or amputation)							
<60	7 (8%)	0 (0%)	0.87 (0.3-1.8)	0.00 (0.0-0.4)	91.4 (85-98)	100.0 (100-100)	0.003
60-75	24 (4%)	1 (0%)	0.40 (0.3-0.6)	0.03 (0.0-0.2)	96.1 (95-98)	99.4 (98-100)	0.004
75+	8 (3%)	0 (0%)	0.41 (0.2-0.8)	0.00 (0.0-0.4)	96.1 (93-99)	100.0 (100-100)	0.05

Table 7-6 Revision indication and procedure by age group and prosthesis

Age group	TKR	PKR
<60	Infection (two stage) x3 Loosening (revision) x2 Pain (patellar resurfacing) x2 Dislocation (unspecified revision) Pain (unspecified revision)	Disease progression (primary TKR) x3 Pain (primary TKR) x2 Disease progression (lateral PKR) Dislocated bearing (bearing exchange and femoral component revision)
60-75	Loosening x 12 Infection (two stage) x 4 Bearing dislocation (unspecified revision) Pain (patellar resurfacing) Instability (unspecified revision) Pain (unspecified) Malalignment (unspecified revision) Stiffness (unspecified revision) Patella revision (failed patella resurfacing x 1, loose patella x 1)	Disease progression (primary TKR) x 4 Disease progression (lateral PKR) x 3 Bearing exchange (dislocation) x 2 Pain (primary TKR) x 2 Instability (hinged TKR) Unknown (primary TKR)
75+	Infection (two stage) x 3 Loosening x 3 Pain (patellar resurfacing) x 3 Unspecified indication (Above knee amputation)	Disease progression (primary TKR) x 3 Disease progression (lateral PKR) x 2 Tibial loosening (primary TKR) Pain (primary TKR)

Table 7-7 List of reoperations by age group and prosthesis

Age group	TKR	PKR
<60	Washout (wound dehiscence) x 2 Washout (infection) x 2 MUA (Stiffness) x 3	Arthroscopy (pain) x 2 Arthroscopy and washout (Pain – performed elsewhere) Arthroscopy, and debridement (unspecified) x 2 MUA (Stiffness)
60-75	Arthroscopy (pain) x 2 Arthroscopy and biopsy (suspected infection) x2 Change of poly (dislocation x 1, infection x 1, prosthetic complication x 1) Debridement (infection) x 5 Debridement, exploration and washout (infection) x 1 EUA (stiffness x 1) EUA and arthroscopy (diagnostic op) x 1 Excision of bone fragment x 1 Excision of lateral patella x 1 MUA (stiffness) x 17 Patella resurfacing (pain) x 1 Washout (infection) x 4	Arthroscopy x 5 Arthroscopy and washout x 1 MUA x 7
75+	Washout (infection) x 2 Washout and debridement (infection) MUA (stiffness) x 2 Debridement (infection)	MUA (Stiffness) x 2
EUA examination under anaesthetic; MUA manipulation under anaesthetic; TKR total knee replacement; PKR partial knee replacement;		

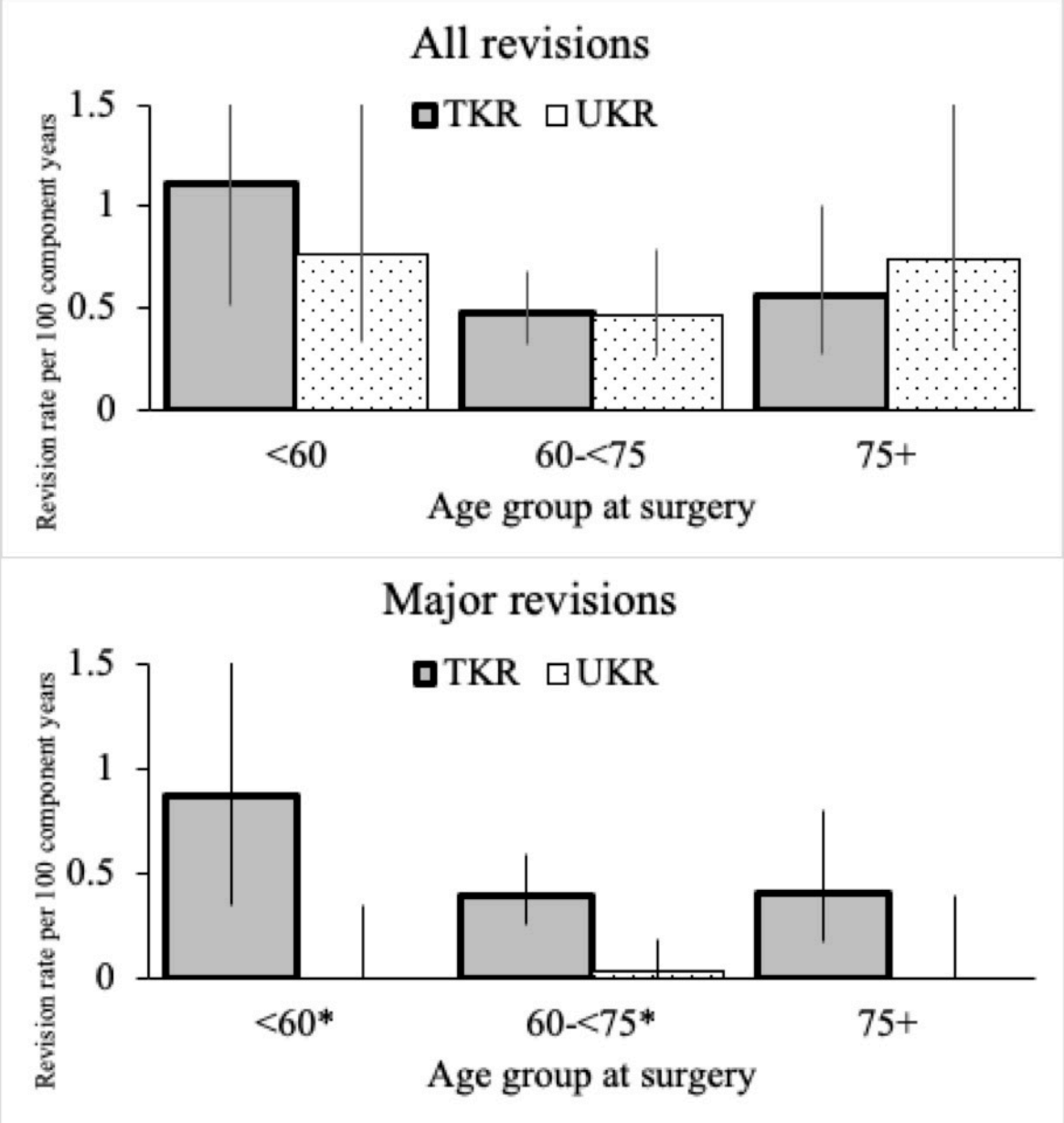


Figure 7-3 Revision rate by age, prosthesis, and revision severity
Comparison of revisions by age group, prosthesis type and extent of revision required. Star (*) indicates significant difference ($p<0.05$). Line represents 95% confidence interval. Major revision defined as any operation undertaking more complex than a single stage primary TKR or amputation. NB: As matching was generated within age strata, estimates cannot compare between age groups, but rather only between prostheses within each age group.

For the composite outcome measure of revision/re-operation or no improvement in OKS the failure rate of TKR in <60 was 8% higher, in 60-75 was 5% higher, in >75 was 4%

higher (none significant) and in all age groups combined was 5% higher (p=0.02; Figure 7-4).

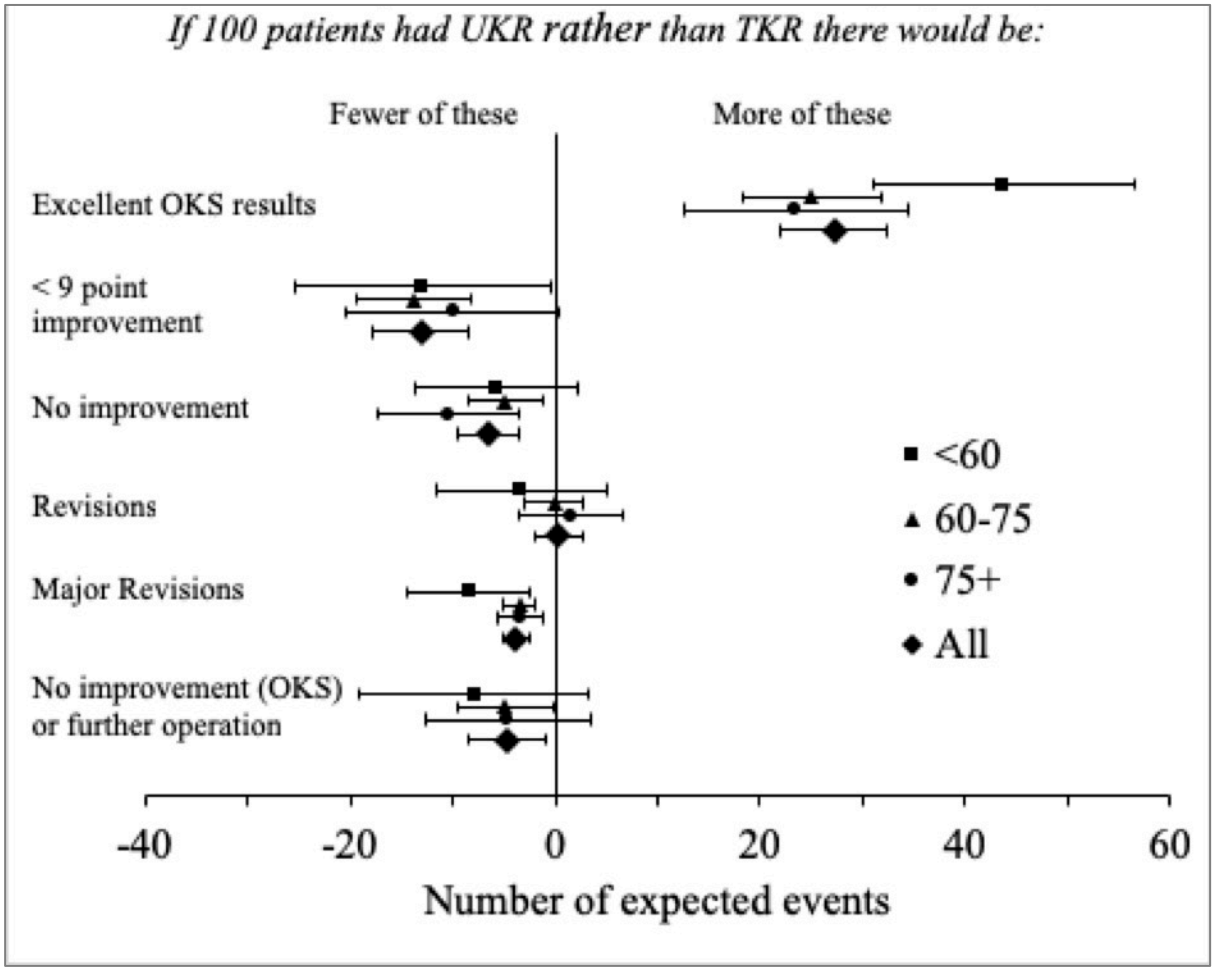


Figure 7-4 Differences between TKR and PKR adverse event rates
Comparison of incidence rate difference by age group. Rate is per 100 patient years. Point estimate and 95% confidence interval provided. OKS Oxford Knee Score, Major Revision defined as any operation with greater than a single stage primary TKR or amputation.

The sensitivity analysis revealed no major deviations in results from those presented suggesting the matching and analysis was a valid interpretation of the data.

Table 7-8 Revision indication and outcome by age group and prosthesis unmatched

Age group	TKR	PKR
<60	Patellar dislocation Two stage revision (infection) x 6 Loosening x 4 Patellar resurfacing x 5 Pain (unspecified) x 2	Primary TKR (ACL injury) Bearing exchange (dislocation x 3) Bearing exchange and femoral component revision (bearing dislocation) Disease progression (primary TKR) x 4 Disease progression (lateral PKR) x 1 Two stage primary TKR x 1 Tibial component revision (malposition) x 1
60-75	Dislocation Two stage revision (infection) x 7 Instability x 3 Loosening x 14 Malalignment Patella resurfacing x6 Unspecified (pain) x 1 Unspecified x 1	Primary TKR (loosening) Primary TKR (AVN Lateral femoral condyle) Bearing exchange (dislocation) x 2 Lateral PKR (disease progression) x 7 Primary TKR (disease progression) x 9 Two stage primary TKR (infection) x 1 Two stage TKR with stemmed tibia (infection) x 1 Hinged TKR (instability) x 1 Primary TKR (unexplained pain) x 6 Primary TKR (Unknown -revised overseas)
75+	Two stage revision (infection) x 4 Loosening x 7 Patellar resurfacing x 5	Loosening (primary TKR) x 1 Bearing dislocation (exchange) x 1 Disease progression (primary TKR) x 3 Disease progression (lateral PKR) x 3 Infection (two stage primary TKR) x 1 Infection (two-stage TKR with stemmed tibia) Pain (primary TKR) x 1

7.5. Discussion:

When considering relative merits of different types of knee replacement, it is important to match patients and to consider not only how good the functional outcome and pain relief is but also the failure rate. In this study PKR provided better outcome scores than TKR in all age groups, with the difference being particularly marked in young patients. Traditionally failure of a joint replacement has been considered as revision. There were

no significant differences in revision rate. However, if failure is defined in a way more relevant to patients, for example if there is no improvement in symptoms or further surgery is required, then in all age groups PKR had a lower failure rate than TKR. This was statistically significant when all age groups were combined. This study therefore supports the use of PKR, when appropriate, although the relative merits are different in different age groups (Figure 4).

Most knee replacements are done in patients between the age of 60 and 75[235]. In this age group the OKS was appreciably better (five points, $p<0.001$) with PKR than TKR. Furthermore about 30% ($p<0.001$) more PKR patients achieved excellent outcomes and 5% ($p=0.005$) fewer had no improvement in OKS compared to pre-op. The revision rate was slightly higher with PKR (5.2% v 4.6%; NS). However, the major revision rate (0.6% v 3.1%, $p<0.01$) and reoperation/revision rate (7.1% v 9.3%, NS) was lower with PKR. The composite failure of worse outcome than pre-operation or further surgery occurred less frequently with PKR than TKR (13% v 18%, $p=0.02$).

In the elderly (>75) the OKS was better after PKR (5yr difference 4 points, $p<0.01$, 10yr difference 2 points, NS). By ten years the average age would be about 90 and due to increasing frailty this is not surprising. Over the whole study period 6% ($p=0.01$) less PKR patients had no improvement in OKS compared to pre-op. The revision rate was higher with PKR (4.5% v 6.4%, NS). However, the major revision, revision/reoperation rate and composite failure of worse than pre-op or reoperation were lower with PKR.

In younger patients (<60) every outcome favoured PKR. At ten years the OKS was markedly better (12 points, $p<0.001$) and 37% ($p<0.001$) more patients achieved

excellent outcomes. The major revision rate, the revision rate and the reoperation/revision rate were lower (p=0.003, p=0.54, p=0.25). In addition, the composite failure of worse OKS than pre-op or revision/reoperation was lower (p=0.23).

The most surprising finding was that in young patients the survival of PKR was not worse than TKR. Although it was better, the difference was not significant. However, this may have been because the numbers were small as in the non-matched data the revision rate was significantly better. Several factors may contribute to this. Firstly the PKR were done for bone-on-bone arthritis, in whom PKR are known to do well[17, 47, 52, 107, 108]. However in young patients PKR is often used for early arthritis, without bone-on-bone and in this situation it is unreliable and has a high revision rate[123, 124]. This likely contributes to the high revision rate seen in registries. Secondly in young active patients TKR tend to be revised because the implant or fixation fail due to higher stresses on the implant. With PKR, due to the mobile bearing the implant is unlikely to fail[236, 237], and because the retained cartilage and bone are strong in the young there disease progression or loosening is unlikely. It was also surprising that the function of PKR in the young was so much better with PKR than TKR. This may be because knee kinematics are virtually normal after PKR whereas it is abnormal after TKR[185, 238].

Revision is the generally accepted definition of failure as this is the data national registries collect. There are a number of problems with this. One, highlighted by the study, is amputation. One patient with a failed TKR had an amputation (Table 4). This would not have been reported to a register so would not be considered a revision despite being a catastrophic outcome; for this study however it was considered a revision. Furthermore, TKR revisions tend to be more major undertakings with worse outcomes than after

PKR[91, 239], which makes a comparison based on revision alone inappropriate. Major revision was therefore analysed separately. Finally, patients are probably more concerned about symptom relief than revision. They would, for example, consider an excellent outcome after a revision to be a success, whereas a register would consider this a failure. Conversely, a patient would consider an implant that did not help their symptoms and was not revised to be a failure whereas a register would consider it a success. To address this, the proportion of patients who are worse post-operatively than pre-operatively was determined and a composite outcome measure introduced in which failure is either no improvement post-operatively or a re-operation/revision.

The main strengths of this study are that the PKR were used for the recommended indications[44, 47, 52] and were matched to TKR that were done in knees with a disease pattern appropriate for PKR. The numbers were relatively large, the data quality was good, and the median follow up was 10 years. As such it probably represents one of the best comparisons that exist between PKR and TKR. As there is nothing similar in the literature, it is difficult to compare with other studies. However, an age dependent analysis found higher satisfaction with PKR than TKR in patients under 55 years of age[151]. Studies based on National Joint Registries have shown much higher revision rates with PKR then TKR and slightly better OKS with PKR[17, 89, 195, 215, 216, 240]. These findings are different probably because many PKR were implanted for early arthritis[50].

The main weakness is that PKR were implanted by two designer surgeons who did large numbers of PKR, whereas multiple surgeons implanted the TKR. The study may therefore not be generalisable. However the TKR cohort was from a randomised trial that found minimal differences between different designs of knee replacement so probably do

reflect the typical results of TKR[231]. There are now multiple published series showing that if surgeons using Oxford PKR adhere to recommended indications they achieve similar ten-year results to the designer surgeons[107-109, 194, 241-243]. Therefore, providing the recommended indications for PKR are used the results are likely to be generalisable. The recommended indications are satisfied in about half of patients requiring knee replacements[47, 60] and the evidence suggests that to get good results surgeons should use PKR for at least 20% and ideally up to 50% of knee replacements[194, 213, 244]. Furthermore, even if the designer surgeons obtain better results this would affect all age groups equally, and would not account for the trend of better outcomes in younger patients. It is not certain that all TKR included in the matching would have been appropriate for PKR as there was not good data on co-morbidities, or the degree of lateral wear and matching could not be performed on these. Further, it is unknown if these results are transferable to fixed bearing PKR. Finally, both cohorts were observational and there was no randomisation. Whilst matching was performed on the data available, it is unlikely that all confounding factors have been controlled for, and the need for a rigorous, well-designed controlled trial remains on this important topic.

In conclusion, when all age groups were combined, PKR provided better functional outcomes with more excellent results and fewer cases in which the post-operative score was less than preoperative. Although there was no significant difference in revision rate PKR did have significantly fewer major revisions and reoperations/revisions. Also, PKR had significantly less failures, defined as no improvement in outcome or revision/reoperation. Similar trends were seen within each age group, with PKR being particularly favourable in young patients. This study therefore suggests, providing the

recommended indications are applied, PKR should be used when indicated in all age groups.

8. Lifetime revision risk of partial knee replacement[3]

8.1. Introduction

Clear communication of risks and benefits of proposed interventions are required for patients to make educated decisions, and to provide informed consent. Patients tend to have difficulty interpreting revision rates. The chance of having a revision during their lifetime is a simpler notion that is preferred by patients when communicating risk [245]. Lifetime revision risk can be expected to be highly dependent on an individual's age at surgery, and lifetime risk of revision at different ages has been estimated for total knee replacement (TKR) but not for partial knee replacement (PKR). About half of patients needing knee replacement can potentially be treated with either TKR or PKR (Section I), and the decision as to which is most appropriate depends, in part, on revision rates. For patients to decide whether to have a PKR or TKR it would therefore be helpful for them to know their lifetime risk of having a revision if they had a PKR.

In the absence of a large series of PKR followed up until all patients have died, lifetime risk of revision can be calculated based on annual revision rates and death rates in different age groups. Death rates can be determined from national statistics. Annual revision rates should be based on data from well documented patient series. However, these tend to be of limited duration so long-term predictions are required, which can be done with parametric survival models. There are different models that may give higher

[3] This chapter has been accepted for publication: Kennedy JA, Burn E, Mohammad HR, Mellon SJ, Judge A, Murray DW. Lifetime revision risk for medial unicompartmental knee replacement decreases with older age at intervention. Knee Surg Sports Traumatol Arthrosc [accepted 14 Jan 2020].

or lower long-term revision rates. It is therefore useful to use a number of different models to assess the accuracy of the long-term predictions.

To help inform patients, surgeons, and health providers, the aim of this chapter was to estimate lifetime revision risk for patients of different ages undergoing PKR.

8.2. Methods

A state-based Markov model (Figure 8-1) was constructed with transition probabilities for revision informed from a large cohort of consecutive PKR and transition probabilities for mortality informed from the United Kingdom Office for National Statistics. This model was used to estimate the percentage of patients that would be revised over the course of their lifetime. As a secondary analysis, assumptions that revision risk would reduce after 90 years of age were tested, and revision rate from the NJR was tested.

Between June 1998 and March 2009, 1000 consecutive medial Oxford PKRs were carried out through a minimally invasive approach in 818 patients by two surgeons (Mr C. Dodd, and Professor D. Murray) who were involved with the design of the prosthesis. All patients met the recommended indications as described by Goodfellow et al [175]. The pathological diagnosis was bone–on-bone anteromedial osteoarthritis with functionally intact ligaments in 977 knees and spontaneous osteonecrosis of the knee in 23. The mean follow up of this cohort is 10 years (range 5 to 17). This patient series has previously been reported in detail [104] and was discussed in Chapter 4.

Patients were followed up by research physiotherapists independent of the surgical and clinical teams involved in the care of the patients. Patients were assessed pre-operatively and at one, five, seven, ten, twelve and fifteen years post-operatively. All patients were contacted to ascertain the incidence of revisions. Revision was defined in the same manner as the National Joint Registry [224], as component removal, exchange or addition. It therefore included insertion of a new bearing for bearing dislocation or washout, addition of a lateral PKR for disease progression or conversion to a total knee replacement (TKR). If a patient had died, information about the status of their knee and any further operation was obtained from primary and secondary care records, and from the patient's relatives where appropriate.

Statistical analysis: To extrapolate revision risk, a multi-state Markov model was constructed with three health states: 'unrevised', 'revised', and 'dead' (Figure 1)[246]. Individuals began as unrevised and then remained so until death or until revised. Such a model reflects the competing risk nature of revision. Transition probabilities to 'revised' were informed from parametric regression models fitted to the cohort revision data. A number of alternative distributions for parametric models were fitted separately, these were exponential, Gompertz, Weibull, log normal, log logistic and generalised gamma distribution. The different models allow the revision risk to increase, decrease, or stay the same over time. Akaike's information criterion[247] (AIC) was calculated for each model as an estimator of the relative quality of each model. The AIC estimates the trade-off between information lost from modelling data, and the number of assumptions introduced to the model. In other words, it provides information regarding the risk of overfitting and underfitting. It is used to compare models for the same data, with a lower number suggesting a higher quality model. Transition probabilities to death were informed from

the Office for National Statistics (ONS) National Life Tables [22]. Subjects entered the model at the age of interest following their PKR. Each year, subjects could remain in their current health state, or transition to a new health state. Each of these transitions is represented by arrows in Figure 1, and had a defined probability of occurring. The simulation was run separately for a cohort of 1000 patients for each age of interest. Confidence intervals were calculated via bootstrapping, with 250 estimations.

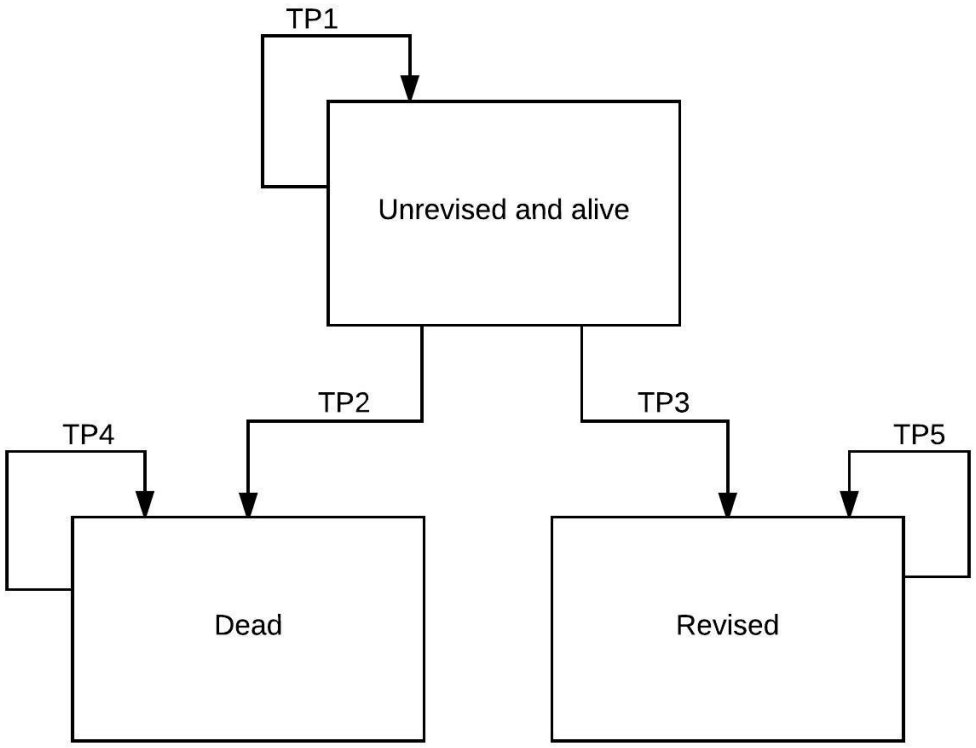


Figure 8-1 Schematic of Markov Model

Because of uncertainties about the generalisability of this study, as well as the regression models themselves, a sensitivity analysis was performed to assess their effects on the results. The first analysis was to examine the lifetime risk from the NJR report for mobile bearing PKR. The second analysis tested an assumption that elderly patients are less likely to be offered revision due to comorbidities. For this, an age of 90 was arbitrarily chosen beyond which the risk of revision was halved. For this analysis, revision risk was modelled with an exponential model as this had the best fit to the data. The model selection was validated by estimating incidence rate per 100 component years from ten years' worth of predictions, which would allow us to compare to observed values from the cohort.

Four knees in three patients could not be traced, and their final status remains unknown. They were excluded from further analysis. There were no missing values for age at surgery or sex. Statistical analyses were performed in R [248] using the survHE package [249].

8.3. Results

The mean age of the cohort was 66.6 years (SD 9.6 years, range 33-88), and mean follow up 10.3 years (range 5 to 17; Table 1). There were 52 revisions, occurring at a mean age of 66.3 years (SD 8, range 49 to 80) and mean follow up of 5.6 years (SD 4 range 2 months to 15 years). Twelve of these revisions occurred in patients younger than 60 at intervention. The ten-year survival was 94% (452 at risk, 95% CI 92 to 96), and the fifteen-year survival 91% (55 at risk, 95% CI 83 to 98).

Table 8-1 Cohort demographics for 1000 designer centre PKR

N	1000
N revisions	52
Age breakdown: N <60 (%) N 60 to <75 (%) N 75+ (%)	 242 (24%) 552 (55%) 206 (21%)
Mean body mass index (SD)	28.5 (5)
N female (%)	487 (49%)
Mean follow up in years (range)	10.3 (5 to 17)
N number, SD standard deviation	

The exponential model had the best fit for estimation of revision probability (AIC 642.8), when compared with the Gompertz (AIC 644.0), Weibull (AIC 644.5), log logistic (AIC 644.7), log normal (AIC 645.7), and generalised gamma (AIC 646.4) models. The exponential model predicted similar component time incidence rates to that observed in the Oxford cohort (Figure 8-2). Therefore, the exponential model was used for the main analysis.

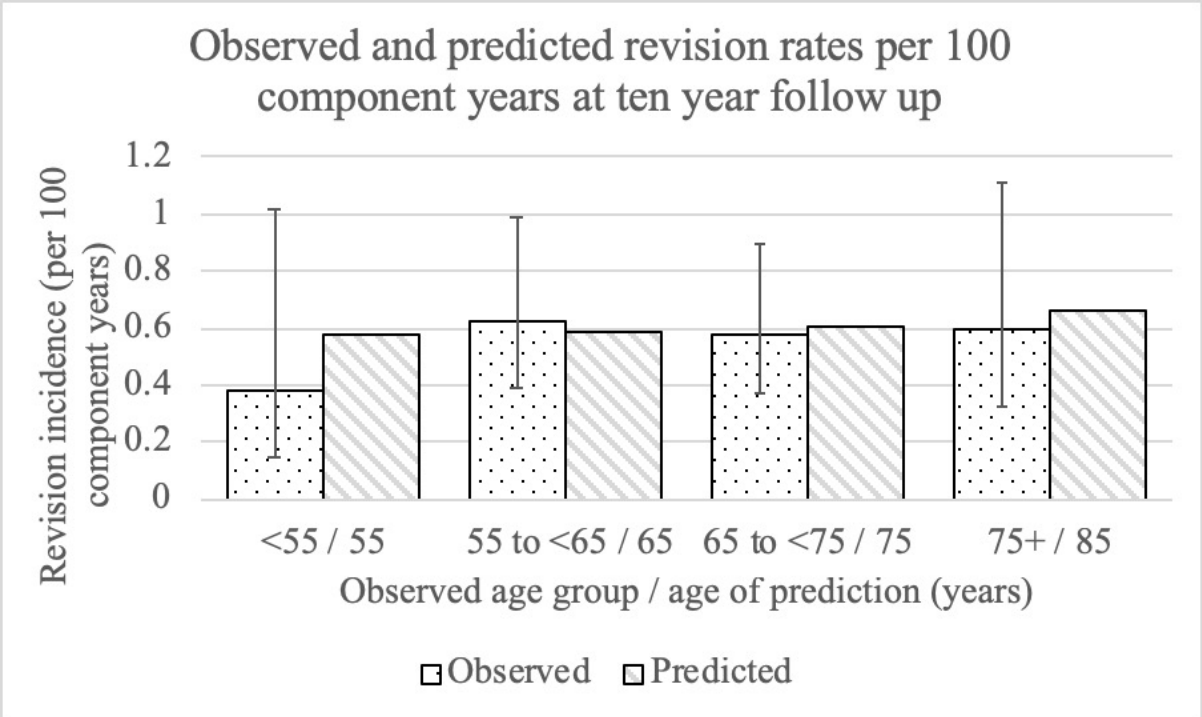


Figure 8-2 Observed and predicted revision rates per 100 component years at ten year follow up
Component time incidence rates after a ten-year simulation to match the mean ten-year observed follow up of this cohort was predicted. Predictions were very similar to observed rates.

The estimated lifetime revision risk increases with younger age at operation (Table 2, Figure 3). The possible outcomes in the years following surgery are shown in Figure 4. Point estimates for lifetime revision risk from the exponential model were 15% (95% CI 12-19), 11% (8-13), 7% (5-9) and 4% (3-5) for those aged 55, 65, 75 and 85 years at operation respectively. The uncertainty around long-term predictions are reflected in the large confidence intervals in younger patients, which decrease with older age. The different models produced differing estimates (Table 2). The variability between model point estimates from age 55 to 85 respectively was 10% (12-22), 4.5% (10-14), 1.2% (7-8), and 0.1% (3.7-3.8%).

Table 8-2 Lifetime revision risk point estimates from different models (95% confidence interval)

Model	Age at PKR			
	55	65	75	85
Exponential*	14.9% (12 to 19%)	10.7% (8 to 13%)	6.8% (5 to 9%)	3.7% (3 to 5%)
Gompertz	22.5% (11 to 55%)	14.1% (8 to 28%)	7.8% (5 to 13%)	3.8% (3 to 5%)
Weibull	16.2% (12 to 24%)	11.5% (9 to 17%)	7.1% (6 to 11%)	3.8% (3 to 5%)
Log logistic	15.5% (11 to 26%)	11.1% (8 to 17%)	7.0% (5 to 10%)	3.8% (3 to 5%)
Log Normal	12.5% (10 to 19%)	9.6% (7 to 14%)	6.6% (5 to 10%)	3.8% (3 to 5%)
Generalised Gamma	16.0% (12 to 24%)	11.4% (9 to 18%)	7.1% (6 to 10%)	3.8% (3 to 5%)
*The Exponential distribution was used for the base-case analysis PKR partial knee replacement				

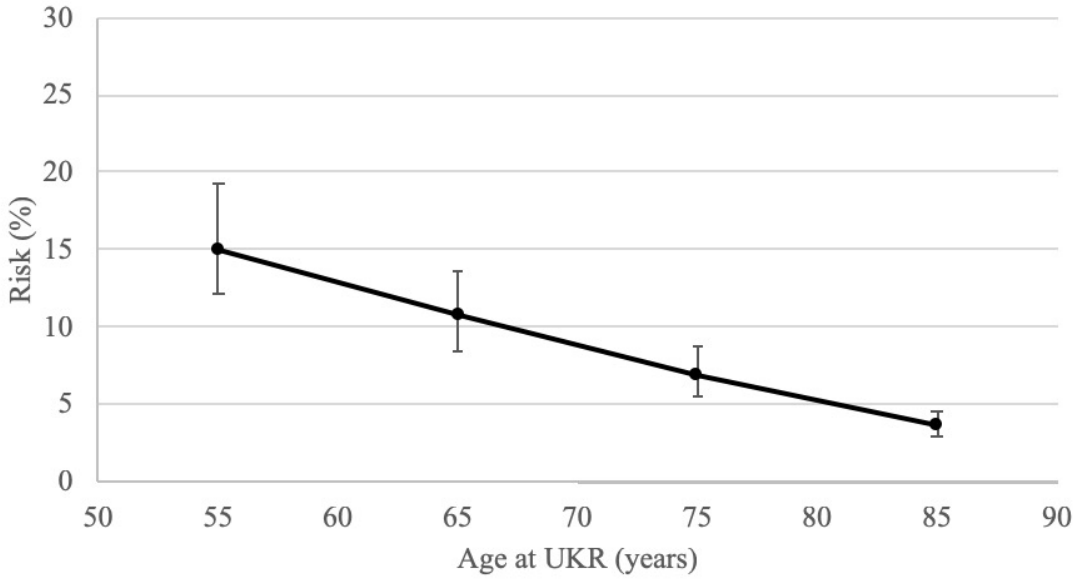


Figure 8-3 Estimated lifetime revision risk with 95% confidence intervals

The sensitivity analyses had the following results: Halving the revision rate from 90 years of age led to estimates of 15%, 10%, 6% and 3% respectively. Increasing the revision rate to that seen in the NJR increased the lifetime revision risk to 25%, 16%, 8% and 3% for those 55, 65, 75 and 85 years at operation respectively.

8.4. Discussion

The risk of revision in a patient's lifetime is low. As would be expected, higher rates were found in younger patients. The youngest modelled patient age was 55, and patients of this age were found to have a lifetime revision risk of 15% (12 to 19). This reduced to a lifetime risk of 4% (3 to 5) for those of 85 years of age at operation. Surgeons and patients will find these results encouraging, as it is widely expected that patients younger than 60 at operation will almost certainly require revision surgery in their lifetime. The graphs shown in Figure 4 highlight the various states that the patients may be as time passes following the surgery, and demonstrate, even in the young how low the risk of revision actually is.

Communication of risk has become increasingly important in patient-centred medicine [245]. As part of the consent process risks and benefits of intervention must be clearly communicated, and there is reasonable evidence to suggest that 5 or 10-year revision risks are difficult for patients to interpret. The James Lind Alliance Priority Setting Partnership, a public-patient involvement group, highlighted that the relationship between timing of joint replacement and best outcome is of great importance to patients[250]. This is a particular concern for young patients, as they are widely expected to

outlive their primary joint replacement. Thus, if and when revision surgery may occur, becomes a major factor in deciding whether to proceed with surgery. Lifetime revision risk estimates are one way of quantifying the likelihood that they will outlive their prosthesis.

Lifetime revision risk has not previously been estimated for PKR. Burn and colleagues [251] recently looked at 10,000 total knee replacements; and using similar predictive modelling techniques predicted for patients of 50 years of age a 34% lifetime risk of revision, dropping to about 3% for those undergoing TKR at age 80. Further, Evans and colleagues [252] undertook a long term analysis, albeit without age stratification, and using data predominantly from the Finnish arthroplasty registry concluded that the 25 year revision rate was about 18% for TKR, and 30% for PKR. Bayliss et al [253] published detailed lifetime risk estimates for TKR, using different methodology, based on a dataset of over 50,000 patients with a mean follow up of five years. Like this study, they found that lifetime risk reduces with increasing age and in older patients the lifetime risk of revision was similar with PKR and TKR. Their data would suggest that at age 55 the lifetime risk of revision was about 20% for women and 35% for men. This study found no significant difference between men and women, and found that at 55 the PKR had a lifetime risk of revision of about 15%. This suggests that, providing the PKR is used appropriately, in young women the lifetime risk of revision is similar in PKR and TKR, whereas in young men the lifetime risk may actually be less in PKR. Even if the life time risk of PKR and TKR were similar PKR would be advantageous because revision is simpler and is usually a conversion to a TKR [115]. Furthermore PKR provide better PROMs [17], lower morbidity and mortality [3] and a faster recovery[143].

Young age is considered to increase the risk of revision as their relatively higher activity levels place increased mechanical loads and wear on the implant and bone-implant interface. In this context, when compared to TKR, medial Oxford PKR has theoretical reasons for reducing the revision rate. The fully congruent bearing has low contact stresses so should minimise wear [158, 159], and transmits predominately compressive forces to the bone-implant interfaces so should minimise loosening [160]. Furthermore, the instrumentation aims to restore ligament tension and function [160], thereby restoring normal knee kinematics [185]. In the observed cohort, the youngest patients have the lowest risk of revision due to disease progression [254]. Although this may seem counterintuitive, it suggests that younger patients may have better quality retained cartilage and bone, and are less likely to fail from lateral osteoarthritis or aseptic loosening, which represent the two main modes of PKR failure. These factors all tend to decrease the revision rate of PKR compared to TKR resulting in a similar lifetime risk of revision.

Many surgeons feel TKR is the best procedure in the elderly, as TKR will not require a revision whereas PKR may. However, as the life expectancy is relatively shorter in the elderly the lifetime risk of a revision of a PKR is very low (Figure 4), so other factors need to be considered. In the elderly the rapid recovery, and lower incidence of major medical complications and death are major advantages of PKR [3, 255]. In a matched study of over 100 000 knee replacements, it has been shown that in the first three months following surgery the risk of death is about 50% less with PKR compared to TKR, and out to 4 years it is about 25% less [3]. Therefore, the decreased risk of medical complications and death almost certainly will outweigh the slight increased lifetime risk of revision.

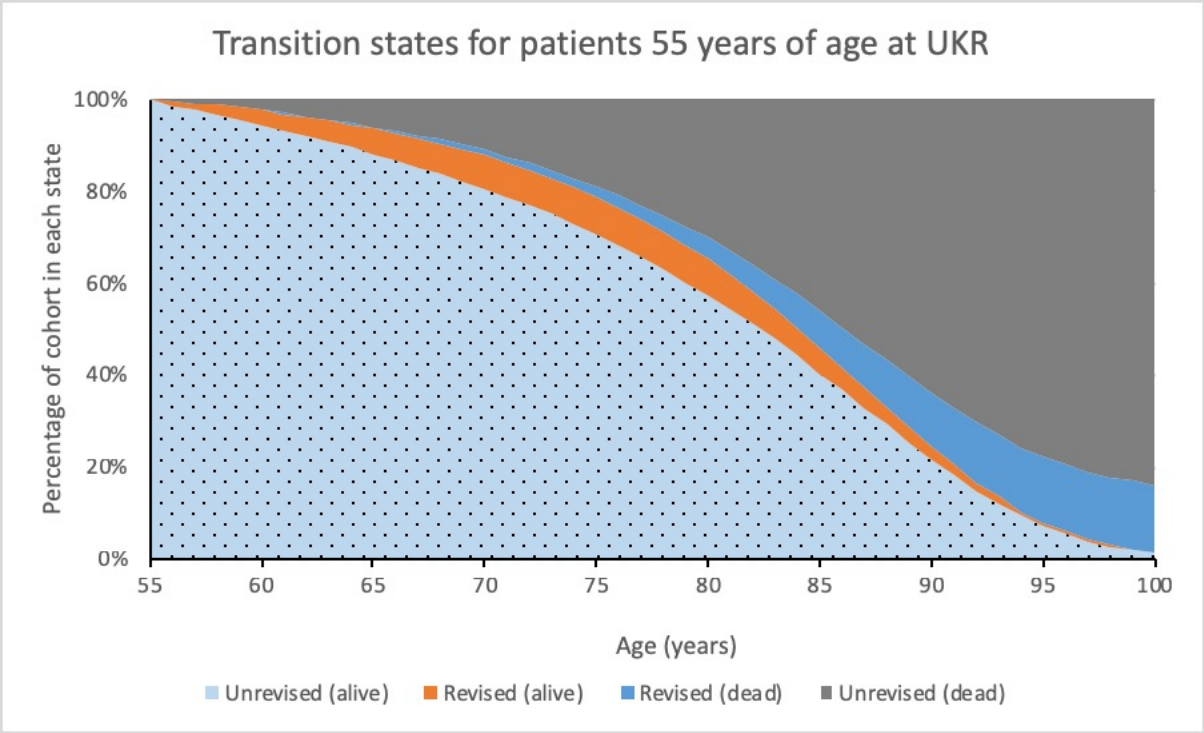


Figure 8-4 Transition states for patients 55 years of age at partial knee replacement

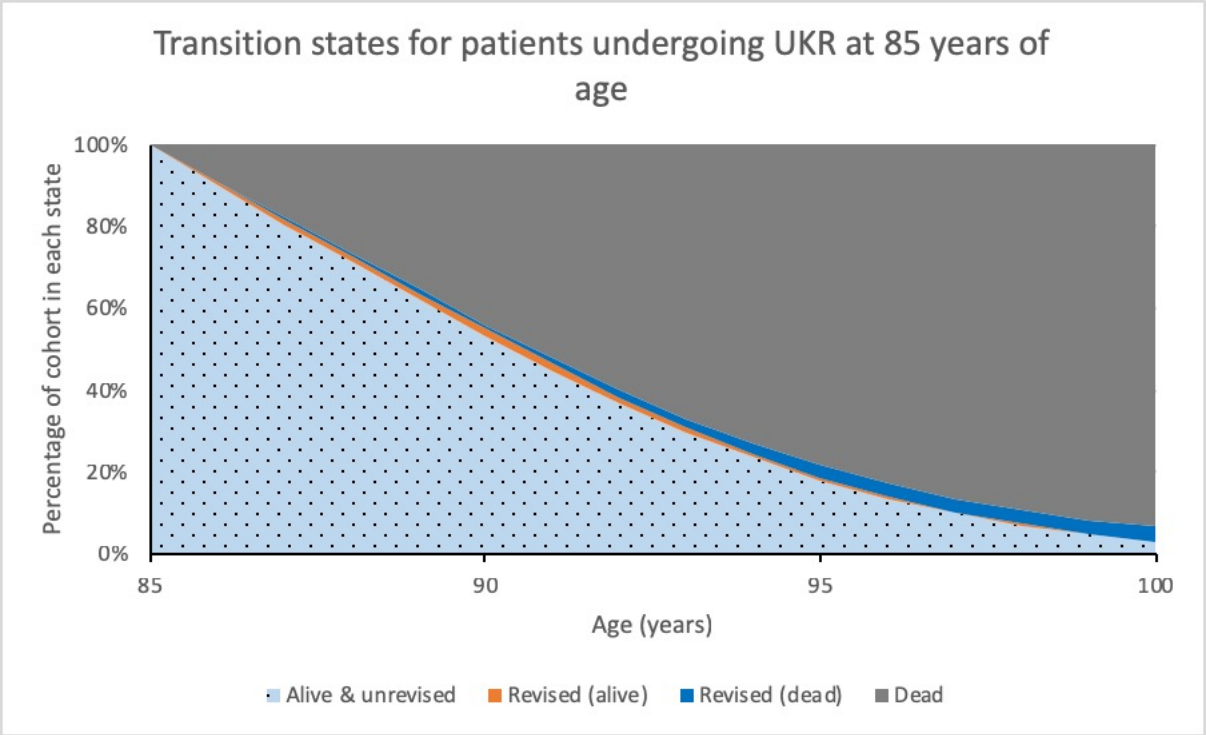


Figure 8-5 Transition states for patients 85 years of age at partial knee replacement
Graphical representation of the competing risk of death and revision in patients of different age groups. Note the difference in scale on the x-axis.

There are limitations of the study: The use of a designer centre series where all patients met established indications to inform revision risk, limits its generalisability. However, in multiple studies it has been shown that provided surgeons use the recommended indications and therefore use PKR for at least 20% of knee replacements they will have similar revision rates to the designer centre[107, 194, 226-229]. Therefore, the results are likely to be generalisable to surgeons using the recommend indications. As part of the sensitivity analysis lifetime revision risk based on data reported in the NJR was modelled, and whilst these estimates were higher, as low volume surgeons who may be using inappropriate indications are included, there were still only one in three requiring revision in those 55 years of age, which is substantially lower than what many would expect.

Although the dataset was substantially smaller (1000 patients) than Bayliss', it had double the mean follow up (10 years) and the revision hazard was modelled with parametric survival methods, which allowed estimation of revision risk beyond the observed data, and allowing construction of a Markov model. Component time incidence rates were calculated at ten year follow up and found almost identical estimates to the observed data at all ages except the very young (55 years) (Figure 2). In the very young the revision rate in the model (0.6% per year) was higher than the observed data (0.4% per year), which suggests that in the young it is a conservative estimate of the revision rate and therefore of the lifetime risk. The results were only slightly influenced by the different parametric models (Table 2), which model the revision rate increasing or decreasing in the long term suggesting that the conclusions are robust.

In conclusion, these estimates of lifetime risk of revision will help patients and surgeons in their decision-making process about whether to receive a medial Oxford PKR. They support the use of PKR as a definitive prosthesis provided it is used for the recommended indications.

9. Lifetime revision risk of total knee replacement

9.1. Introduction

This chapter follows on from the previous chapter where lifetime revision risk was estimated for PKR. As it is preferred by patients relative to time specific risk (i.e. 10% risk over 10 years), it is important to provide comparative information so that the lifetime revision risk can be weighed up between PKR and TKR.

Lifetime revision risk has been previously estimated for TKR using different methodology and a different dataset by Bayliss et al[253]. They found that younger patients had a higher risk of revision. Using data taken from community general practitioners, they had over 50,000 patients, with a mean follow up of 5 years. They estimated yearly revision rates within 5-year age-bands, and transitioned patients through this risk to estimate their lifetime risk. The methods used in this chapter estimate the lifetime revision risk in a different dataset using parametric methods, with a mean follow up of ten years.

The aim of this section is to predict the lifetime revision risk of total knee replacement using the same model as used for PKR in Chapter 7. Further, as the risk of age is known to affect the risk of revision for TKR, as opposed to what was found for PKR, this was also explored.

9.2. Methods

A multistate Markov Model was used to predict the lifetime risk of revision for patients of different ages undergoing TKR (Figure 1). The revision probability was estimated from a large, prospective randomised controlled trial of TKR, and the probability of mortality was estimated from the United Kingdom's Office for National Statistics.

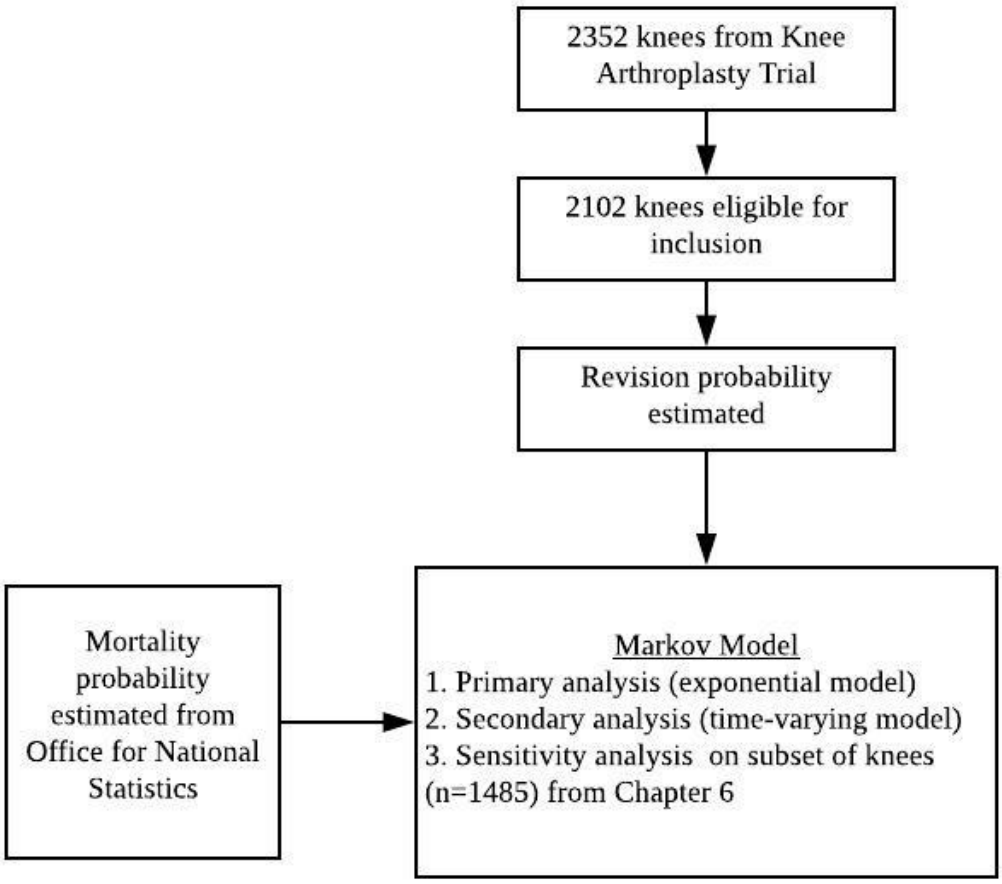


Figure 9-1 Study design for predicting lifetime revision risk for total knee replacement

The cohort was the Knee Arthroplasty Trial (KAT)[231]. KAT is a multicentre randomised controlled trial undertaken in the United Kingdom to prospectively evaluate different aspects of knee arthroplasty design. 2352 participants were recruited between July 1999 and January 2003. Patients received yearly postal questionnaires with the primary outcome measure being the OKS. Postal and telephone reminders were undertaken to complete data collection. Hospitals were contacted for details of readmissions. For this study, the randomisation was not taken into account, thus forming a prospective cohort. The mean follow up was ten years.

Our outcome was revision, and this was defined similarly to the National Joint Registry of England, Wales, Northern Ireland and the Isle of Man[215], meaning that any component removal, addition or exchange were considered revisions. In addition amputation and periprosthetic fractures requiring open reduction and internal fixation were counted as revision.

Statistical analysis: To extrapolate revision risk, a multi-state Markov model was constructed with three health states: 'unrevised', 'revised', and 'dead'[246]. Individuals began as unrevised and then remained so until death or until revised. Such a model reflects the competing risk nature of revision.

Transition probabilities to 'revised' were informed from the parametric regression model used primarily in Chapter 7, the exponential model, which was fitted to the cohort revision data. This model assumes that the risk remains constant over time. As age is intimately related to revision risk with TKR, age was included as a covariate. The primary analysis (called 'exponential model') used only the exponential probabilities. Transition

probabilities to death were informed from the Office for National Statistics (ONS) National Life Tables [22]. Subjects entered the model at the age of interest following their PKR. Each year, subjects could remain in their current health state, or transition to a new health state. Each of these transitions is represented by arrows in Figure 1, and had a defined probability of occurring. The simulation was run separately for a cohort of 1000 patients for each age of interest. Confidence intervals were calculated using the 95% confidence interval of the exponential revision risk, and recalculating the expected revisions that would occur using the model, thus providing the 95% confidence intervals of the estimate.

It is well recorded that age at surgery is related to revision risk, but it is not clear whether that risk reduces over time. That is, if a patient who had surgery at age 55 has been followed for ten years, it is unknown if they have same probability as being revised as someone undergoing their primary surgery at 65 years of age. As such an alternative model to the exponential model was explored, and modelled the risk to reduces over time in line with their initial risk. For the purpose of this chapter, this is called the 'time-varying' model.

A second sensitivity analysis explored the concept that not all knees undergoing TKR can receive PKR. Those receiving TKR who could have had PKR have been shown to have slightly better function when compared to those who are candidate for TKR[256]. It is unknown if there is a selection bias present on revision risk. As such, a sensitivity analysis was performed using the subset of knees who were matched in Chapter 6. Those knees with inflammatory arthritis, in valgus, or with a deficient anterior cruciate ligament were excluded so that those analysed should have been eligible for medial PKR.

9.3. Results

The mean time from surgery to data extraction was 11 years (10 to 13 years). There were 2102 knee replacements performed at a mean age of 71 years (Table 1).

Table 9-1 Demographics of patients in the Knee Arthroplasty Trial

Number of knee replacements	2102
Mean age in years (sd, range)	71 (8, 38 to 93)
Number female (%)	939 (45%)
Mean weight in kilograms (sd)	82 (16)
sd standard deviation, % percentage	

The predicted lifetime revision risk using both models, as expected, decreased with increasing age (Figure 9-2). With the time varying model, the risks were about 16% (95% CI 11 to 22%), 7% (5-11), 3% (2-6) and 1% (0-4%) in those 55, 65, 75, and 85 years of age at surgery. With the exponential model, the risks were much higher, being about 34% (25-46) in those 55 years of age, about 12% (9-15) in those 65 years of age, 5% (3-6) in those 75 years of age, and about 1% (0-3) in those 85 years of age.

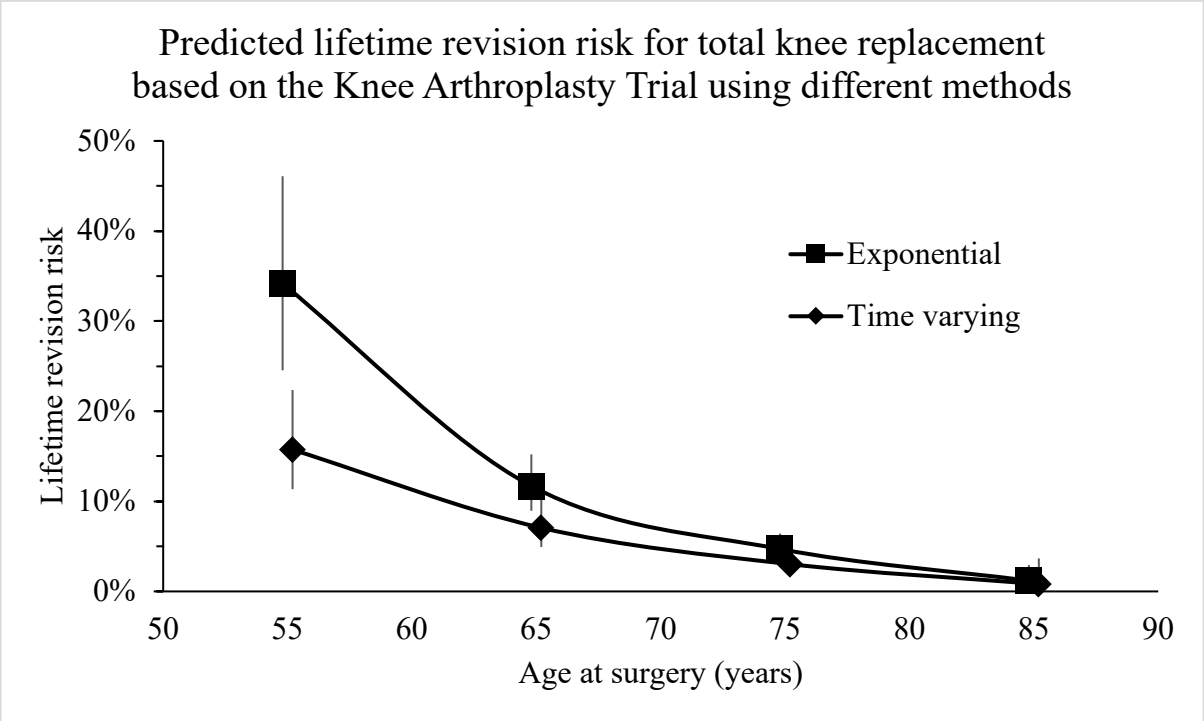


Figure 9-2 Lifetime predictions for total knee replacement based on Knee Arthroplasty Trial using different models
Points offset for clarity

There was a non-linear effect of age on revision risk (Figure 9-3), with significantly higher risk of revision in younger patient groupings. This was approximately 1.5% per year (95% CI 1.0 to 2.2%) in those 55 years of age, dropping steeply to about 0.6% (0.5 to 0.8%) at 65 years of age. From this age the risk continued to decrease, but less steeply, being about 0.4% (0.3 to 0.5%) at 75 years of age, and 0.2% (0.1 to 0.4%) at 85 years of age.

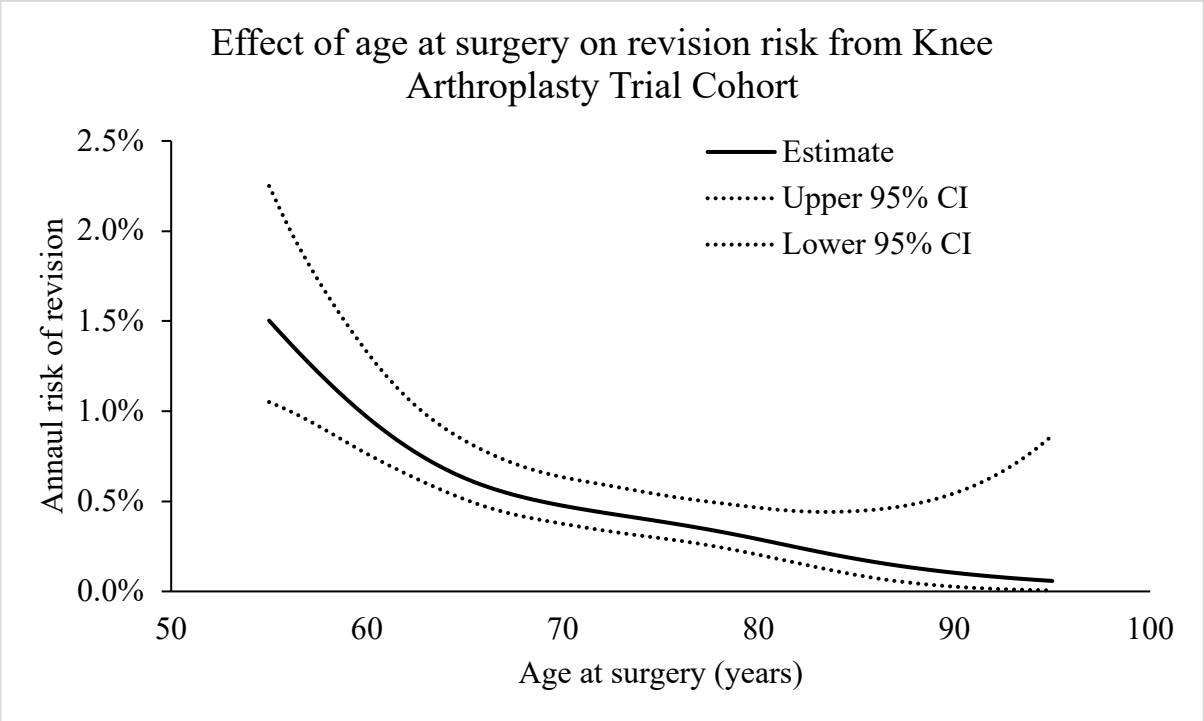


Figure 9-3 Effect of age at surgery on revision risk from Knee Arthroplasty Trial Cohort

The sensitivity analysis, performed on the subset of knees matched in Chapter 6 (demographics provided in Table 9-2), did not reveal any major differences to the risk age presented on the cohort overall (Figure 9-4).

Table 9-2 Demographics of subset of patients from Knee Arthroplasty Trial who were matched to the designer centre partial knee replacements

Number of knee replacements	1485
Mean age in years (sd, range)	69 (8, 39 to 92)
Number female (%)	707 (48%)
Mean weight in kilograms (sd)	81 (16)
Mean preoperative Oxford Knee Score	21 (7)

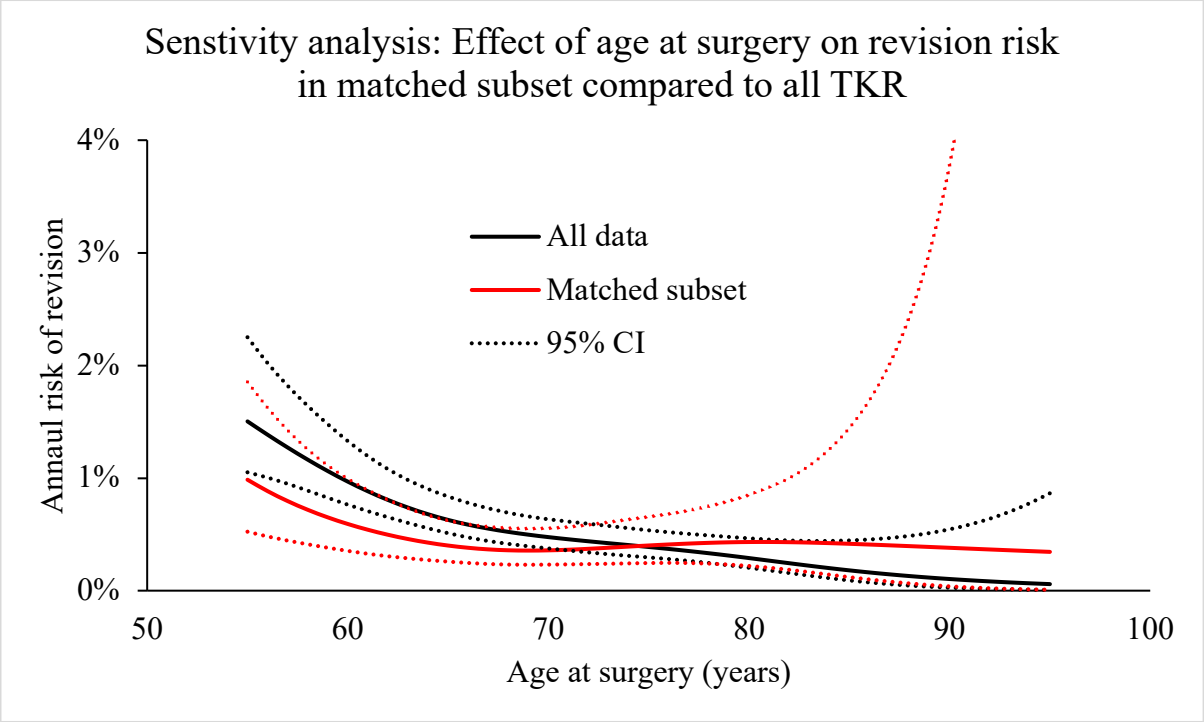


Figure 9-4 Comparison of the effect of age at surgery on revision risk between the Knee Arthroplasty Trial cohort, and the subset matched to designer centre partial knee replacements

9.4. Chapter Discussion

The lifetime revision risk of total knee replacement is low using this novel methodology. Further a significant non-linear effect with age is reported, with those in younger patient groupings being particularly at risk. From the primary analysis, in those about 55 years of age at operation, the lifetime risk was about one in three (34%, 95% CI 25 to 46), falling to about one in ten in those 65 years of age, one in 20 for those 75 years of age, and one in 100 for those 85 years of age at operation.

Burn and colleagues [251] looked at 10,000 total knee replacements; and using similar predictive modelling techniques predicted for patients of 50 years of age a 34% lifetime risk of revision, dropping to about 3% for those undergoing TKR at age 80. Further, Evans and colleagues [252] undertook a long term analysis, albeit without age stratification, and using data predominantly from the Finnish arthroplasty registry concluded that the 25 year revision rate was about 18% for TKR, and 30% for PKR. Bayliss and colleagues [253] published detailed lifetime risk estimates for TKR, using different methodology, based on a dataset of over 50,000 patients with a mean follow up of 5 years. Their study suggested that at age 55 the lifetime risk of revision was about 20% for women and 35% for men. Their estimates at around age 80 were about 1-2% for both males and females. Very similar revision rates across the various ages were predicted using the models, and in particular suggests that the exponential model is more accurate than the time-varying. In Chapter 7, patients of age 55 undergoing medial PKR would have a lifetime revision risk of about 15%, falling to about 4% in those at age 85.

In young patients, these estimates suggest that one in three will require a revision in their lifetime. On the one hand, this will be better than what most surgeons counsel patients of this age to expect: which would be that they would definitely require a revision in their lifetime. On the other, one in three will require a revision, which will require complex reconstructions[91, 92]. If the patient were eligible for medial PKR, as about half are (Section I), their lifetime revision risk at this age would be about 15%, which is substantially lower than that predicted in this study.

In older patients, the lifetime risk of revision is low, no matter what prosthesis is used. This study has identified a risk of about 5% in those 75 years of age, and 1% in those 85

years of age, and these are very similar to those found in other studies[251, 253]. Again, about four in ten patients in this age group may be eligible for PKR (Section I), and had they received medial PKR then their lifetime revision risk would be similar (7% and 4%). The major advantages of PKR in this age group are the substantially lower morbidity and mortality [3].

This study has limitations. It has only examined one outcome, that of primary revision, it has not attempted to identify re-revision incidence or other outcomes that are important to patients such as function. Further, mortality probability was estimated from the Office for National Statistics, and does not take into account the healthy patient selection bias. The estimates of revision were based on KAT data, which was a multi-surgeon, multi-centre study involving centres of varying expertise in knee surgery. This thus provides high levels of external validity (generalisability), but comparisons with results from specialist centres may be unfair. It has not explored covariates such as gender. Finally, the projection of revision incidence relies heavily on assumptions that may or may not be justified. These assumptions were tested by undertaking more than one scenario.

In conclusion, this study has estimated the lifetime revision risk for TKR and found the risk to decrease with increasing age, being 34% (25-46) in those 55 years of age, about 12% (9-15) in those 65 years of age, 5% (3-6) in those 75 years of age, and about 1% (0-3) in those 85 years of age at primary total replacement.

9.5. Comparisons of PKR and TKR: Section discussion

This section has compared the outcome of PKR and TKR using traditional outcomes (observed function and implant survival), and the novel concept of lifetime revision risk. Particularly with long term (10 year) outcomes, partial replacement had significantly higher function as measured by the Oxford Knee Score in younger age groups (younger than 75 years at primary) when compared to total replacement. However, in those 75 years or older the function, though better, was not significantly different. Further, revision rates were found not to be significantly different at ten years in any of the age groups, with a trend toward better fewer revisions with PKR in younger groups, and TKR in older groups.

The lifetime risk of revision is low for both prostheses compared to what surgeons would have expected, particularly for partial replacement. In patients undergoing partial knee replacement, the lifetime revision risk was estimated at 15% (95% CI 12-19), 11% (8-13), 7% (5-9) and 4% (3-5) for those aged 55, 65, 75 and 85 respectively (Figure 9-5). The predictions for total knee replacement were more difficult to model due to the effect that age has on revision risk. Using the same model as that used for partial knee replacement presented estimates of 34% (25-46), 12% (9-15), 5% (3-6), and 1% (0-4) for those aged 55, 65, 75 and 85 years at surgery.

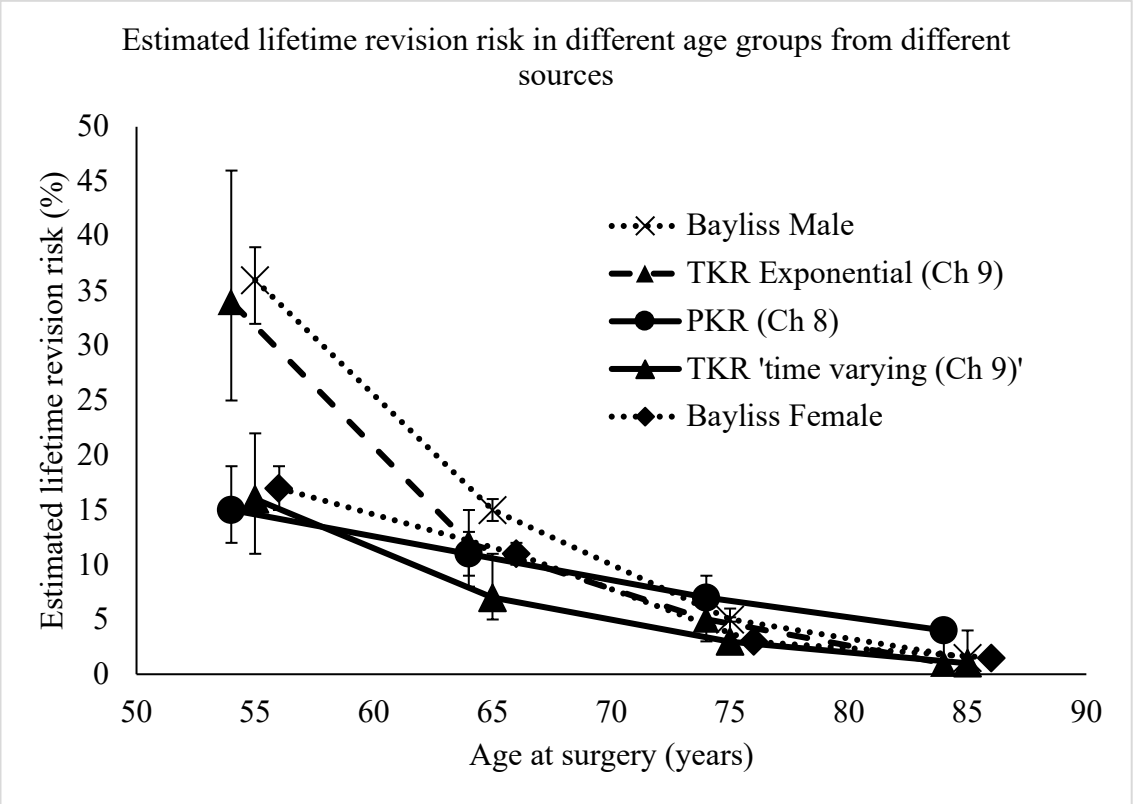


Figure 9-5 Comparison of estimated lifetime revision risk from different sources. Bars represent 95% confidence interval. Points offset for clarity

Putting the results together for different age groups there appears to be significant advantages in receiving PKR in younger patients (younger than 55 to 60 at primary operation). There is significantly better function, which at ten years was of a magnitude of 10 points on the Oxford Knee Score, fewer revisions (though not significant), fewer major revisions (significant), and a lower lifetime revision risk.

In older patients, the findings were more nuanced. With PKR the only significant finding was of fewer major revisions. There was slightly better function at ten years (2 points, though not significant), slightly more revisions (not significant), and a similar lifetime

revision risk. However, the major advantage in this age group, which is not measured in these studies, is that of lower morbidity and mortality [3, 69, 152].

For those in the middle, the outcomes also slightly favour PKR, but are not as extreme. With PKR there is significantly higher function in the Oxford Knee Score at ten years (5 points), there were similar revision rates, but major revisions were fewer. Lifetime revision risk was also similar.

The main limitation to these results is that the results are from observational cohorts that were matched, rather than the gold standard randomised controlled trial. The main findings of this matched study have, however, been replicated in the Total Or Partial Knee Arthroplasty Trial (TOPKAT)[66], where there were no differences in revision rate (though age stratified results were not provided for revision), and a slight preponderance towards better scores in younger patients. Further, the PKR cohort is from a designer centre, using two very experienced designer surgeons. In contrast, the TKR results were from a multicentre, multisurgeon pragmatic trial looking into the results of TKR. The results of PKR are far more dependent on usage than with TKR[72], suggesting that even if high volume surgeons were used for TKR the results are unlikely to change significantly. Further, the results in young patients are the most striking, and it tends to be the most experienced TKR surgeons who undertake replacement in this age group. Additionally, in terms of generalisability of the PKR results, the designer centre results were compared to non-designer centres in Section 2, and found to be identical. Therefore, these results apply to surgeons undertaking partial knee replacement for the recommended indications, and not to the part-time partial knee user in early arthritis.

In contrast, the strengths of these studies include the large numbers of patients included: 1,485 in the matched observational study, which is almost three times as many as the largest randomised trial to date (TOPKAT), and the long follow up of 10 years, which is twice as long as TOPKAT. Further the lifetime revision risk estimates used novel methodology allowing long term extrapolation, and was based on both of these cohorts with a much longer mean follow up than the other studies on the topic[251, 253].

In conclusion, these studies have found substantial benefits to PKR in the hands of experienced surgeons when compared to TKR in all age groups, but particularly in those younger than 55 years of age at operation.

9.6. Comparisons of PKR and TKR: Section summary

Partial and total replacement can both be used in the treatment of severe osteoarthritis of the knee. Substantial benefits have been identified with partial replacement, including lower morbidity[3, 69, 152, 220], lower mortality[3, 69, 152, 220], better function[17], more normal knee movement[185], and higher satisfaction[217]. However, registries report higher revision rates[1, 154, 155, 179]. The relative merits of partial and total replacement in different age groups has not been studied in detail.

The first study (Chapter 7) matched two cohorts, one a designer cohort of 1000 medial PKR, and the other, the Knee Arthroplasty Trial (KAT), a multicentre, pragmatic randomised controlled trial of total knee replacements which was combined into a prospective cohort of TKR. TKR that would not have been eligible for medial PKR were

excluded on the basis of intraoperative findings, and matched to the PKR on multiple variables. At five and ten years OKS was found to be better with PKR (significantly in all age groups and all time points except in those 75+ at ten years). This was particularly marked in those younger than 60 years at primary, who at ten years had a median OKS 10 points higher with PKR than with TKR. Further, in all age groups revision rates were found to be similar. The concept of major revision was also introduced, which was a revision to anything more than a single stage primary TKR, and in all age groups this was significantly lower with PKR.

Lifetime revision risk is a concept that refers to the risk of a revision over a patient's lifetime, rather than over the observed period only. It is preferred by patients when communicating about risk[245]. Using a designer centre cohort of 1000 partial knees with a mean ten year follow up, the lifetime revision risk was estimated using novel methodology. A multi-state Markov model was used with revision risk estimated from parametric survival distributions, and mortality estimated from population data from the Office for National Statistics. Revision surgery was defined as per the National Joint Registry, with any component addition, exchange or removal counted as revision. The results demonstrated that age was an important factor, with lifetime revision risk estimated at 15% (95% CI 12-19), 11% (8-13), 7% (5-9) and 4% (3-5) for those aged 55, 65, 75 and 85 years at surgery respectively.

Following this, a large multicentre cohort of 2102 total knee replacements, also with a mean ten year follow up, was used to estimate the revision risk for total knee replacements using the same methodology. However, the models used for total knee replacement were more complex due to the intimate relation of age on revision risk (with younger patients

being at significantly higher risk of revision, unlike those with partial knee replacement, see Section 2). For this reason two models were created, one was using the same methods as used for the partial knees (parametric survival model using exponential distribution), the other allowing the revision risk to reduce as the patient aged (time varying). The exponential model estimated lifetime revision risk to be 34% (25-46), 12% (9-15), 5% (3-6), and 1% (0-4) for those aged 55, 65, 75 and 85 years at surgery respectively, whilst the time varying model estimated risk at 16% (95% CI 11 to 22%), 7% (5-11), 3% (2-6) and 1% (0-4%) respectively.

Putting the results together, it appears that in younger patients the lifetime revision risk for partial knee replacement is no higher than total knee replacement, and possibly lower (15% and 11% for PKR in those 55 and 65 years at surgery, compared to 16-34% and 7-12% in those with TKR). In older patients, partial knee replacement is similar to a little higher than total knee replacement (7% and 4% for PKR at 75 and 85 years of age, compared to 3-5% and 1% for TKR). Unmeasured, and of great importance in the elderly, is perioperative morbidity and mortality[3].

The results will surprise some as the revision rates for PKR are markedly different compared to those reported in the registries. However, this is not without precedent, and as reported in Section II the results are achievable outside of the designer surgeon. Multiple surgeons have, in fact, published similar revision rates with the Oxford PKR [107, 227, 229, 257]. Further, whilst these are the first estimates for lifetime revision risk for PKR, the results for TKR are similar to other published lifetime risk estimates by Bayliss et al[253], Burn et al[251], and Evans et al[252].

The main limitations of the work are that the comparison was not made as a randomised controlled trial, but rather a matched comparison of observational cohorts. This may lead to confounding from unmeasured variables. Further the comparison was between a cohort by two experienced, designer surgeons using a single device, and a multicentre, multisurgeon pragmatic trial used as a prospective cohort, using different designs of TKR. However, no significant differences were found between the TKR designs[231] so this is unlikely to have confounded the results. Surgeon usage has been demonstrated to significantly affect the results of PKR[71, 73], but there is very little effect seen on the results of TKR[72]. Further, the most striking findings were found in the youngest age group, and the TKR in this age group are most likely to have been undertaken by experienced surgeons. The lifetime risk estimates include assumptions inherent to modelling data, and the primary analysis had a constant rate of revision which may not reflect reality. Finally, revision was defined as per the joint registry, therefore a bearing relocation following dislocation was treated the same as a complex two stage revision for infection. The outcome or lifetime revision risk for subtypes of revision was not explored.

In conclusion, these studies have found substantial benefits to PKR in the hands of experienced surgeons when compared to TKR in all age groups, but particularly in those younger than 55 years of age at operation

10. Conclusions and future work

10.1. Summary of findings

Knee replacement continues to increase and is now the most commonly performed Orthopaedic operation in the United Kingdom[1]. Historically knee replacement was performed in elderly patients due to concern over implant wear and requirements for revision surgery. The disease process, most commonly osteoarthritis, was severe. The implants designed at the time performed well, and surgeons and manufacturers stretched the indications to cater for more patients, both in terms of disease severity and in patient age, with knee replacement being performed on one end of the spectrum in increasingly young patients, and on the other, increasingly frail, elderly patients.

Broadly speaking knee replacement has evolved into two designs: partial knee replacement (PKR) and total knee replacement (TKR). PKR has many benefits over TKR, including more normal knee movement[185], lower morbidity[3, 70, 152, 220], lower mortality[3, 70, 152, 220], and is cheaper[113] and quicker operation to perform. However, it has a higher rate of revision surgery reported in registries[1, 87, 179]. It currently remains unknown how PKR might compare with TKR in different age groups, particularly with regards to the proportion of patients who may be eligible, and the outcomes. Furthermore, many discussions with regards to PKR centre on the controversy around bias involved in design centres and high volume centres[94]. Thus, it remains unknown if a selection bias may occur with some of these studies or whether the results might be generalisable.

From the designer centre, 1424 consecutive primary knee replacements were identified (excluding patellofemoral replacement). Eight-hundred and twenty three were PKR

(medial or lateral, 58%), and in all age groups more PKR were performed than TKR (<55 years 63%; 55 to <65 years 64%, 65 to <75 years 57%, and 75+ years 53%). There was a significant effect with age (p=0.01). This study was at risk of selection bias due to the high number of cases being performed as day cases, and as the designer centre a referral bias cannot be excluded.

From a high volume centre in the USA, those considered eligible for medial Oxford PKR was determined from a consecutive series of 457 knees that had undergone either medial PKR or TKR. The data was categorised into age at surgery (<50, 50-60, 60-70, 70-80, and 80+), and the proportion considered eligible for PKR was calculated. PKR was found to be significantly associated with age (p<0.001), with more younger patients being eligible for medial PKR. Further, the accuracy of radiographs in determining eligibility was identified as being about 90%. As a high volume PKR centre the risk of selection bias could not be excluded.

From a multi-surgeon private Orthopaedic Practice in Melbourne, Australia, 402 consecutive knee replacements were identified. This practice resembles the population of the joint registry, and does not advertise as a PKR centre. Using radiographs, eligibility was determined as being 62% in those under 60 years, 64% in those 60 to 75, and 56% in those older than 75 years at primary surgery (p=0.03). This study was limited by the accuracy of radiographs, but was very similar to the estimates from the other centres, suggesting that referral bias did not play a large role. Overall, across the three studies there appeared to be an association with increasing age reducing PKR eligibility, but about one in two being eligible no matter the age group. However, these studies were all limited in that they have not explored the outcome of the PKR.

A consecutive series of 1000 medial Oxford PKR was identified from the designer centre with a mean 10 year follow up and divided into age groups consistent with registry analyses (<55, 55-65, 65-75, 75+). The mean 10 years Oxford Knee Score was found to be consistent amongst age groups, and further, even with large numbers in each age group there was no difference in survival between the age groups. In fact, there was a slight trend to better survival in the younger age groups. This was an important finding as all joint registries report much higher revision rates in younger patients.

To validate the finding of revision rate, two other cohorts of knee replacement were identified. One was from the USA and included 194 medial PKR, the other was from New Zealand and included 759 medial PKR. The mean follow up was 6.9 years for New Zealand, and 3.9 years for USA, with the USA patients being younger (mean age 63.3 years vs about 66 years, $p<0.001$), and heavier (mean BMI 32.1 vs about 29, $p<0.001$), than those seen in Oxford and New Zealand. Despite this, there was no significant difference in any age group between the revision rates, and the overall revision rate was identical at 0.49 revisions per 100 component years.

The relative merits of medial Oxford PKR and TKR have not been assessed for patients of different age groups in a meaningful way. 1000 consecutive medial PKR from the designer centre were matched with 2,252 TKR from the Knee Arthroplasty Trial. The TKR patients were excluded if they had an intraoperative recording valgus alignment or deficient anterior cruciate ligament. This left 190 patients <60, 937 patients 60-75, and 358 patients 75+. Oxford Knee Score was found to be significantly better (10 points, $p<0.01$) with younger patients at ten years, reducing to 6 points ($p=0.04$) and 2 points

(p=0.24) in older patients. Implant survival was not significantly different between the two prosthesis in any age group; however, PKR had fewer major revisions (defined as requiring more than a single stage, primary knee replacement).

Lifetime revision risk conceptualises the risk of revision throughout the remaining patient lifetime, and takes into account competing risks such as background mortality. Using novel methodology, the risk of medial Oxford PKR revision for patients aged 55, 65, 75 and 85 was calculated. Younger patients were found to have higher risk of revision, with lifetime risk for 55 year olds calculated to be 15% (95% CI 12 to 19), for 65 year olds 11% (8 to 13), for 75 year olds 7% (5 to 9), and for 85 year olds 4% (3 to 5). These estimates will be helpful for patients, surgeons and health providers.

Using a similar model, lifetime revision risk for total knee replacement was estimated using the cohort from the Knee Arthroplasty Trial. The risk of revision was determined for patients aged 55, 65, 75, and 85 years of age at primary replacement. The risk was estimated to be 34% (95% CI 25 to 46) in those aged 55, 12% (9 to 15) in those 65 years, 5% (3 to 6) in those 75 years, and about 1% (0 to 3) in those 85 years of age. As revision risk was significantly associated with age, a second model was considered where revision risk would reduce. For this the estimates were: 16% (11 to 22), 7% (5 to 11), 3% (2 to 6) and 1% (0 to 4) in those 55, 65, 75, and 85 years of age at surgery. A sensitivity analysis was performed using only those considered eligible for medial PKR and the risk was not found to be significantly different. Therefore, comparing these to the PKR estimates, it suggests that the risk is similar to lower with PKR in those <65 years of age, whilst in those 75 years of age or greater there is a lower risk with TKR.

10.2. Discussion of findings

The findings in this thesis apply to those knees that would be appropriate for PKR, and support the use of the PKR when used by expert surgeons in all age groups.

Younger patients, which for knee replacement tend to refer to those aged younger than 60 years at operation, tend to be more active and have a longer life expectancy[6, 258]. The consequence of this is that their knee is expected to undergo a revision due to device failure in their lifetime. The cause of this revision is primarily loosening of the implant, including both septic and aseptic[195], and for the latter is likely to be due to their high activity levels. This is particularly troublesome as revision procedures in this context will often require the resection of increasing amounts of native tissue. The proportion of knees that could receive PKR was examined in Section I, and it was estimated that more than half (about 60%) of those undergoing knee replacement in this age group could receive PKR. As examined in Section II, in those receiving PKR, the revision rate with PKR was no higher than that seen with TKR in the registry. However, as examined in Section III, in contrast to TKR, the revision procedure undertaken with PKR was overall much less invasive, with no patients requiring more than a primary TKR (as opposed to 8% of matched TKR patients requiring major revision). Further, when the revision rates were extrapolated over the patients' lifetimes, the point estimate for lifetime revision risk for a patient of age 55 with PKR was 15% (95% CI 12 to 19), whilst with TKR it was 34% (95% CI 25 to 46).

Older patients tend to be more limited in their activity, have shorter life expectancies, and are increasingly frail relative to younger patients[6, 258, 259]. With patient safety as a key

priority, the goals in this group are to provide a procedure with minimal morbidity and mortality that alleviates pain, and restores function. Further operations are important to avoid due to the physiological deleterious effects. Many surgeons would consider the older age groups to require a TKR due to the presence of multiple compartment arthritis. This thesis examined the indications for Oxford PKR (Section I) and found that about one-third to one-half of the older age groups would be eligible to receive PKR (between 36% and 50% depending on the chapter). This is in stark contrast to national use in the United Kingdom which shows just 3% of those older than 80 years receive PKR[148]. In Section II, the outcomes were examined, and it was found that there was a trend towards higher rates of disease progression in this older age group, with a ten year implant survival of 93%. The number requiring further bone resection was <1%. When compared with TKR in Section III, the Oxford Knee Score was found to not be significantly different (though was slightly lower with TKR), and neither was the revision rate (though was slightly better with PKR). This work has built upon that performed by Liddle et al[3], who showed in an age-standardised analysis that if 400 knee replacements were performed as PKR instead of TKR a life would be saved. Further, the incidence of stroke, heart attack and pulmonary embolus were significantly less with PKR[3]. Lifetime risk for PKR was estimated to be 7% (95% CI 5 to 9) at 75 years of age, and 4% (95% CI 3 to 5) at 85 years of age. For TKR the estimates were 5% (3 to 6) and 1% (0 to 3) respectively.

The age group between those considered young, and those considered elderly, roughly representing those aged between 60 and 75 years of age at operation, are the group receiving the largest number of knee replacement[21]. Similar to the other age groups, Section I identified that about half of patients were found to eligible to receive PKR. Section III identified that function and implant survival were similar between PKR and

TKR, though the revisions were substantially less involved with PKR. In this age group either procedure can be considered, with consideration given to the significant benefits in morbidity and mortality as identified by Liddle et al[3]. Lifetime risk at age 65 for PKR was estimated to be 11% (CI 8 to 13), for TKR it was 12% (CI 9 to 15).

The substantial limitation of working with predominantly designer centre data was identified early in the course of this thesis, which spurred a search for other centres with data. Validation within registries was considered, and an application discussed with the Australian Registry. There were multiple concerns regarding the quality of data within registries in general, including an absence of information regarding the philosophy of use, which is strongly suspected of playing a role in the high revision rate of PKR[38]. Proxy measures used previously to examine this have included measures of caseload and usage[71-73]. However, due to multifactorial reasons including suspected local surgeon disinterest, the application did not proceed. As such it was decided to analyse prospectively followed cohorts from surgeons who voice a philosophy of PKR use that is similar to the 'Oxford' philosophy (See Chapter 1.3, Selection, page 7). By examining outcomes from outside the designer centre, the findings could be supported or refuted. Whilst the follow up was shorter, with fewer patients, overall the results from the designer centre were supported. However, the generalisation remains limited to those surgeons who would be considered 'expert' surgeons.

10.3. Implications of thesis

This thesis has explored three main ideas: the influence of age on selection for knee replacement between different sources, the influence of age on outcomes between different sources, and the generalisability of designer centre findings.

Through three studies the proportion of patients eligible for partial knee replacements has been estimated. Whilst this has been explored by other authors, these are the first studies to explore the effect of age and has provided a link between radiographic and usage estimates. The remarkable consistency between the studies should reassure surgeons that about one in every two patients could receive a partial knee replacement.

With regard to patient outcome, this thesis reports the first finding of a remarkably low revision rate in younger patients (those < 55) with partial knee replacement when used by surgeons who use partial replacement consistently across age groups. This was externally validated in two other centres that use partial knee replacement in high usage. Further, when compared to total knee replacement, PKR appears to provide much better function, and in experienced hands the risk of revision was not as high as reported in joint registries, and arguably is the same between PKR and TKR in younger age groups.

Finally, for each outcome, comparisons were made between designer and non-designer centres to explore the possibility of designer centre bias. With regard to PKR eligibility and revision risk, there was little difference between the designer centre and the non-designer centres. This therefore provides external validity to the findings presented in this thesis.

The revision rates presented in this thesis are significantly less than that reported in joint registries. Though not examined specifically in this thesis, this may be attributable to the use of PKR as a 'pre-TKR' intervention in early arthritis, and a lower threshold to revision.

This information should be of use to patients, surgeons, and health care commissioners.

10.4. Limitations and future work

The main limitation of each outcome examined was the use of a designer cohort as a comparator. Designer cohorts are at risk lacking external validity, typically ascribed to unmeasured factors in patient selection, and surgical skill. This thesis has therefore examined the most important outcomes at external centres and found little difference. However, these external centres have fewer patients and shorter follow up and thus later validation may be warranted.

Further, the findings in this thesis do not apply to the use of the 'device', but rather the 'surgeon-device' composite. The external centres all use partial knee replacement for about half of their knee replacements, and only a small proportion of these are used in younger patients. This stands in contrast to what is recorded in the registry, where much larger proportions of PKR are used in younger patient groupings. Therefore, a TKR surgeon who uses PKR part time in younger patients, in whom the surgeon may be unwilling to perform TKR, will likely not achieve the results presented in this thesis.

Gold standard comparisons between treatment options are randomised controlled trials, in which this thesis contains zero. It was however reassuring to see that the five year results of the Total Or Partial Knee Arthroplasty Trial (TOPKAT), were not dissimilar to those presented in this thesis.

The most important study to be performed following this thesis would be to re-analyse adverse events between PKR and TKR, but only in the eldest age group. A comparison of adverse events was undertaken by Liddle et al in 2014[3], but had an age standardised analysis with a mean age of 68 years: patients of this age do not suffer as many medical complications as their older peers and thus the effect size is likely to be attenuated. It may be that the difference in revision rate between PKR and TKR would be similar to the difference in major medical complications; in which case there would be a very strong case for PKR implantation in this age group.

A second study of interest would be to define the role of magnetic resonance imaging (MRI) in patient selection. Large cohort studies have identified MRI findings of osteoarthritis in over 70% of those with asymptomatic knees over 65 years of age with normal radiographs. A suspicion is that an MRI finding of arthritis in an asymptomatic lateral compartment may prevent surgeons from utilising PKR, when there is no evidence that these findings continue to definite compartment degradation.

Finally, some work should be directed towards bridging the gap between the philosophy of PKR use in early arthritis alone, to use as a more established device in the knee surgeon's arsenal. It currently remains unclear whether good surgeons who achieve good

results undertake more PKR, or whether these surgeons were trained to this level (and indeed if any and all surgeons can be trained to achieve these results).

11. Appendices

A. Outcome scores

The Oxford Knee Score consists of 12 questions which are graded 0-4, giving a possible score of 0-48 (with 48 being the best outcome). Its questions relate to function and pain. The EQ-5D is a health economics questionnaire that relates to general quality of life. It consists of five questions relating to mobility, self-care, usual activities, pain/discomfort and anxiety/depression. These questions are graded, and the score is calculated and scaled to between 0 and 1 (with 1 being perfect health).

Revision is a hard deadline and is variably defined between authors. The most consistent definitions are those used by the joint registries, and this roughly corresponds to any implant insertion, removal or exchange within the originally operated knee.

Date: ☐☐/☐☐/☐☐

Op date: : ☐☐/☐☐/☐☐

Patient Name & no. (Sticky Label)

LEFT/RIGHT

PROBLEMS WITH YOUR KNEE

During the past 4 weeks.....

☯ **tick one box for every question**

1

During the past 4 weeks.....

How would you describe the pain you usually have from your knee?

None	Very mild	Mild	Moderate	Severe
❒4	❒3	❒2	❒1	❒0

2

During the past 4 weeks*.....*

Have you had any trouble with washing and drying yourself (all over) because of your knee?

No trouble at all	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
❒4	❒3	❒2	❒1	❒0

3

During the past 4 weeks*.....*

Have you had any trouble getting in and out of a car or using public transport because of your knee? (whichever you would tend to use)

No trouble at all	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
❒4	❒3	❒2	❒1	❒0

4

During the past 4 weeks*.....*

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

No pain/more than 30 mins	16 to 30 mins	5 to 15 mins	Around the house only	Not at all - pain severe when walking
❒4	❒3	❒2	❒1	❒0

5

During the past 4 weeks*.....*

After a meal (sat at a table), how painful has it been for you to stand up from a chair because of your knee?

Not at all painful	Slightly painful	Moderately painful	Very painful	Unbearable
❒4	❒3	❒2	❒1	❒0

PLEASE TURN OVER

Oxford Knee Score© Department of Public Health, Institute of Health Sciences, Old Road, Oxford OX3 7LF (Dawson et al 1998)

6

During the past 4 weeks.....

Have you been limping when walking, because of your knee?

Rarely/never	Sometimes, or just at first	Often, not just at first	Most of the time	All of the time
❒4	❒3	❒2	❒1	❒0

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
❒4	❒3	❒2	❒1	❒0

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
❒4	❒3	❒2	❒1	❒0

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
❒4	❒3	❒2	❒1	❒0

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
❒4	❒3	❒2	❒1	❒0

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
❒4	❒3	❒2	❒1	❒0

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
❒4	❒3	❒2	❒1	❒0

TOTAL SCORE **/48**

American Knee Society Score (AKSS)

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 movement in any position)

AP	Points	✓
<5mm	10	
5-10mm	5	
>10mm	0	

Med-Lat	Points	✓
<5°	15	
6-9°	10	
10-14°	5	
>15°	0	

Flexion 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	

Flexion ROM (continued)		
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	

Maximum Flexion: _____

Extension: _____

Subtotal: □□□/100

DEDUCTIONS

Flexion contracture			Extension Lag			Alignment		
	Points	✓		Points	✓	**ASIS – Knee- Ankle**	Points	✓
0-4°	**0**		0	**0**		Normal Knee (in 5-10° valgus)	**0**	
5-9°	**-2**		1-9°	**-5**		Minor Valgus Knee (in 0-4° valgus)	**-10**	
10-15°	**-5**		10-20°	**-10**		Moderate Valgus Knee (in 11-15° valgus)	**-10**	
16-20°	**-10**		>20°	**-15**		Severe Valgus or Varus (>15° or < 0°)	**-20**	
>20°	**-15**					**Goniometer Measurement** in degrees: Please circle **valgus or varus**		°

Total Deductions □□/50

Objective Knee Score □□□/100

FUNCTION SCORE

Walking			Stairs			Support (deductions)		
	Points	✓		Points	✓		Points	✓
Unlimited	50		Normal	50		No Support	0	
500m-1km	40		Down with rail	40		Stick	-5	
100-500m	30		Up & down with rail	30		2 sticks	-10	
<100m	20		Unable down	15		Crutches/walker	-20	
Housebound	10		Unable	0				
Unable	0							

Functional Knee Score □□□/100

Comments:

Charnley ABC
A: Single knee affected ☐
B: Both knees affected ☐
C: Multiple arthritis or medical infirmity ☐

TEGNER ACTIVITY SCORE

Please circle the number, which best describes the activity you are able to do.	
10	**Competitive Sports**: soccer – National & International Elite
9	**Competitive Sports**: soccer – lower divisions, ice hockey, wrestling, and gymnastics
8	**Competitive Sports**: bandy, squash/badminton, athletics (jumping etc.), downhill skiing
7	**Competitive Sports**: tennis, athletics (running), motocross, speedway, handball, basketball **Recreational Sports**: soccer, badminton, ice hockey, squash, athletics (jogging), cross-country.
6	**Recreational Sports**: tennis, badminton, handball, basketball, downhill skiing, jogging at least 5 times a week
5	**Work**: heavy labour (building, forestry) **Competitive Sports**: (cycling/cross-country skiing) **Recreational Sports**: (jogging on uneven grounds at least 2 times a week)
4	**Work**: moderate heavy labour eg. truck driving, heavy domestic work **Recreational Sports**: cycling, cross-country skiing, jogging on even ground at least 2 times a week
3	**Work**: light labour eg. nursing **Competitive and recreational sports**: swimming, walking in forest possible
2	**Work**: light labour Walking on uneven ground possible but walking in forest impossible
1	**Work**: sedentary work, walking on even ground possible
0	**Sick Leave / Disability** pension due to knee problems

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

SELF-CARE

I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities*)

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT

I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

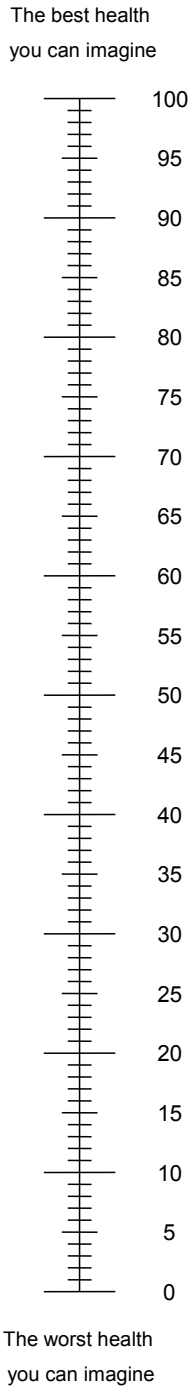
I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

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- We would like to know how good or bad your health is TODAY.

- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = ☐



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