Elective, aseptic revision knee arthroplasty - Epidemiology and Patient-relevant outcomes

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Abstract

Revision total knee arthroplasty (rKA) is further surgery to address a problem with an existing knee replacement. This includes 'urgent' procedures (such as for infection or fracture) and elective, aseptic procedures (such as for malalignment or aseptic loosening). The need for rKA is predicted to increase as more and more primary knee arthroplasties (pKA) are implanted. However, compared to pKA, little is understood about the epidemiology of rKA or patient-relevant outcomes following surgery.

The purpose of this thesis was to explore and investigate delivery of elective, aseptic rKA, including any patient-relevant outcomes. The overarching aims were: (1) to investigate the epidemiology of elective, aseptic rKA in the United Kingdom (UK) to understand its incidence, trends over time and reasons for surgery; (2) to investigate the validity of existing patient reported outcome measures (PROMs) to measure joint function from the perspective of the patient; and (3) to investigate patient-relevant outcomes following elective, aseptic rKA by diagnosis to support better shared decision making with patients.

Since the National Joint Registry (NJR) began, annual rKA numbers were found to have steadily increased. While increases have levelled off in recent years, more than double the procedures are performed today compared to 15 years ago. Previously, aseptic loosening and component wear were the most common reasons for rKA. Today, infection is the leading cause for surgery, being particularly common in patients requiring a second or a third rKA.

Many different PROMs were found to be in current use to measure pain and joint function following elective, aseptic rKA. However, evidence to support these instruments was limited. Further research is needed to establish the content validity and measurement properties of these instruments, aiming to create a core outcome set.

Patient-relevant outcomes following rKA included the need for further surgery, joint function, quality of life and frequency of complications. A systematic review found evidence was limited to uncontrolled, case series. Implant survivorship following elective, aseptic rKA was estimated as ~96% at 1 year, ~91% at 5 years and ~87% at 10 years, with most studies identifying large improvements in pain and joint function.

Analysis of routinely collected national data found elective, aseptic reasons for rKA generally had better outcomes than 'urgent' indications. Notably, patients revised for stiffness and unexplained pain showed significant variation in improvements in pain and joint function. To assist surgeons in the discussion of risks and benefits of rKA with patients, an online Shiny application was developed.

To better understand the decision to offer surgery for unexplained pain, a qualitative study explored surgeons' experiences. This identified the following themes: *(1) I need to understand a patient's journey and their expectations; (2) A difficult consultation; (3) I'm the 'fixer'; (4) It's complicated asking for help; (5) I'm uncomfortable operating for truly unexplained pain; and (6) It's a wound I carry with me.*

In conclusion, this thesis has quantified current rKA practices in the UK and trends over the past fifteen years. Further research is needed to develop a core outcome set to measure pain and joint function following elective, aseptic rKA. Patients revised for stiffness and unexplained pain had unpredictable outcomes following elective, aseptic rKA and this should be considered in shared decision-making prior to surgery.

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List of Abbreviations

ASA . . . . . American Society of Anesthesiologists

AOANJRR . . Australian Orthopaedic Association National Joint Replacement Registry

BASK . . . . . British Association for Surgery of the Knee

BMI . . . . . Body Mass Index

BOA . . . . . British Orthopaedic Association

BPT . . . . . Best Practice Tariff

COASt . . . . Clinical Outcomes in Arthroplasty Study

COKS . . . . . Change in Oxford Knee Score

COS . . . . . Core Outcome Set

COSMIN . . . COnsensus-based Standards for the selection of health Measurement INstruments

CPRD . . . . . Clinical Practice Research Datalink

DAIR . . . . . Debridement, antibiotics and implant retention

e-RS . . . . . NHS e-Referral Service

EPR . . . . . Electronic Patient Record

ESP . . . . . European Standard Population

GDPR . . . . . General Data Protection Regulation

GIRFT . . . . Getting It Right First Time

HES . . . . . Hospital Episode Statistics Admitted Patient Care

HQIP . . . . . Healthcare Quality Improvement Partnership

HRG . . . . . Health Resource Group

HRQoL . . . . Health-Related Quality of Life

IQR . . . . . Interquartile Range

JLA PSP . . . James Lind Alliance Priority Setting Partnership

KA . . . . . Knee Arthroplasty

KAT . . . . . Knee Arthroplasty Trial

LOS . . . . . Length Of Stay

MDS . . . . . Minimum Data Set

MDT . . . . . Multi-Disciplinary Team

MRC . . . . . Major Revision Centre

MUA . . . . . Manipulation Under Anaesthesia

NAR . . . . . Norwegian Arthroplasty Register

NHS . . . . . National Health Service

NJR . . . . . National Joint Registry for England, Wales, Northern Ireland, the Isle of Man and the States of Guernsey

NPS . . . . . Northgate Public Services

OA . . . . . Osteoarthritis

ONS . . . . . Office for National Statistics

PPI . . . . . Patient and Public Involvement

PJI . . . . . Prosthetic Joint Infection

PROMs . . . . Patient-Reported Outcome Measures

QoL . . . . . Quality of Life

RCT . . . . . Randomised Controlled Trial

REC . . . . . Research Ethics Committee

RKCC . . . . . Revision Knee Complexity Classification

RWE . . . . . Real-world evidence

SD . . . . . Standard deviation

SF-36 . . . . . 36-Item Short Form Survey

SIP . . . . . Surgeon, Implant and Patient factors

SPC . . . . . Statistical Process Control

STAR . . . . . Supportive Treatment After Replacement

TKR . . . . . Total Knee Replacement

UK . . . . . United Kingdom

WHO . . . . . World Health Organisation

1 Introduction

Contents

1.1 Thesis purpose

The purpose of this thesis is to explore and investigate the delivery of elective, aseptic revision knee arthroplasty (rKA), including any patient-relevant outcomes. The overarching aims are:

1. To investigate the epidemiology of elective, aseptic rKA in the United Kingdom (UK) to understand its incidence, trends over time and reasons for surgery;

2. To investigate the validity of existing patient reported outcome measures (PROMs) to measure joint function from the perspective of the patient; and
3. To investigate patient-relevant outcomes following elective, aseptic rKA by diagnosis to support better shared decision making with patients

1.2 Definitions

- *Primary knee arthroplasty (pKA)* refers to the first operation to artificially replace one or more compartments of a native knee joint. The knee joint has three compartments: medial tibiofemoral, lateral tibiofemoral and patellofemoral. pKA may involve replacement of one, two or all three of these compartments. Osteoarthritis (OA) is the most frequent indication for surgery, and is the sole diagnosis for 96.6% of all pKA performed in the United Kingdom [1].

- *Revision knee arthroplasty (rKA)* will be defined as any procedure following pKA where a joint replacement component is added, removed or modified, or a debridement, antibiotics and implant retention (DAIR) procedure, an arthrodesis or an amputation [1]. This definition matches that introduced by the National Joint Registry (NJR) in June 2018 [2]. According to this definition, isolated exchange of a polyethylene insert, secondary patella resurfacing, replacement of a further compartment of the knee after partial knee replacement and washout of a knee replacement are all considered revision procedures. Further surgery to a previously revised knee will be termed a *re-revision* or described according to the following sequence: *pKA*, *first rKA*, *second rKA*, *third rKA*, and so on.

- *Re-operation* will be defined as further surgery to a pKA or rKA that does not meet the criteria for revision (or re-revision). This will include procedures such as manipulation of the knee joint under anaesthesia (MUA) and re-alignment of the extensor mechanism.

Table 1.1: Top Ten Research Priorities for Problematic Knee Arthroplasty

1.	What are the causes of persistent pain following a knee arthroplasty? How can the pain be prevented or minimized?
2.	What is the best way to diagnose and treat infection of a knee arthroplasty?
3.	What are the most effective ways to organize healthcare and avoid delay to improve the results and patients' experience of revision knee surgery?
4.	What factors determine (predict) whether revision knee surgery is likely to work?
5.	What can be done after and/or before revision knee surgery (including physiotherapy and exercise) to optimize the result?
6.	What is the psychological impact of a problematic knee arthroplasty and what support do people need before, during and after revision knee surgery?
7.	How should we measure the outcomes following revision knee surgery in a way that is meaningful to patients, and is surgery cost-effective?
8.	Is there a way to manage some types of problematic knee arthroplasty to avoid revision knee surgery (through physiotherapy, lifestyle change, and/or self-management)?
9.	What causes knee stiffness following knee arthroplasty? How can it be avoided and how is it best treated?
10.	What are the best forms of surgery to use for revision knee surgery (including choice of implant and technique)?

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1.3 Research priorities for patients with a problematic knee arthroplasty

A recent James Lind Alliance Priority Setting Partnership (JLA PSP) led by the British Association for Surgery of the Knee (BASK) identified the top ten research priorities for patients with a problematic KA [3]. These are shown in Table 1.1. This thesis will create new evidence to contribute to Priority #7 above.

1.4 Surgical evaluation of revision knee arthroplasty

Revision knee arthroplasty can be considered to be a *complex* intervention (Table 1.2). This term was originally defined in reference to the presence of several, interacting component parts [4]. However, many different aspects of an intervention can make it complex. These include variability in outcomes; a range in the difficulty of behaviours exhibited by those delivering or receiving the intervention; or the presence of flexibility and tailoring in the intervention itself [5]. A *simple* intervention can be considered to provide contrast. The prototypical example is a drug trial, where the patient either takes the drug or does not. However, as others

Table 1.2: Examples of complexity associated with studying rKA

- What exactly is the intervention under study? Are all types of rKA the same?
- How should the outcome be measured?
- Are patients willing to enrol in a clinical trial after a previous failed intervention?

have pointed out, it can be difficult to identify truly *simple* interventions in the real world [6]. Nearly all surgical evaluation can be thought to concern *complex* interventions, with skill and experience linked to the outcome.

In 2000, the Medical Research Council published a framework to characterise the process of development through to implementation of a complex intervention [4]. This framework was designed to resemble the phases of drug development. A "continuum of increasing evidence" was described from theory (preclinical) through to long term implementation (Phase IV) [4]. This framework was subsequently updated to incorporate new study methodologies and to remedy the limitations identified with the original description (such as the need for a linear sequence of development) [5]. This thesis will follow the new complex interventions guidance from the Medical Research Council.

1.5 Indications for revision knee arthroplasty

Primary knee arthroplasty is, by definition, the first procedure to replace the articular surface of a joint. Patients undergoing pKA nearly always present to their surgeon at a planned outpatient appointment with pain and poor function arising on a background of osteoarthritis [1]. This homogeneity allows pKA procedures to be reasonably grouped together for investigation – for example, in a randomised controlled trial comparing different types of joint replacement prosthesis [7]. In contrast, rKA procedures are more heterogeneous. Patients may present as an emergency or electively, with a variety of diagnoses and few or many previous surgeries to the joint. The main goal of treatment can vary. For example, a patient with an infected arthroplasty may prioritise eradication of this over improvements in pain and joint function; or, a patient with a periprosthetic fracture may prioritise a stable limb that allows early mobilisation.

A key simplifying assumption that will be employed in this thesis is to focus mainly on elective, aseptic rKA. I will consider these to be rKA for any indication, except malignancy, infection or fracture. Elective, aseptic rKA account for around 85% of procedures [1]. Within this group, I will consider the main source of heterogeneity to be the indication for rKA. An overview of different indications for rKA (including septic and urgent indications) is provided in Table 1.3. In some instances, there may be more than one reason to operate. For example, a patient with malalignment of their KA may also develop aseptic loosening. Where necessary, a rKA will be assigned a single, dominant diagnosis to reflect the relative *importance* of the diagnosis. Table 1.3 is ordered from most important to least important diagnosis. This system was originally developed by the AOANJRR based on expert opinion [8]. To continue the example above, the implant would be presumed to have loosened due to abnormal force transmission due to malalignment. This system is imperfect and may misrepresent some cases. Furthermore, there is limited understanding of how surgeons classify indications for rKA and the definitions provided may not be used by all. The NJR lists fourteen different indications on their minimum data set form (providing 2^{14} theoretical combinations) [2]. While many of these combinations will never be realised, it is clear that some form of simplification is necessary. Finally, some investigators have differentiated between the *type* of rKA procedure. This might include setting rules to assign rKA as *major* or *minor* procedures [9] or stratifying revisions by the type of pKA implant [10; 11; 12]. This source of potential heterogeneity will not be investigated in the thesis.

1.6 Epidemiology of revision knee arthroplasty

Over the past decade, leading up to the Covid-19 pandemic, national joint replacement registers have reported increasing volumes of pKA each year [1; 13; 14]. Over 103,000 pKAs were recorded on the NJR in 2019, compared to 76,000 procedures in 2009 [1]. It has been suggested that these increases reflect ageing patient populations with a greater prevalence of osteoarthritis [15] and increases in the demand

Table 1.3: Indications for revision knee arthroplasty

Rank	Indication for revision	Definition
1	Infection	Failure due to the presence of microorganism(s) within a joint. The diagnosis of prosthetic joint infection is complex, with criteria available from the European Bone and Joint Infection Society (EBJIS) [26] and the Musculoskeletal Infection Society (MSIS) [27].
2	Malalignment	Failure due to component alignment. Optimal component alignment for KA is debated, and different surgeons may employ different alignment strategies [28].
3	Loosening/Lysis	Failure due to loosening of the joint prosthesis without the presence of a mechanical cause or infection.
4	Component wear	Failure due to progressive removal of material from a prosthesis.
5	Dislocation/Instability	Failure due to abnormal and excessive displacement of a KA.
6	Fracture	Failure due to a break in the continuity of the bone (femur, tibia or patella).
7	Progressive arthritis	Failure due to loss of articular cartilage and bone damage in compartments of a knee not already replaced.
8	Stiffness	Failure due to limited range of motion of a KA.
9	Unexplained pain	Failure due to pain without a diagnosis to explain symptoms. A diagnosis of exclusion.
10	Other	Failure due to other pathology, not encompassed above.

for surgery from younger patients [16]. In turn, several studies have predicted that the volume of pKA will rise further over the coming decades [17; 18; 19; 20].

The majority of patients undergoing pKA will never require rKA [21; 22]. At ten years around 4% of pKA are revised [1] and, over the longer-term, a recent systematic review found that three-quarters of pKA implants lasted 25 years or more [22]. However, a greater prevalence of pKA, coupled with increases in life expectancy [23] and use of implants in patients who place the greatest demands on them (for example, young patients [16; 24] and those with obesity) have created expectations for a sharp rise in the requirement for rKA [17]. On the other hand, there is recent evidence to suggest that increases in the incidence of pKA and rKA may be slowing down, rather than speeding up [25].

In the UK, count data for annual numbers of pKA and rKA are regularly published by the National Joint Registry (NJR) [29]. These also show a 'levelling off' for increases in both pKA and rKA. However, while these data are useful for resource planning, without a reference to the size and structure of the underlying population, further inferences are limited. For example, these data do not help us to understand whether increases in joint arthroplasty activity reflect growth in population size, ageing of the population or a *true* increase in the rate of intervention. Several studies have described international variation in the intervention rate

for rKA [30; 25]; however, the failure to standardise for differences in population structure limit interpretation beyond the sample population. Following on from this, it is evident that comparatively little is understood about the epidemiology of rKA by diagnosis, complexity or number of previous surgeries, despite considerable variation in patient-reported outcome measures [31], costs and resource utilisation between these procedures [32; 33; 34].

A further reason to understand delivery of rKA is the recent introduction of *Revision Networks* in England [35; 36]. This refers to a system where rKA are delivered by a fewer surgeons undertaking greater volumes and working within designated units. The guiding principles underpinning this model of care include the triage of complex work to specialist centres and avoidance of low-volume practice [35; 37]. This concept for healthcare delivery is familiar from many other areas of the NHS, including cardiovascular, cancer and trauma networks [38; 39]. A recent publication examined the volumes of rKA performed in different surgical units across the UK [40]. However, more detailed information is needed to better understand this care pathway beyond that available from aggregate data. This includes information on the characteristics of the patients being operated on in different types of surgical unit, the patterns for referral and the procedures themselves.

1.7 Patient-relevant outcomes following elective, aseptic revision knee arthroplasty

This thesis will investigate *patient-relevant outcomes* following elective, aseptic rKA. The domains of outcome to be studied have been extrapolated from evidence developed for pKA [41] after discussion with the SORE (Surgery Or REstraint for elective, aseptic revision) knee arthroplasty Patient and Public Involvement group, which was set-up to support the delivery of this thesis. This section will define the outcome measures of interest and provide a brief summary of what is already known. A formal review of the literature will be provided in Chapter 4. Before

discussing specific outcome measures, this section will begin with a theoretical discussion of the definitions for *success*, *revision* and *failure*.

Success, revision and failure

Implant survivorship is widely used to judge the success or failure of joint replacement. The advantages of this approach include its objectivity, ease of measurement and ability to identify a discrete point in time at which the event took place. However, revision (and re-revision) surgery are relatively uncommon, and so this endpoint lacks sensitivity to judge the outcome [42]. Implant survivorship dichotomises the joint replacement population into *revised* or *not revised* at a given point in time. An important limitation is evident when the *not revised* group is interpreted to mean that the intervention has been a *success*. This is easily understood with the following examples. First, consider the patient in pain following pKA. When the outcome for that patient is measured using implant survivorship alone, the procedure is considered to be a success until a revision occurs. Second, consider the patient who undergoes one or more re-operations that do not qualify as a revision. The impact of these operations is not accounted for. In recognition of these limitations, there have been an increasing number of calls over the past decade to measure the outcome from surgery from the perspective of the patient [43; 42; 44].

It is also important to consider the similarities and differences between the terms *revision* and *failure* - though this thesis will largely use the terms interchangeably. In many cases, revision surgery is indicated because a prosthesis has failed. The joint replacement revised because a component has worn out or become loose provides a nice exemplar. However, not all revisions are for a failed implant. For example, consider the partial knee replacement that itself is mechanically sound and asymptomatic, but requires revision because another compartment of the knee has worn out. This idea of a difference between *revision* and *failure* can also be explored in a temporal sense. Consider a knee replacement that is loose and painful in a patient who requires medical optimisation before surgery. The joint may be

considered to have failed long before it is revised. Indeed, a failed knee replacement may never be revised - for example, in a patient who chooses to avoid further surgery or dies before a scheduled revision operation. However, defining the time to a failure is often difficult as joint replacements are not under continuous surveillance and not all failures are symptomatic. For time-to-event analyses in this thesis, the *time-to-(re-)revision* (calculated from the difference in dates between joint replacement surgeries) will be considered to be the same as the *time-to-failure*.

Implant survivorship

A definition for re-revision KA has been provided above. Deere et al [45] recently reported on implant survivorship following first and multiple rKA procedures using data from the National Joint Registry (NJR) for England, Wales, Northern Ireland, the Isle of Man and the States of Guernsey. This study included both elective and urgent procedures and reported Kaplan Meier survivorship estimates of 96.4% at 1-year, 87.4% at 5-years and 82.9% at 10-years following first rKA.

Patient-reported outcome measures

Whilst clinicians can recognise impairment and disability, only patients can report symptoms and quality of life [43]. Prioritising patients' views has become an essential component of delivering patient-centred surgery [46]. Patient-reported outcome measures (PROMs) are increasingly used to capture this perspective. PROMs measure patients' perceptions on the impact of a condition or a treatment on their health [47]. PROM instruments can broadly be divided into two types: *generic* and *disease-specific*.

Generic PROMs The Constitution of the World Health Organisation (WHO) defines health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" [48]. Some instruments have been designed to measure health in a general way and can be used across a range of conditions and patient groups [49]. These are termed generic PROMs and

measure HRQoL. Examples include The 36-Item Short Form Survey (SF-36) [50] and the EQ-5D [51].

Disease-specific PROMs Other PROM instruments are designed for a specific health condition. These are termed disease-specific PROMs. Within this thesis, instruments measuring domains of pain, function, combined pain and function, joint-related health status or patient activity have been termed *joint-specific* PROMs. The individual PROM instruments of interest will be identified from a systematic review in Chapter 3 and discussed accordingly. PROMs have been defined as self-report instruments in this thesis. Any instrument partly or entirely completed by a clinician does not meet this definition. As such, examples of instruments that would not be considered PROMs include: The Knee Society clinical rating system [52] and the Bristol Knee Score [53].

Mortality

Death is a rare adverse event following knee replacement surgery. The NJR recently estimated that the overall cumulative percentage probability of death was 0.31% (95% CI 0.30-0.33) at 90-days following pKA [54]. This probability corresponded most closely to the risk observed for patients aged 70-74 years. As might be expected, the observed mortality rate was lower for younger patient groups, and higher for older patient groups. For rKA, the overall mortality rate was approximately double that of pKA, with a Kaplan-Meier estimate of 0.60% (95% CI 0.52-0.69) at 90-days. Several studies have observed a higher mortality rate for septic compared to aseptic rKA [55; 56; 57]. The Norwegian Arthroplasty Register (NAR) reported 90-day mortality of 1.2% following revision for PJI [58]. Another study found that, at 5 years, the mortality rate for septic revisions was 25.9% compared to 12.9% for aseptic revisions [56]. These mortality rates need to be interpreted in the context of other patient predictors (such as age and comorbidity burden); however, the apparently high figures have been used to support recent calls for multi-disciplinary team (MDT) management of these cases [59]. An important

methodological point is worth highlighting. When studying mortality following joint replacement, researchers must be cognisant of the 'healthy surgical patient effect' [60]. This is where patients undergoing joint replacement have been observed to have lower mortality rates than their counterparts in the general population with similar disease profiles. This is likely to be due to residual confounding, where patients selected for joint replacement surgery are healthier than those not selected, but some of the factors responsible for their better health are not measured [61].

Serious complications

A serious complication can be defined as an adverse event requiring re-admission to hospital. Serious complications have recently been reported for many types of elective orthopaedic surgery including arthroscopic partial meniscectomy [62], arthroscopic shoulder surgery [63] and elective shoulder replacement [64] using national, routinely collected data. These complications can be divided into medical (such as cardiac, central nervous system, deep venous thrombosis, pulmonary embolism, genitourinary, renal, and respiratory complications) or surgical (such as deep surgical site infection and wound dehiscence).

Hospital admission impact

For pKA, patients also identified the duration of the hospital admission for the index surgery and the requirement for high-dependency or intensive care were also important factors influencing their decision to choose surgery [41].

1.8 Unexplained pain after revision knee arthroplasty

Some patients enter the rKA care pathway with pain, but no diagnosis is ever reached to explain their symptoms. These patients are termed as having *unexplained pain*. This group is of interest as there is uncertainty as to how they are best managed. A recent review noted the low quality of the evidence base, finding only one randomised controlled trial of a pharmacological intervention for

the management of chronic pain after KA and no trials on multi-disciplinary interventions [65]. Lack of evidence is known to be an important driver of unwarranted variation in care.

The NIHR STAR study recently reported on the increasing burden of long-term pain after pKA [66], highlighting the complexity of interventions for this condition and the need for evaluative science to develop new care pathways [5; 67]. The programme highlighted the need for a multi-disciplinary approach, with appropriate expertise recruited from healthcare professionals across primary and secondary care (e.g. pain management clinicians, physiotherapists, occupational therapists and general practitioners) [65]. However, a notable omission was that rKA was not considered as a potential treatment for unexplained pain. This is despite previous research suggesting rKA might have some efficacy for this patient group [31].

Previous research from our group has helped us to understand the ways a problematic knee replacement impacts on patients' lives and the impact of rKA [68]. This thesis will investigate patient-relevant outcomes following surgery for unexplained pain and surgeon considerations around the decision to offer surgery to this patient group.

1.9 Thesis scope and structure

The scope of this thesis is to investigate the epidemiology of, and patient-relevant outcomes following, elective, aseptic revision knee arthroplasty (rKA). The main concepts from which the thesis is built were introduced earlier in the chapter. Each subsequent chapter will include an introduction, to define the aims and to describe further concepts as necessary, followed by methods, results and discussion sections. The final chapter will summarise the main findings from each chapter and directions for future research.

- **Chapter 2: Epidemiology of revision knee arthroplasty.** The first part of the chapter investigates trends over time in the national delivery of rKA.

The second part of the chapter examines the operative practice of a high-volume revision centre, in order to define the complexity of the operative caseload and patterns of referral.

- **Chapter 3: Usage and measurement properties of PROMs in elective, aseptic rKA.** The first part of the chapter includes (i) a scoping review to identify PROMs currently used to measure joint function and HRQoL following elective, aseptic rKA; and (ii) a systematic review using the COnsensus-based Standards for selection of health status Measurement INstruments (COSMIN) checklist to investigate the measurement properties and the quality of the evidence for PROM validation studies in this population. The second part of the chapter investigates the measurement properties of the Oxford Knee Score for elective, aseptic rKA since no validation study was found, despite routine use of the instrument in the NHS PROMs programme.

- **Chapter 4: Patient relevant outcomes following elective, aseptic rKA compared to non-operative management.** This chapter combines three systematic reviews. Review 1 investigates randomised and non-randomised comparative studies of patient-relevant outcomes of elective, aseptic rKA to one or more alternative forms of treatment. Review 2 investigates uncontrolled studies of patients treated with non-operative management for a failed KA due to an elective, aseptic indication. Review 3 investigates uncontrolled studies of patients treated with elective, aseptic rKA.

- **Chapter 5: An investigation of patient relevant outcomes by diagnosis using routinely collected data from the NJR, HES, NHS PROMs and Civil Registrations of Deaths.** This chapter investigates patient relevant outcomes for different indications for elective, aseptic and urgent rKA using data from a national cohort of over 30,000 rKA. The systematic review in Chapter 4 did not provide sufficient information to support patients to understand the risks and benefits of rKA for different indications. This

information is critical to support patients with the decision to choose surgery or not.

- **Chapter 6: The experience of surgeons treating unexplained pain after knee replacement: a reflexive thematic analysis.** This chapter includes a qualitative study to gain a deeper understanding of the experience of surgeons treating patients with unexplained pain after knee replacement.
- **Chapter 7: Conclusions and future work** This chapter summarises the main findings from the thesis and directions for future work.

2

Epidemiology of revision knee arthroplasty

Contents

This chapter investigates the epidemiology of rKA in the UK for the past fifteen years. This includes the number of rKA performed each year, the reasons for surgery and analysis of trends over time. The background literature describing the epidemiology of rKA has been provided earlier. While the focus of this thesis is on elective, aseptic rKA, I have included all rKA in this chapter (including 'urgent' cases), since this information may be of interest to readers whose scope extends

beyond that of the thesis. The chapter begins with analysis of national trends in rKA activity. The second part of the chapter investigates operative activity at a high-volume revision centre, using data not available within national datasets, to better understand the complexity of these cases and the patterns of referral.

This chapter has been published as two papers:

- *Sabah SA, Knight R, Alvand A, et al. No exponential rise in revision knee replacement surgery over the past 15 years: An analysis from the National Joint Registry. Osteoarthritis and Cartilage. 2022. doi: 10.1016/j.joca.2022.08.016*
- *Sabah SA, von Fritsch L, Khan T, et al. Revision total knee replacement case-mix at a Major Revision Centre. J Exp Orthop. 2022;9(34). doi: 10.1186/s40634-022-00462-2*

2.1 National trends in revision knee arthroplasty over the past 15 years

2.1.1 Aim

The aim of this study was to investigate trends in the incidence and the main indication for rKA over the past 15 years in the UK.

2.1.2 Methods

This study is reported according to the RECORD checklist [69]. Ethical approval was obtained from the London-Bromley Research Ethics Committee (20/LO/0428) and data access approvals were obtained from the NJR. Data for patients who chose not to consent to the NJR audit were not included.

2.1.2.1 Study dataset

The NJR is a prospective register of primary and revision joint arthroplasty procedures in England, Wales, Northern Ireland, the Isle of Man and the States of Guernsey. Data collection started in 2003 and the submission of records to

the NJR is mandatory for both National Health Service (NHS) and independent centres within its geographic remit. Records are submitted to the NJR using Minimum Data Set (MDS) forms that specify the procedures to be recorded. Each form is specific to a particular joint (e.g. knee) and broad category of procedure (e.g. primary or revision). For example, data for rKA are collected on K2 forms and include patient demographics, operation details and surgeon details.

The NJR originally defined *revision joint arthroplasty* as any "operation performed to remove and replace one or more components of a total joint prosthesis, for whatever reason" [70]. There were several modifications to the definition over the study period and to procedure specifications on MDS forms. The most recent definition of *revision* is "any operation where one or more components are added to, removed from or modified in a joint arthroplasty or if a Debridement And Implant Retention (DAIR) with or without modular exchange is performed" [29].

2.1.2.2 Timeframe

Data from 1st January 2006 to 31st December 2020 were analysed. This provided fifteen years of data for analysis, and excluded data from the first three years of the NJR (2003-2005) which are known to have the lowest rates of registry compliance [23,24]. I also excluded data from 2021 because: (i) our NJR data extract was created on 3rd February 2022, which provided only a short opportunity for late submission of data; and (ii) population statistics from the Office for National Statistics (ONS) were not available for 2021.

2.1.2.3 Inclusion and exclusion criteria

Study inclusion and exclusion criteria are illustrated in Figure 2.1.

2.1.2.4 Trends over time in the incidence of rKA

The crude incidence of rKA was calculated for each calendar year from 2006 to 2020. The rationale for calculating incidence (rather than count data only) was to standardise for changes over time in the usual resident population. In some cases rKA is planned to be performed as a two-stage procedure: consisting of

two distinct operations on different days. For a given patient, I considered first- and second-stage rKA procedures to be a single procedure when they met the following criteria: the NJR K2 form indicated the intention to treat the patient in stages and a second-stage procedure was performed within 365 days of the first-stage procedure. The year of surgery was taken from the date of the first-stage procedure. To calculate crude incidence, I used the annual total count of rKA procedures (numerator) and the sum of the mid-year population estimates for adults in England, Wales and Northern Ireland (denominator). 95% confidence intervals (CIs) were calculated for these rates using the *phe_rate* function within the *PHEindicatormethods* package in R [71; 72]. I have presented crude incidences as a line graph overlying bars depicting annual total counts. As a further analysis, I have indicated whether or not the rKA procedure was linked to a pKA on the NJR. The proportion of rKA procedures linked to a pKA over time was presented as a line graph overlying stacked bars depicting annual total counts. Due to the large proportion of rKA not linked to a pKA and large changes in this proportion over time, I did not consider it appropriate to present incidences for rKA stratified into first- and subsequent rKA procedures.

I used the methodology above to calculate total counts and crude incidences for pKA and have presented these for reference. It is important to highlight that the incidence of rKA within a given year has little relationship to the incidence of pKA in that year (because very few pKA fail within one year). The incidence of rKA has a more direct relationship to the prevalence of (primary and revision) knee arthroplasty in the population. I did not consider it appropriate to estimate the prevalence of knee arthroplasty given the relatively short existence of the NJR and the longevity of knee arthroplasty implants.

As a supplementary analysis, I also calculated directly standardised rates (DSRs) for pKA and rKA. These allow better comparison of populations with different age-structures. Office for National Statistics (ONS) mid-year population estimates were used to calculate changes in the usual resident population. Since Scotland has its own arthroplasty register and does not contribute cases to the NJR, I filtered out

population data for Scotland. This left data for England, Wales and Northern Ireland, which - for simplicity - I have continued to refer to as the 'UK population'. A further note is that - in recent years - the NJR has started to collect cases from regions that are not part of the UK (i.e. the Isle of Man and the States of Guernsey). I have not accounted for this in mid-year population estimates and, as such, have chosen to accept a small error. The total UK population increased in size every year over the study period, with overall growth of 10.1% from mid-2006 (55,693,967 persons) to mid-2019 (61,333,507 persons). The adult population (i.e. persons aged 18 years or older) increased by 10.9% from mid-2006 (43,511,312 persons) to mid-2019 (48,239,295 persons) [73].

Direct standardisation was performed using Byar's method with Dobson method adjustment as recommended by Public Health England [71]. I used the *phe_dsr* function within the *PHEindicatormethods* package in R for all calculations. The 2013 European Standard Population (ESP) was used as the standard population. This is a theoretical population of 100,000 persons based on European Union states' population projections for 2011 - 2030. The population structure is described in five-year age groups, where the first group is 0-4 years and the last group 90 years and older. Since it is the adult population that is relevant for pKR and rKR, I truncated and recategorised the European Standard Population into the following age groups: *18-49 years/ 50-59 years/ 60-69 years/ 70-79 years/ 80+ years*. To calculate the size of the 18-59 years age group, I calculated the total of all age groups from 20-24 years to 45-49 years, and then added two-fifths of the total of the 15-19 years age group. Finally, the resulting vector was transformed to provide a standard population of 100,000 persons.

2.1.2.5 Trends over time in the incidence of rKA by patient age

To investigate trends over time in the incidence of rKA according to patient age, I stratified the study population into the age groups described above. Crude incidences per 100,000 persons were calculated for each group for each year of analysis and presented graphically.

2.1.2.6 Trends in the main indication for rKA

Each rKA procedure was assigned a single, dominant diagnosis based on the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) hierarchical model [8] (Table 1.3). I then combined data for all years of the dataset and calculated the percentage frequency of each revision diagnosis.

To investigate trends over time in the main indication for revision surgery, I calculated crude incidences per 100,000 adults for each diagnosis for each year of the dataset for all rKA procedures and presented these using grouped barplots. As a supplementary analysis, I calculated the annual percentage frequency of each revision diagnosis.

I then investigated first- and subsequent rKA procedures. I defined the following groups: *first linked rKA* (the earliest revision procedure for a given patient-side linked to a primary knee arthroplasty on the NJR); *second linked rKA* (the next revision procedure for a given patient-side linked to a first linked rKA); *third or more linked rKA* (subsequent revision procedure(s) linked to a second linked rKA); and *no linked primary* (revision procedure(s) not linked to a primary procedure).

2.1.2.7 Software

Statistical analyses were performed using R version 4.1.2.

2.1.3 Results

2.1.3.1 Data cleaning and linkage

A flowchart to illustrate attrition of study records during data cleaning is provided in Figure 2.1.

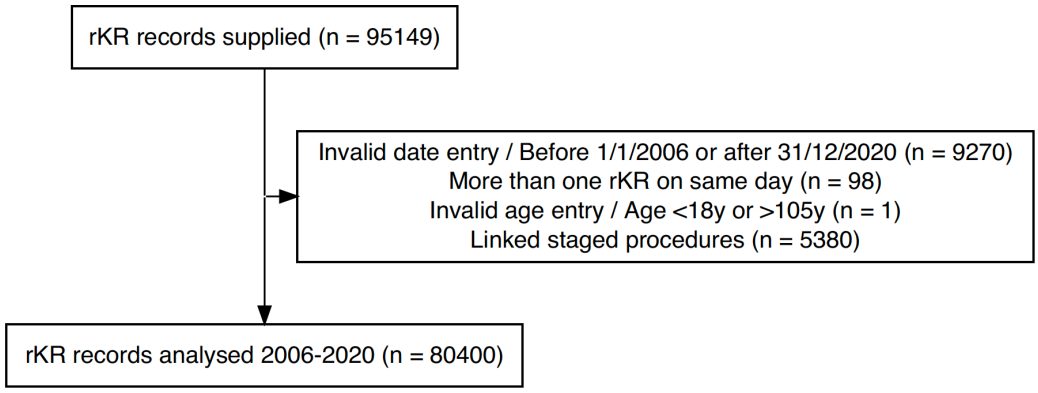

Figure 2.1: Flowchart demonstrating attrition of study records during data cleaning.

2.1.3.2 Trends over time in the incidence of rKA

The annual totals of rKA procedures submitted to the NJR and the crude incidences are presented in Table 2.1 and Figure 2.2. Annual totals of rKA procedures reported to the NJR increased year-on-year from 2006 to 2019, with the exception of 2013 and 2018. There were 2743 rKAs reported to the NJR in 2006, compared to 6819 rKAs in 2019. Annual increases in the incidence of rKA became smaller over the study period, indicating a slowing in the rate of increase. There was a 43.6% reduction in total number of rKA procedures in 2020 (during the Covid-19 pandemic) compared to 2019. The annual total count of rKA increased by 149% over the study period. The incidence of rKA increased from 6.3 per 100,000 adults in 2006 (95% CI 6.1 to 6.5) to 14 per 100,000 adults in 2019 (95% CI 14 to 14). There were large increases in the incidence of pKA over the study period from 116 per 100,000 adults in 2006 (95% CI 115 to 117) to 227 per 100,000 adults in 2019 (95% CI 226 to 228) (Figure 2.2).

Table 2.1: Annual totals and incidences of rKA

	Years														
	2006	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Annual totals of rKR procedures															
All rKR	2743	3776	4254	4667	5142	5269	5994	5646	6142	6371	6552	6623	6559	6819	3843
No linked primary	2621	3187	3111	2987	3017	2958	2964	2684	2709	2553	2442	2274	2001	1958	1084
First linked rKR	118	553	1059	1568	1957	2100	2715	2608	2985	3315	3541	3783	3926	4208	2303
Second linked rKR	4	29	77	99	148	186	276	307	378	409	446	442	499	503	356
Third or more linked rKR	0	7	7	13	20	25	39	47	70	94	123	124	133	150	100
Incidence rates of rKR															
Crude incidence rate per 100,000 adults	6.3 (6.1 - 6.5)	8.6 (8.3 - 8.9)	9.6 (9.3 - 9.9)	10.4 (10.1 - 10.7)	11.4 (11.1 - 11.7)	11.6 (11.2 - 11.9)	13.1 (12.7 - 13.4)	12.2 (11.9 - 12.5)	13.2 (12.9 - 13.5)	13.6 (13.2 - 13.9)	13.8 (13.5 - 14.2)	13.9 (13.6 - 14.2)	13.7 (13.3 - 14)	14.1 (13.8 - 14.5)	7.9 (7.7 - 8.2)
Age-specific incidence rate per 100,000 persons															
18-49 years	0.4 (0.3 - 0.5)	0.6 (0.5 - 0.7)	0.6 (0.5 - 0.7)	0.9 (0.8 - 1)	1 (0.9 - 1.1)	0.8 (0.7 - 0.9)	1 (0.9 - 1.2)	0.9 (0.8 - 1)	1 (0.8 - 1.1)	0.9 (0.8 - 1.1)	0.9 (0.8 - 1)	0.9 (0.8 - 1)	0.8 (0.7 - 0.9)	0.7 (0.6 - 0.8)	0.4 (0.4 - 0.5)
50-59 years	5.5 (4.9 - 6.1)	7.4 (6.8 - 8.1)	9.7 (9 - 10.5)	10.8 (10.1 - 11.7)	11.6 (10.8 - 12.5)	11.7 (10.9 - 12.6)	14.8 (13.9 - 15.7)	13.1 (12.3 - 14)	13.3 (12.5 - 14.2)	13.1 (12.3 - 13.9)	13.2 (12.4 - 14)	12.8 (12.1 - 13.7)	11.4 (10.7 - 12.1)	12.3 (11.5 - 13.1)	6.2 (5.7 - 6.7)
60-69 years	16.6 (15.5 - 17.8)	23.7 (22.4 - 25)	24.1 (22.8 - 25.4)	25.8 (24.6 - 27.2)	27.8 (26.5 - 29.2)	28.1 (26.8 - 29.4)	31.8 (30.4 - 33.3)	29.2 (27.8 - 30.5)	30.7 (29.4 - 32.1)	31.5 (30.2 - 32.9)	31.6 (30.2 - 33)	32.1 (30.7 - 33.5)	32.3 (30.9 - 33.7)	32.2 (30.8 - 33.6)	16.6 (15.6 - 17.6)
70-79 years	26.1 (24.5 - 27.8)	34.9 (33.1 - 36.9)	39.4 (37.4 - 41.4)	40.8 (38.8 - 42.8)	44.8 (42.7 - 46.9)	46.7 (44.6 - 48.9)	48 (45.8 - 50.2)	44.8 (42.7 - 46.9)	50.5 (48.3 - 52.7)	50.9 (48.8 - 53.1)	52 (49.9 - 54.2)	50.9 (48.8 - 53)	48.8 (46.9 - 50.9)	50.1 (48.2 - 52.2)	28.5 (27.1 - 30)
80+ years	19.1 (17.3 - 21.1)	23.9 (21.9 - 26.1)	27 (24.9 - 29.3)	28 (25.9 - 30.3)	29.7 (27.5 - 32)	29.8 (27.6 - 32)	33.4 (31.2 - 35.8)	34 (31.7 - 36.3)	35 (32.8 - 37.4)	38.1 (35.8 - 40.6)	38.7 (36.3 - 41.1)	39 (36.7 - 41.5)	40.4 (38 - 42.9)	41.1 (38.8 - 43.6)	26.2 (24.3 - 28.2)

The percentage of rKA procedures linked to a pKA on the NJR increased from 4.4% in 2006 to 71.3% in 2019 (with a further increase to 71.8% in 2020) (Figure 2.3).

Directly standardised rates of pKR and rKR are plotted together with crude incidences in Figure 2.4. These rates may be useful for other countries or regions wishing to compare their rate of intervention to the UK, accounting for differences in population age structure.

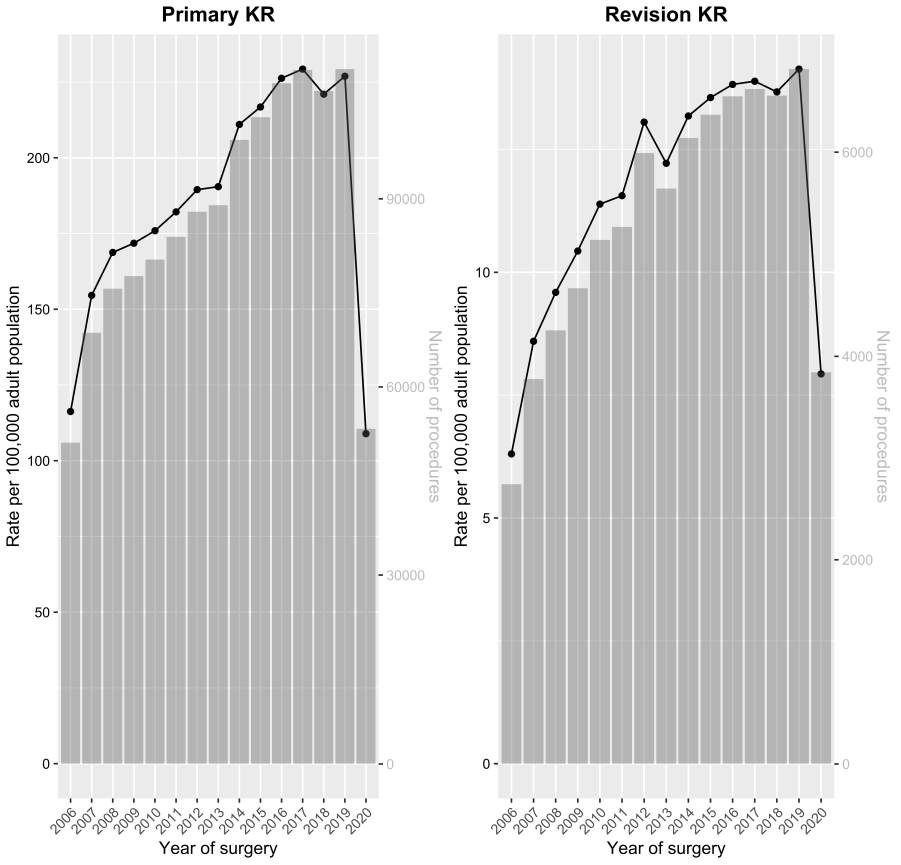

Figure 2.2: Annual crude incidences (line, left y-axis) and total counts (bars, right y-axis) of pKA and rKA from 2006-2020. Note the differences in y-axis scales for pKA and rKA

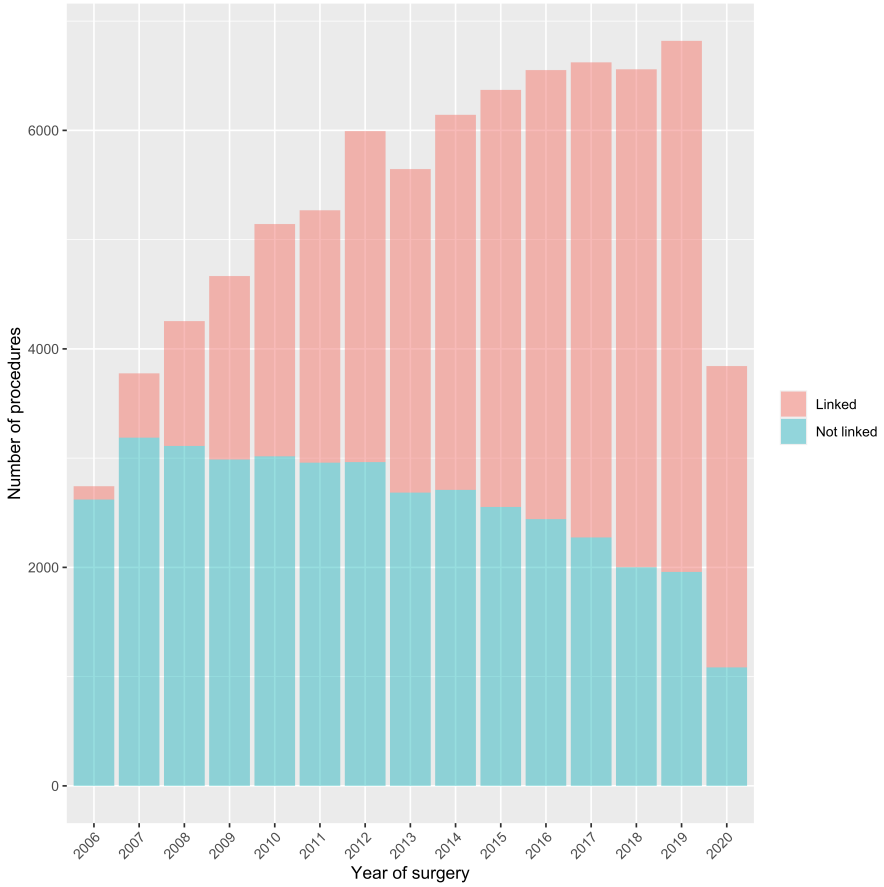

Figure 2.3: Annual total counts of linked and not linked rKA

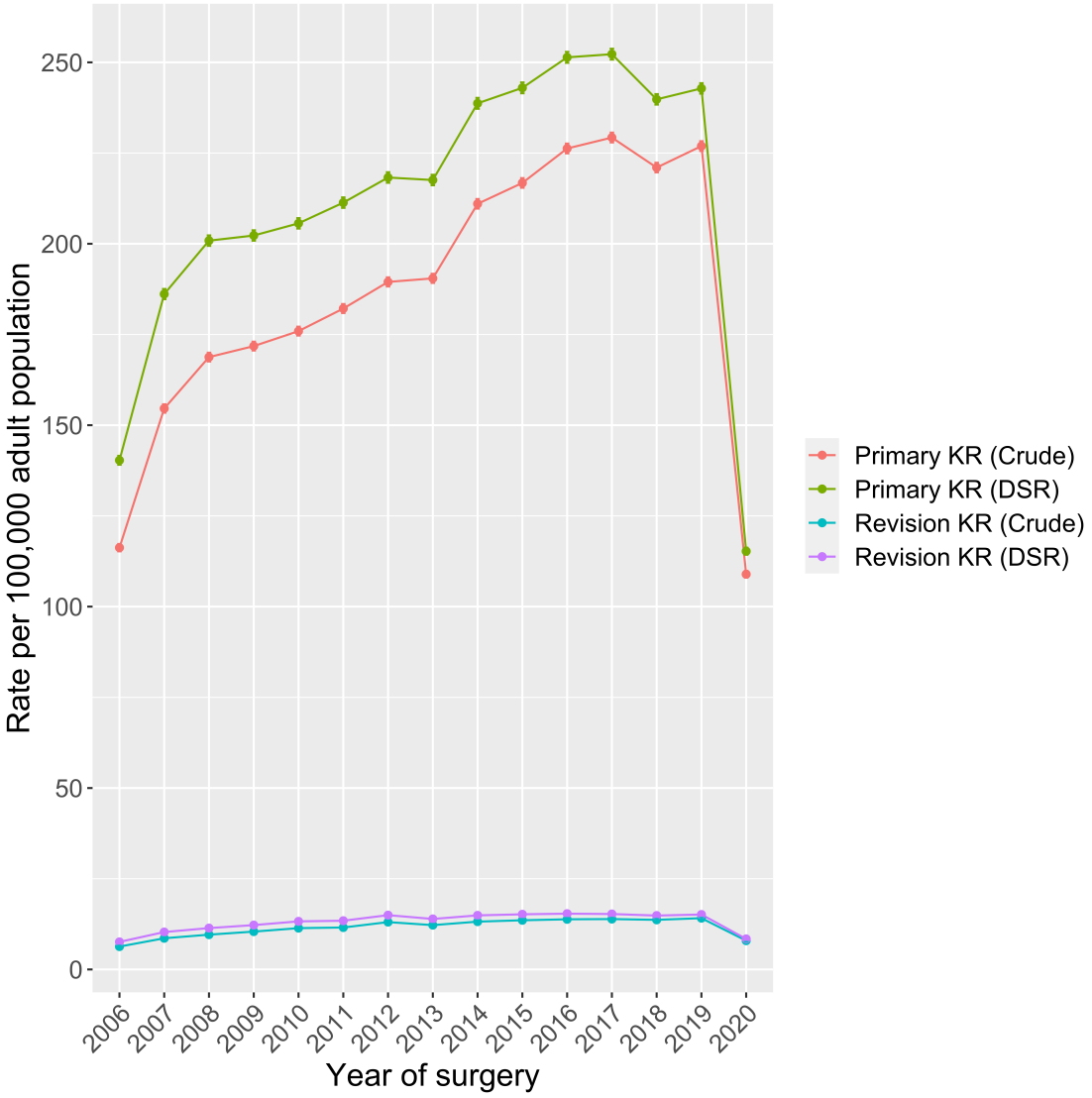

Figure 2.4: Directly standardised rates (DSR) (using European Standard Population 2013) and crude rates of pKR and rKR from 2006-2020.

2.1.3.3 Trends over time in the incidence of rKA by patient age

The incidence of rKA increased for all age groups over the study period. The largest increases were seen in the 70-79 year age group, followed by the 80+ year age group. These two age groups also had the highest incidences of rKA among the age groups studied. In 2019, the incidence of rKA for patients aged 70-79 years was 50 per 100,000 adults [95% CI 48 to 52]) (Figure 2.5).

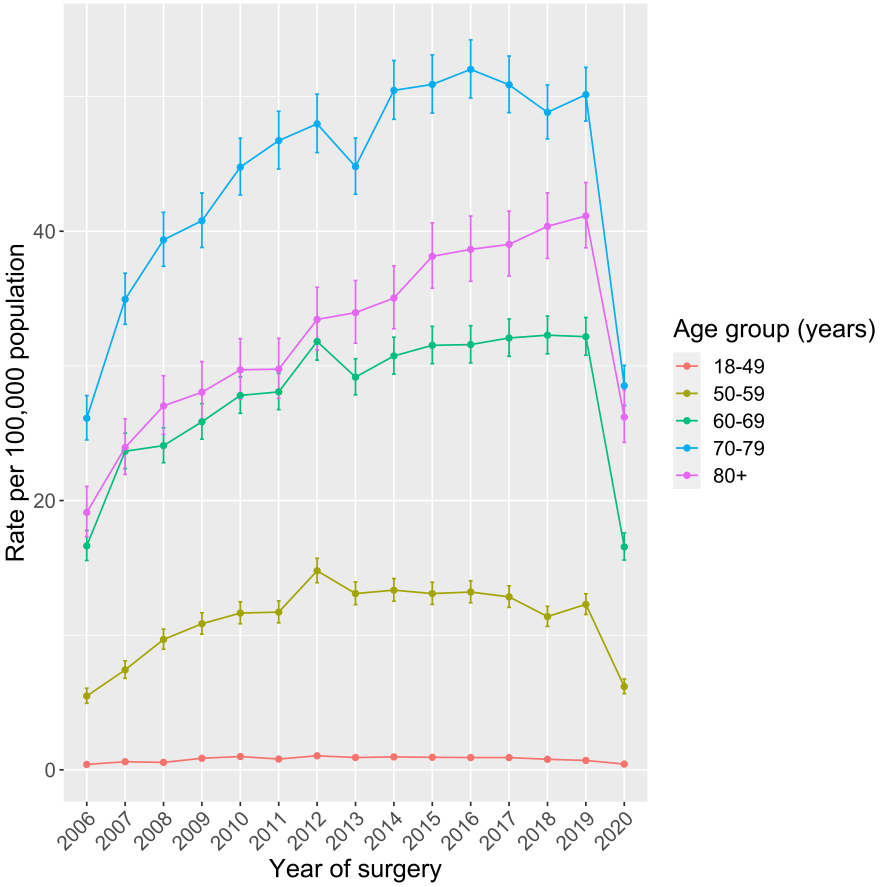

Figure 2.5: Annual incidences of first linked rKA from 2006-2020 by age group.

2.1.3.4 Trends in the main indication for rKA

For all years of the study combined, aseptic loosening was the most frequent indication for rKA (20.5%), followed by infection (16.4%) and then instability (15.4%) (Figure 2.8). The incidence of rKA for aseptic loosening peaked in 2012 and subsequently declined (Figure 2.6). Meanwhile, the incidence of rKA for infection increased nearly every year - from 0.9 per 100,000 adults in 2006 (95% CI 0.8 to 1) to 2.7 per 100,000 adults in 2019 (95% CI 2.6 to 2.9). Infection was the most common indication for rKA in 2019, followed by progressive arthritis (2.5 per 100,000 [95% CI 2.3 to 2.6]), then aseptic loosening (2.3 [95% CI 2.2 to 2.5]). The incidences of rKA for instability, periprosthetic fracture, progressive arthritis and stiffness demonstrated nearly year-on-year increases over the study period. However, rKA for unexplained pain and 'other' reasons peaked in 2012 and have since declined.

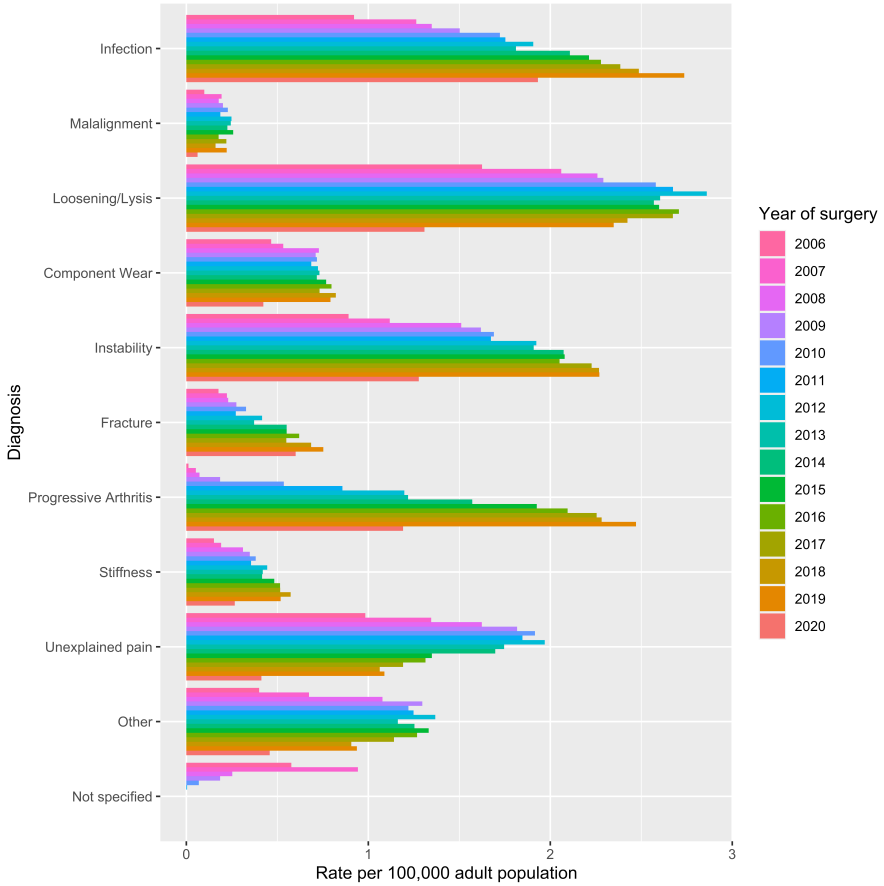

Figure 2.6: Grouped barplots demonstrating annual incidences for all rKA by indication for surgery from 2006-2020. Diagnoses are ranked in hierarchical order (greatest importance at the top).

Changes in the annual *proportions* of each revision indication are presented in Figure 2.7. These data are best interpreted with reference to the total number of rKA in a given year. For example, whilst the *proportion* of rKA for aseptic loosening/lysis was lower in 2019 compared to 2006, the crude incidences was higher in 2019 compared to 2006.

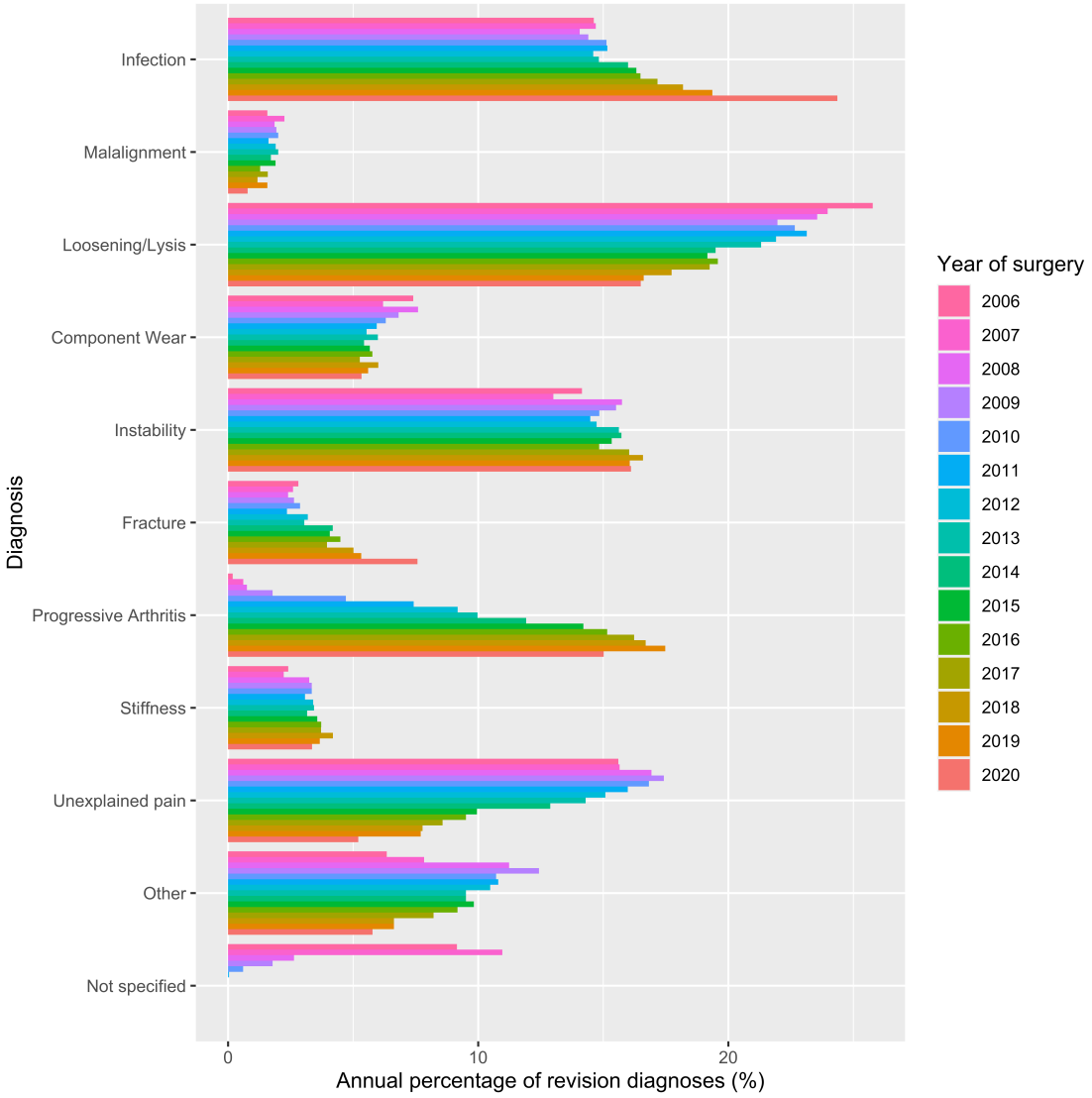

Figure 2.7: Grouped barplots demonstrating changes in the annual proportions of each revision diagnosis for all rKR from 2006-2020. Diagnoses are ranked in hierarchical order (greatest importance at the top).

For re-revision procedures (which were linked to a pKA), infection was the most frequent indication for revision (Figure 2.8). Infection accounted for 17.2% for *first linked rKA*, 36.7% for *second linked rKA* and 50.7% for *third or more linked rKA*.

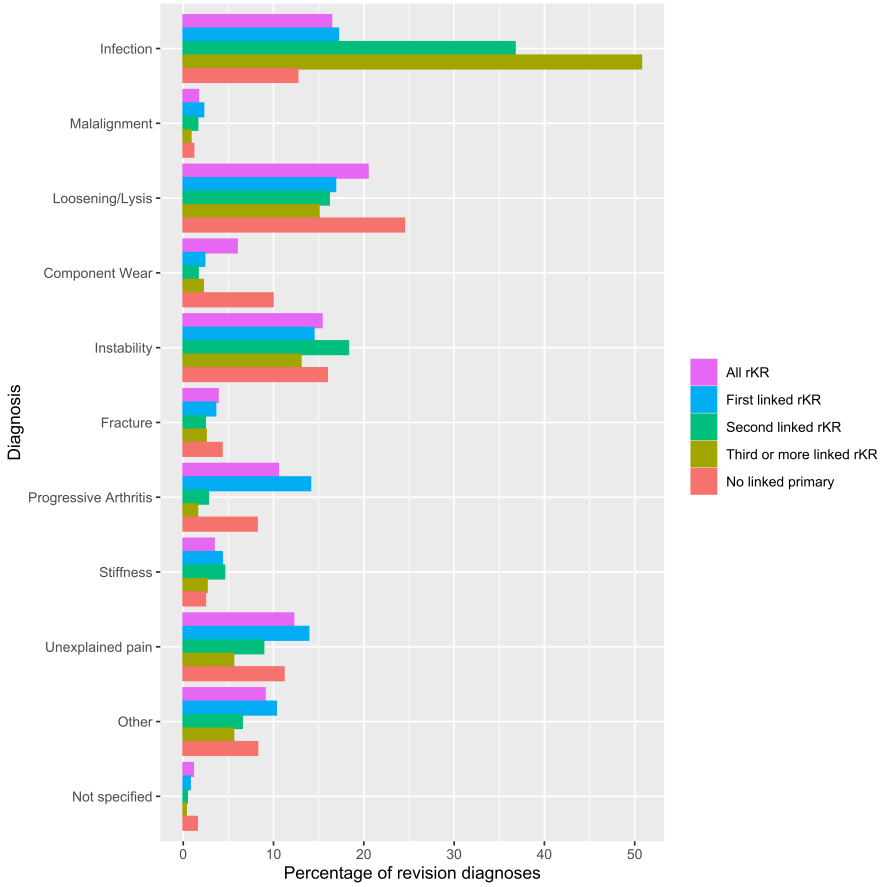

Figure 2.8: Percentage frequency of each indication for first and re-revision KA. Diagnoses are ranked in hierarchical order (greatest importance at the top). For a given procedure (e.g. First linked rKA), the sum of all diagnoses is 100 percent.

2.1.4 Discussion

Over the past fifteen years, annual reports of rKA to the NJR increased by 149%. While the incidence of rKA is still increasing, the rate of this increase appears to be slowing down rather than increasing exponentially as previously projected [17; 74]. There was a 43.6% reduction in total rKA procedures in 2020 compared to 2019 due to the impact of Covid-19. This is similar to the reduction of ~50% reported for primary joint arthroplasty [75]. The percentage of rKA procedures linked to a pKA on the NJR increased from 4.4% in 2006 to 71.3% in 2019.

The highest incidences for rKA were in patient groups aged 70 years and older. These older patient groups also experienced the greatest increase in the incidence of rKA over the study period. For all years of the study combined, aseptic loosening

was the most frequent indication for rKA (20.5%), followed by infection (16.4%). However, in recent years, procedures for infection appear to be increasing and those for aseptic loosening reducing. In 2019, infection was the most frequent indication for rKA. For rKA procedures linked to a pKA, infection accounted for 17.2% for *first linked rKA*, 36.7% for *second linked rKA* and 50.7% for *third or more linked rKA*.

Lewis et al [25] recently reported incidences for rKA using registry data from Australia, Sweden and the United States. Their study provides an exemplar for international registry collaboration. Similar to our study, they observed slowing of the rate of increase of rKA procedures over a fifteen year period. For the year 2017, they reported an incidence of rKA of 19.5 per 100,000 persons in Australia, 9.4 per 100,000 persons in Sweden and 11.8 per 100,000 (insured) persons in the United States (from the Kaiser Permanente Joint Replacement Registry). I have identified a rate of rKA of 14.1 per 100,000 adults in 2019. It is important to note our use of a different denominator, which I believe reflects the population of interest. However, in order to provide closer comparison to the aforementioned study (ignoring differences in population age structures), the incidence of rKA in the UK in 2019 was 11.1 per 100,000 total population (i.e. adults and children). More recently, a follow-up study from Lewis et al [76] reported trends in the indications for rKA. They found increases in the proportion of revisions for infection and decreases in the proportion of revisions for wear across the three registries they studied. I observed largely similar trends in the UK. To provide greater interpretation, our study has taken the approach of presenting crude incidences, as well as reporting changes in proportions of rKA for each diagnosis over time. I have also explored the indications for re-revision KA procedures, demonstrating the the high prevalence of infection.

The information I have presented here should be considered to complement that presented by the NJR in its annual reports. The NJR regularly present count data (i.e., totals) of procedures, which can be used to understand overall surgical activity. This has useful applications - for example, for workforce planning and budget allocation. The approach here of calculating incidences has shown that the

observed increases in annual totals of rKA reflected both an increase in the size of the adult population and an increase in the intervention rate. One of the strengths of this study is its reproducibility and openness. All results are derived directly from the underlying source data and the statistical code used to prepare the data is provided as a supplementary file [77]. I believe that this is the first study using the NJR dataset to take this approach.

However, there are a number of limitations to our study that should be noted. It is likely that some of the trends I have described represent changes in reporting practices, rather than operative activity. I have provided some mitigation by excluding the earliest years of the NJR dataset, but surgeon compliance for reporting of rKA procedures continued to improve over the study period [78; 79; 29]. Latest figures from the NJR data quality audit suggested that only ~5% of rKA procedures were not reported to the NJR in 2018/19, and this proportion is expected to shrink further in coming years. I have used a diagnosis hierarchy to classify a single dominant diagnosis for rKA when the NJR allows multiple indications to be specified. I recognise that there is subjectivity in this process, and the hierarchy I have adopted may not reflect the *true* order of importance for all cases. Whilst I have chosen to present the proportion of diagnoses for first and subsequent rKA procedures, I caveat that readers give consideration to the high proportion of unlinked rKA procedures over the study period. As such, this analysis is biased towards indications that result in earlier revision procedures and may change as the registry matures.

Our study has shown the profound effect of the Covid-19 pandemic on rKA activity. Waiting lists for surgery are currently at record levels [80] and operative activity will need to increase to treat the backlog of patients. The recent observation that many areas of the UK have struggled to return to pre-pandemic levels of primary joint arthroplasty frames this challenge in stark terms [75]. It is also important to recognise that, prior to the pandemic, annual increases in rKA activity were slowing. There may be positive reasons for this, such as improvements in the

outcome following primary joint arthroplasty [81], or greater adoption of evidence-based indications for surgery. The observation that rates of surgery for 'unexplained pain' have reduced over time supports this, though it is possible that surgeons have simply changed their coding practices. Another possible explanation for the smaller than expected increase in the rate of rKA is a lag in time between increases in primary KA and the need for revision surgery (though it is evident that increases in the incidence of primary KA have also slowed). This may provide an indication of the difficulty associated with increasing capacity for joint arthroplasty procedures in the NHS, particularly for rKA procedures which may be resource intensive [82]. The NJR should consider the approach taken in this study of reporting incidence (rather than count data only) to understand how changes in operative activity over time reflect changes in the underlying resident population.

In conclusion, annual reports of rKA to the NJR have increased by 149% over the past fifteen years. While the incidence of rKA is still increasing, the rate of this increase appears to be slowing down. Infection has become the most common indication for rKA and appears to be prevalent in re-revision KA procedures.

2.2 Revision knee arthroplasty case-mix at the Nuffield Orthopaedic Centre, Oxford

2.2.1 Aim

It is evident that large, routinely collected national datasets provide an invaluable perspective on trends in the number and type of rKA procedures performed across the country. However, their reliance on a limited number of administrative codes means that granularity on these procedures is often limited. By way of contrast, consider the surgeon in the outpatient clinic using an Electronic Patient Record (EPR), which holds information from referral letters, previous outpatient appointments and the results of investigations, such as blood tests or imaging. This information may be useful to evaluate the complexity of rKA procedures.

The aims of the current study were to answer the following research questions:

- *What is the surgical complexity of rKA at a Major Revision Centre (MRC) (according to the Revision Knee Complexity Classification, RKCC)?*
- *When, and from where, are patients referred to a MRC?*
- *How does length of stay (LOS) differ between more and less complex rKA?*

2.2.2 Methods

Institutional Review Board approval was obtained for this study.

2.2.2.1 Data sources

I performed a retrospective analysis of our revision knee arthroplasty database over a four-year period from 1st January 2015 to 31st December 2018. This database was created from revision procedures identified from theatre logbooks and the electronic theatre booking system. The number of procedures in the database was compared to the number of procedures identified in summary-level Hospital Episode Statistics Admitted Patient Care (HES APC) data at the centre over the study period to calculate the rate of case ascertainment [83]. The Office

of Population Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS-4) codes used by NHS Digital to produce these summary figures is provided in Appendix A.

2.2.2.2 Inclusion/Exclusion criteria

Revision knee arthroplasty was defined as any procedure to add, exchange or modify an existing joint arthroplasty. This aligns with the latest National Joint Registry definition [29]. As such, debridement, antibiotic and implant retention (DAIR) procedures with or without modular exchange, and the replacement of a further compartment of the knee (such as secondary patella resurfacing or addition of another unicompartmental knee arthroplasty to an existing one) were classified as revision procedures. Revision knee arthroplasty procedures for malignancy were excluded.

2.2.2.3 Patient demographics

Data were extracted on the following variables: age at revision surgery, gender, body mass index (BMI), and Charlson comorbidity index (Summary Hospital-Level Mortality Indicator [SHMI] specification [84]). Since the focus of this paper was on the activity of the surgical unit, each procedure was considered to have been performed in a unique patient for summary purposes. This meant that patients who underwent multiple rKA over the study period (including staged procedures) contributed more than once to summary statistics.

2.2.2.4 Indication for surgery

For each revision procedure, the indication for surgery was defined as a single, dominant diagnosis based on the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) hierarchical system [8] (Table 1.3.

2.2.2.5 Referral patterns

Non-urgent referrals were received via formal written communication to our department from primary or secondary care. Referrals were triaged by a consultant surgeon and then assessed in the outpatient department. Urgent referrals were received through verbal or written communication to our on-call team, and assessed in our Emergency Department or directly transferred as an inpatient to the surgical ward. I classified rKA procedures as 'unplanned' (for acute admissions via the Emergency Department, and inpatient transfers from other centres) or 'elective' (for patients undergoing planned surgery after assessment in the outpatient department).

For patients who were referred to the major revision centre over the study period, the referral source was classified as follows: primary care, primary arthroplasty unit (<20 revisions per year), revision unit (20-70 revisions per year), and major revision centre (>70 revisions per year). The revision volume thresholds for classification represent those proposed by the British Association for Surgeons of the Knee (BASK) Revision Knee Working Group [40]. Classification was based on publicly available 36-month practice profiles from the NJR website [29]. For each case, the number of previous joint arthroplasty procedures on the affected knee was recorded as: first, second, third, or fourth or more.

2.2.2.6 Technical details of revision surgery

The type of revision procedure was recorded in the same format as the NJR K2 MDS version 7 form [2]. The level of constraint of the revision construct and type of implants used were extracted for single stage and stage 2/2 procedures. The complexity of each case was rated according to the RKCC [after review of the electronic patient record and patient imaging [85] (Table 2.2). This provided a three-point ordinal scale where the complexity of surgery was rated as "less complex" (R1), "complex" (R2) or "the most complex/salvage" (R3) according to patient, implant and surgical factors. Each case was rated by one post-certificate

Table 2.2: Revision Knee Complexity Classification (RKCC)

R1 (Revision 1) Less complex revision surgery
For example: - First revision TKR for aseptic loosening - Revision of a partial knee replacement to a total knee replacement - Polyethylene exchange - Debridement, antibiotics and implant retention (DAIR) procedures - No additional complexity factors (such as patient comorbidities or soft tissue inadequacy)
R2 (Revision 2) Complex revision surgery
For example: - First re-revision operation - First revison for PJI - Bone loss requiring supplemental fixation (e.g. using a cone or sleeve) (AORI 2B) - R1 cases with additional complexity factors
R3 (Revision 3) Most complex and salvage cases
For example: - Multiple previous revision procedures - Bone loss requiring extensive metaphyseal reconstruction or massive endoprosthesis - Requirement for hinged prosthesis due to bone loss or instability - Salvage procedures (e.g. arthrodesis, amputation)

Adapted from:
Phillips JRA, Al-Mouazzen L, Morgan-Jones R, et al. Revision knee complexity classificationRKCC: A common-sense guide for surgeons to support regional clinical networking in revision knee surgery. Knee Surgery, Sports Traumatology, Arthroscopy. 2019;27:10117. doi: 10.1007/s00167-019-05462-x.

for completion of training (CCT) Fellow in knee arthroplasty as well as the senior author (AA) who specialises in revision knee surgery.

2.2.2.7 Hospital admission impact

LOS was recorded for each case and any usage of higher-dependency care. The relationship between length of stay and complexity as rated using the RKCC was presented visually as the cumulative probability of hospital discharge over time using the Stata package *distplot*. The strength and direction of correlation between RKCC and length of stay was measured using Spearman's rank correlation coefficient.

2.2.2.8 Statistical analysis

Descriptive statistics and figures were prepared using Stata (StataCorp. 2019. *Stata Statistical Software: Release 16*. College Station, TX: StataCorp LLC.) and R version 3.6.2.

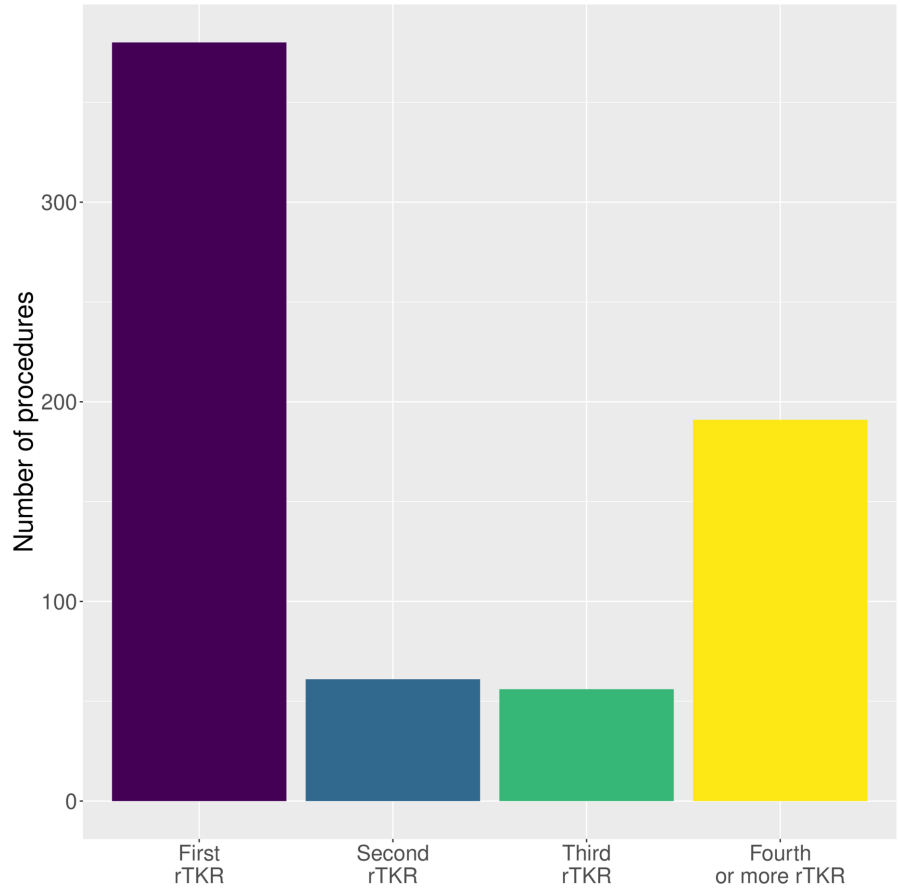

Figure 2.9: Bar chart demonstrating the numbers of first revision, second revision and third or more revision KA procedure performed in the major revision centre over the study period

2.2.3 Results

688 rKA procedures were performed over the study period in 534 distinct patients. These comprised 380 (55.2%) first-revision procedures and 308 (44.8%) re-revision procedures (Figure 2.9).

2.2.3.1 Case ascertainment

The local rKA database identified 188 procedures performed in 2016/7 financial year, compared to 121 procedures reported in HES, representing case ascertainment of 155.4%. Similarly, 189 procedures were identified on the local database in 2017/8, compared to 140 procedures reported in HES (case ascertainment 135.0%).

2.2.3.2 Patient demographics

The mean age at revision surgery was 69.5 years (standard deviation 11.8). 342 procedures (49.7%) were in female patients. 383 procedures (55.7%) were right-sided. The mean body mass index was 30.8 (sd 6.1) (data available for 670/688 procedures (97.4%)). The median Charlson comorbidity index was 0 (IQR 0-4). Patient demographics are summarised in Table 2.3.

2.2.3.3 Indication for surgery

There were 170 (24.7%) unplanned admissions and 518 (75.3%) elective admissions for revision KA. The indication for rKA was: infection (n=345, 50.2%); aseptic loosening/lysis (n=116, 16.9%); dislocation/instability (n=79, 11.5%); progressive arthritis (n=57, 8.3%); unexplained pain (n=28, 4.1%); periprosthetic fracture (n=19, 2.8%); stiffness (n=17, 2.5%); component wear (n=14, 2.0%); malalignment (n=10, 1.5%); and other (n=3, 0.4%). The revision diagnosis is plotted against the number of revision procedures in Figure 2.10).

2.2.3.4 Referral pattern

Among the 534 patients who underwent rKA over the study period, 288 (53.9%) patients were new referrals to the MRC, 209 (39.1%) patients had a previous primary knee arthroplasty at the MRC and 37 (6.9%) patients had a previous rKA at the MRC. Among the 288 new referrals, the referral source was: primary care (65 rKA, 22.5%); primary arthroplasty unit (68 rKA, 23.6%); revision unit (127 rKA, 44.1%); major revision centre (2 rKA, 0.7%); and not available (26 rKA, 9.0%). The two quaternary referrals from other major revision centres were both multiply-revised patients presenting with prosthetic joint infection to our Bone Infection Unit. 140/288 (48.6%) of the referred cases had previously undergone one or more rKA prior to referral. The pattern of referrals is illustrated in Figure 2.11.

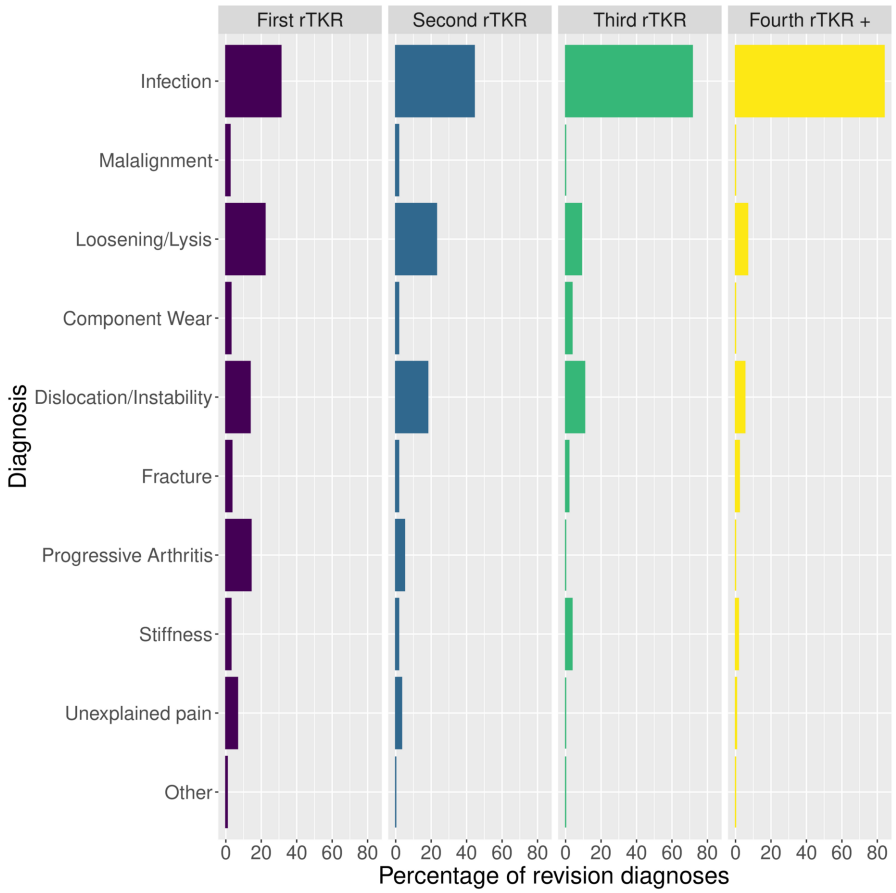

Figure 2.10: Tabplot demonstrating the indications for revision KA. Column percentages are presented for first and subsequent revision procedures and sum vertically to one hundred percent. Prosthetic joint infection was the most prevalent indication for revision.

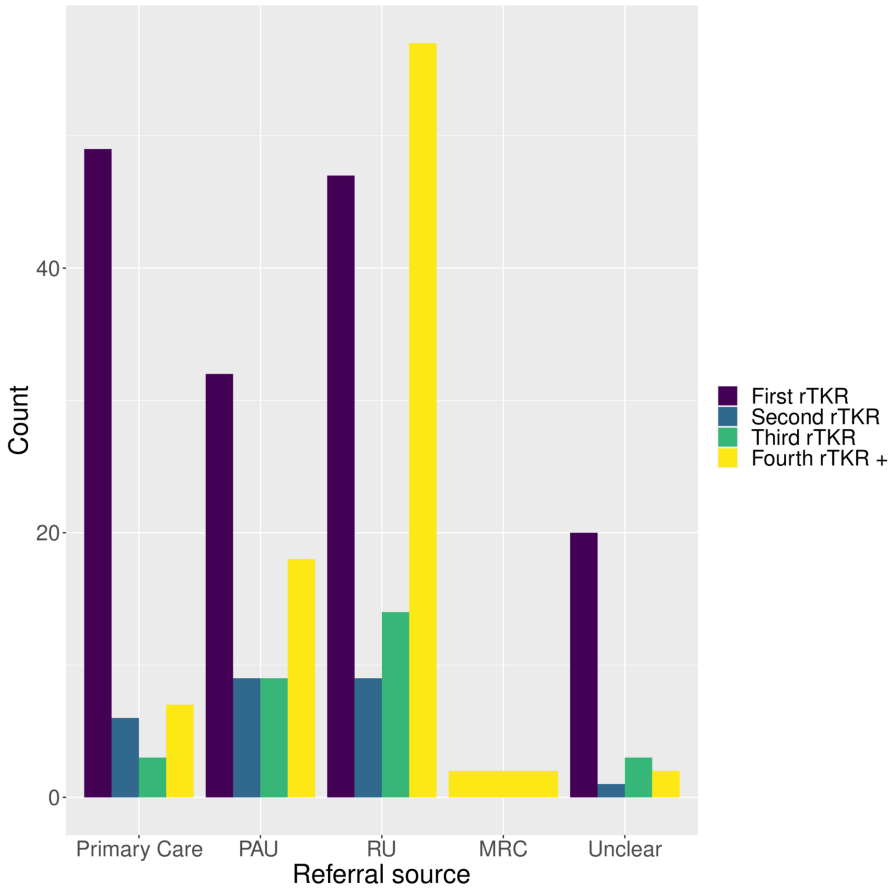

Figure 2.11: Bar-charts demonstrating referral sources to the major revision centre for first and subsequent revision procedures. PAU= Primary arthroplasty unit, RU= Revision unit, MRC= Major revision centre.

Table 2.3: Patient demographics for revision and re-revision knee arthroplasties at the Nuffield Orthopaedic Centre

	Revision KA procedures *n=688*
Female[1] (no. [%])	342 (49.7%)
Age at revision surgery[1] years (mean [sd])	69.5 (11.8)
Body mass index[1] (mean [sd])	30.8 (6.1)
Charlson Comorbidity Index[1,2] (no. [%])	
0	388 (56.4)
1 to 15	272 (39.5)
16 to 30	25 (3.6)
31 to 50	3 (0.4)
Indication for Revision[1] (no. [%])	
Infection	345 (50.2)
Malalignment	10 (1.5)
Aseptic loosening/lysis	116 (16.9)
Component wear	14 (2.0)
Dislocation/instability	79 (11.5)
Periprosthetic fracture	19 (2.8)
Progressive arthritis	57 (8.3)
Stiffness	17 (2.5)
Unexplained pain	28 (4.1)
Other	3 (0.4)

[1] Data aggregated on a procedure level from the perspective of the surgical unit
[2] Summary Hospital-level Mortality Indicator specification

2.2.3.5 Technical complexity of surgery

The overall complexity of the 688 rKA procedures performed over the study period was: R1 n=295 knees (42.9%), R2 n=181 knees (26.3%) and R3 n=212 knees (30.8%). The surgical complexity of the 288 knees referred from external units was: R1 n=96 knees (33.3%), R2 n=92 knees (31.9%) and R3 n=100 knees (34.7%). Among the 209 knees that underwent rKA after primary knee arthroplasty at our centre, the surgical complexity was: R1 n=138 (66.0%), R2 n=38 (18.2%) and R3 n=33 (15.8%). The technical details of revision procedures performed over the study period are described in Figure 2.12.

2.2.3.6 Hospital admission impact

A histogram of length of stay (LOS) is provided in Figure 2.13. This demonstrated a positive skew, with median LOS 8 days (interquartile range 4-14). Higher

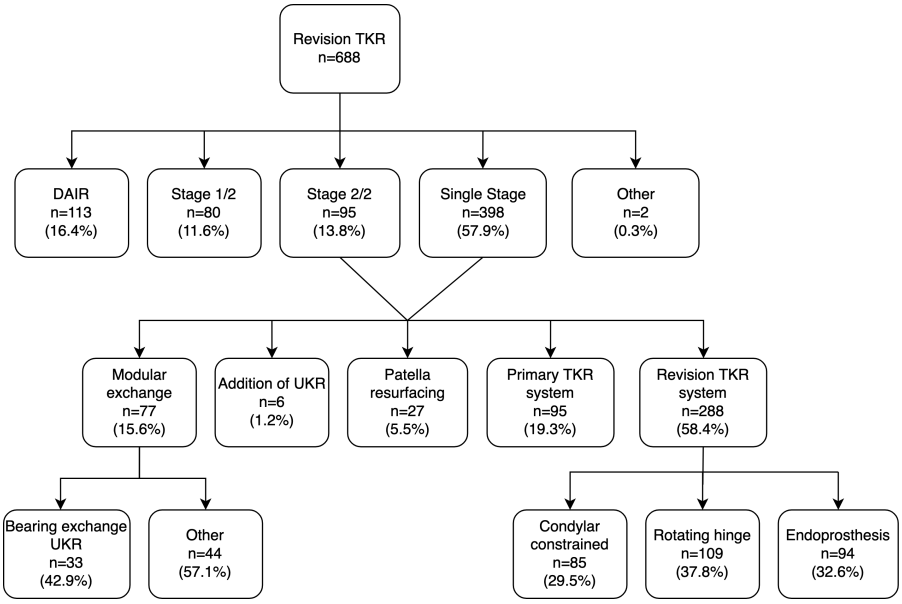

Figure 2.12: Flowchart demonstrating the technical details of revision KA procedures performed over the study period. DAIR = debridement, antibiotics and implant retention; KA = knee arthroplasty; UKA = unicompartmental knee arthroplasty

surgical complexity was associated to longer hospital stay (Spearman rank correlation coefficient 0.38, p<0.0001). The relationship between RKCC and LOS is illustrated in Figure 2.14. 'Less complex' cases had median LOS 5 days (IQR 3 – 9); 'complex' cases had median LOS 9 days (IQR 5 – 15); and 'most complex/salvage' cases had median LOS 11 days (IQR 7 – 19).

330 out of 688 patients (48.0%) were treated in higher-dependency care for at least one night following rKA. Most of these patients (n=317) were observed overnight in an enhanced care environment within our theatre recovery suite on the day of surgery. However, 12 patients out of 688 (1.7%) required transfer out of our centre for formal admission to HDU (for 2 nights [n=9], 3 nights [n=2] and 5 nights [n=1]). One patient out of 688 (0.1%) was transferred to the intensive care unit (ICU) due to an aspiration pneumonia perioperatively.

2.2.4 Discussion

This study has described the surgical practice, patterns of referral and resource utilisation of revision KA at a major revision centre. The surgical complexity of

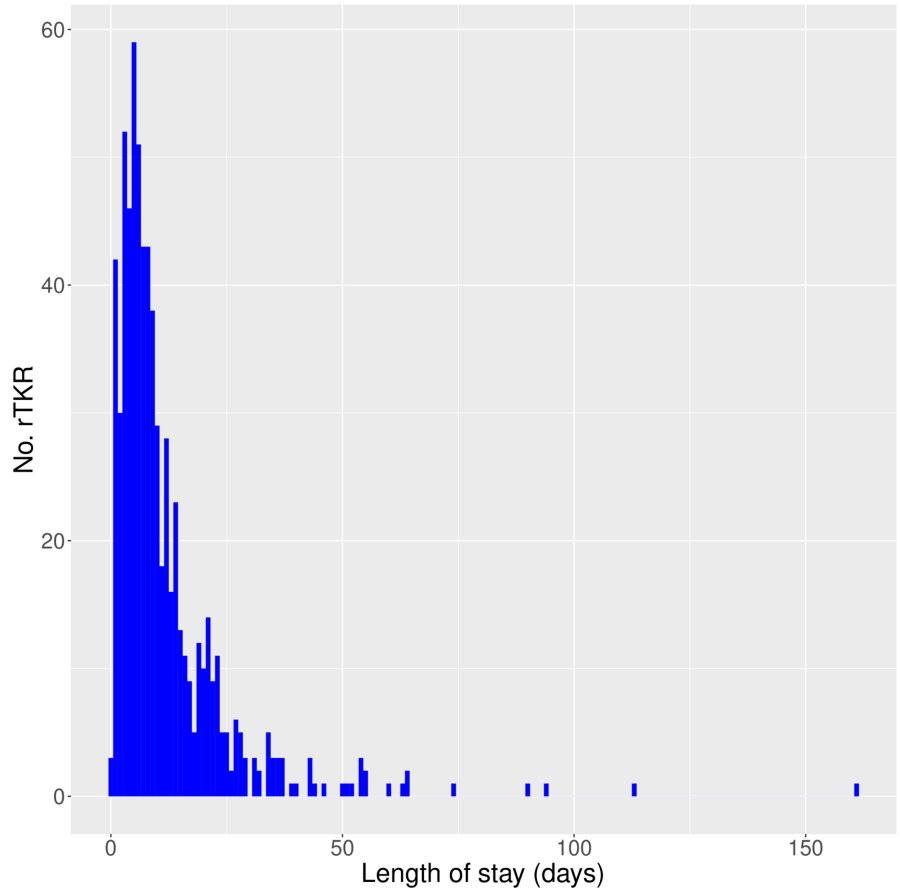

Figure 2.13: Histogram demonstrating length of hospital stay following rKA

rKA procedures performed at the MRC obeyed a 'rule of thirds': one-third of cases 'less complex', one-third 'complex' and one-third the 'most complex/salvage'.

I found that higher case complexity was associated to longer length of hospital stay. The 'most complex' cases had a median LOS of 11 days, compared to 5 days for 'less complex' cases. Assessment of bed capacity will be essential prior to service reconfiguration to prevent 'log-jams' in the system. The approach to this problem in the context of Trauma networks involves 'repatriation' of patients to local units after surgery and similar arrangements may be needed for rKA. Length of stay is also an important driver of hospital costs. Petrie et al [33] recently showed that the most complex cases were inadequately reimbursed [in the NHS model of care by the national tariff, indicating the need for financial uplifts to incentivise this work. One significant financial burden and potential barrier to centres planning to deliver rKA is the requirement for higher-dependency care. In this centre, I found that

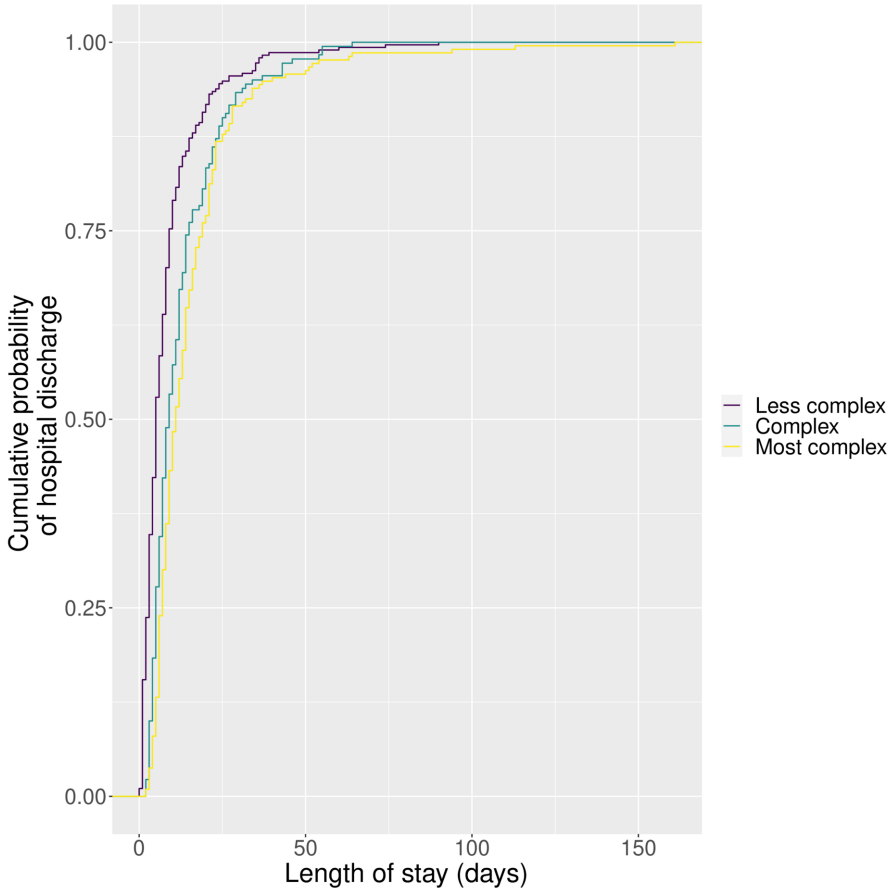

Figure 2.14: Cumulative probability of hospital discharge by length of stay and complexity of rKA (rated according to RKCC as less complex, complex or most complex)

nearly half of all patients undergoing rKA received (mostly planned) 'enhanced' care overnight on the day of surgery (which does not carry additional remuneration) with few patients (<2%) requiring transfer out of our centre for formal HDU/ICU admission. This information is of current relevance given long waiting lists and calls for investment in 'surgical hubs' [86]. A further financial burden to consider for major revision centres is the need to maintain an extensive inventory of revision implant systems. These costs should be reflected in the remuneration of major revision centres – and are likely to be more cost-efficient for the healthcare system overall when compared with large numbers of units 'loaning in' kits.

The methods used in this study are suitable for implementation by other surgical units to gain a more detailed understanding of their own operative practices, which may be used for local service planning. Our approach is likely to provide

an adjunct to models analysing routinely collected data [40] and may overcome some of the limitations associated with this. One important finding here was that publicly-reported rKA activity by NHS Digital underestimated actual operative activity. For example, in 2016/7 the rKA workload reported by HES was 35.6% lower than that identified from our local database. The source of this discrepancy requires further investigation as it may be relevant for hospital reimbursement and the interpretation of publicly reported surgical outcomes [87].

This study has a number of limitations that should be considered. First, the recruitment of cases from theatre logbooks means that only cases managed with surgery were enrolled. As such, the wider role of a major revision centre in providing multidisciplinary team advice, specialist diagnostics and non-operative interventions (with the associated financial implications and pressure on MRC resources) has not been measured. Second, the generalisability of our findings to other major revision centres has not been tested. The high observed prevalence of prosthetic joint infection among referrals is likely to reflect the presence of a specialist Bone Infection Unit at our centre and may be lower in other units. Our study was performed in the UK in the context of an NHS provider. As such our findings may not be generalisable to other countries or healthcare models. Our centre has a high utilisation of unicompartmental knee arthroplasty, which may explain why I observed a high prevalence of 'less complex' rKAs in patients who had their original knee arthroplasty at our centre. A final limitation to consider is that, whilst the RKCC has previously been shown to have good intra- and inter-observer reliability, there may be subjectivity in the classification of some cases [85].

The question as to whether revision surgery in a network model will lead to better surgical outcomes has not been answered here. However, this principle is accepted for other sub-specialties, including major trauma and sarcoma. I have already introduced the idea above of cost-savings through economies of scale – for example, through reduction of 'loan kits'. There is a need for high-quality research to investigate the association of surgeon and unit caseload with clinical outcomes following rKA. In addition, the implementation of a network model must be sensitive

to local intricacies in service provision and the process must involve the surgeons practising in these units as well as patient group representatives [3]. It is important to recognise the impact of centralisation on the patient experience. For example, centralisation may be associated with longer travel times for specialist opinions, surgery and follow-up appointments. Patients may have developed good rapport with their primary surgeon and – particularly for high-volume, highly-skilled primary arthroplasty surgeons with low-volume revision practices, but achieving good outcomes – it may be that some revisions would achieve a better patient experience for an equivalent outcome without tertiary referral.

In conclusion, the surgical complexity of rKA procedures at our MRC was distributed evenly as 'less complex', 'complex' and 'the most complex' cases. Higher surgical complexity was associated to greater length of hospital stay. Among external referrals at our MRC, nearly half of patients had a previous rKA prior to referral. This information is likely to benefit service planning for the development of rKA networks in the near future.

2.2.5 Link to the next chapter

This chapter has investigated the epidemiology of rKA in the UK. The first part of the chapter used routinely collected national data to investigate trends in the delivery of rKA. This found large increases in the incidence of rKA over the past fifteen years. However, I did not observe an exponential rate of increase, as others have predicted [17], instead finding that the rate of increase had slowed down more recently. The indications for rKA were found to have changed over time, with infection becoming the most common indication for surgery. The second part of the chapter used local data from a MRC to characterise referral patterns, case complexity and resource utilisation of rKA procedures in greater detail than is possible from national datasets. Outside the scope of this thesis, I have published on the management of aseptic rKA for failed Oxford medial unicompartmental knee arthroplasties [88].

The next chapters will investigate patient-relevant outcomes following rKA. Pain and joint function are one important domain of outcome within this framework and are commonly measured using PROMs. However, it is not currently known which PROMs are collected for rKA nor whether these instruments are valid in this context. The next chapter will introduce the terminology used to describe PROMs and scope the literature to find PROMS in current use. The chapter will go on to evaluate the measurement properties of these PROMs and the quality of the evidence to support their use.

3

Usage and measurement properties of Patient-Reported Outcome Measures in elective, aseptic revision knee arthroplasty

Contents

This chapter has been published as two papers:

- *Sabah SA, Hedge EA, Abram SG, Alvand A, Price AJ, Hopewell S. Patient-reported outcome measures following revision knee replacement: A review of*

PROM instrument utilisation and measurement properties using the COSMIN checklist. BMJ Open. 2021;11(10):e046169. doi: 10.1136/bmjopen-2020-046169

- *Sabah SA, Alvand A, Beard DJ, Price AJ. Evidence for the validity of a patient-based instrument for assessment of outcome after revision knee replacement: Evaluation of the Oxford Knee Score using the UK National PROMS Dataset. Bone & Joint Journal. 2021;103-B(4):627-634. doi: 10.1302/0301-620X.103B4.BJJ-2020-1560.R1*

3.1 A systematic review of PROM instrument utilisation and measurement properties in elective, aseptic revision knee arthroplasty using the COSMIN checklist

3.1.1 Introduction

The use of PROMs has been introduced earlier. The purpose of this section is to describe the terminology used to evaluate the psychometric properties of PROM instruments and a tool to aid systemic review and selection of these instruments. The ideal PROM is developed or subsequently validated in the population of interest, has good measurement properties and is supported by high-quality evidence. PROM instruments meeting these criteria can be selected for a core outcome set in order to standardise outcome measurement. If there are no suitable PROMs, then further validation studies may be required or the development of a new PROM. For rKA, no systematic review has evaluated PROMs in current use, their measurement properties or the quality of this evidence. This limits meta-analysis of previous research and design of future trials.

3.1.1.1 Selecting the most appropriate health measurement instruments

The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) group have developed tools to guide the selection of the most

appropriate outcome measurement instruments [89; 90]. They have standardised terminology and definitions of measurement properties, and created a taxonomy for their classification which will be used throughout this thesis [91]. For many conditions, the ultimate goal is for the PROM to contribute to a core outcome set (COS), which is "an agreed standardised set of outcomes that should be measured and reported as a minimum in all clinical trials in a specific area of disease" [92].

3.1.1.2 Psychometric properties of PROM instruments

This section will outline the terminology (what it's called) and definitions (what it means) that will be used in this thesis to describe the properties of PROM instruments. These definitions are based on work from the COSMIN group. More comprehensive discussions around these terms and the methods used to develop them are available from the COSMIN handbooks and related resources [89; 90; 91].

- "A *construct* is some postulated attribute of people, assumed to be reflected in test performance" [93]. The Cochrane Handbook defines it as "what (the) PROM (is) trying to measure" [94]. Examples of constructs include pain, function and mood.

- *Validity* is the degree to which an instrument measures the construct(s) it sets out to measure. This can be divided up into specific properties:

  - *Content validity* refers to the extent to which the measure accurately captures and reflects the relevant aspects of the patient's experience, health status, or quality of life that it is intended to assess.

  - *Construct validity* is the degree to which an instrument reflects the dimensions of the construct to be measured (*structural validity*, which involves fitting a model to the measurement instrument) or is consistent with hypotheses (*hypothesis testing*).

  - *Criterion (or comparative) validity* is the degree to which an instrument reflects the 'gold-standard' measure of the construct.

- *Reliability* is the degree to which measurements using the instrument are free from error. Measurement error itself can be systematic or random. Reliability of a PROM can be tested in a number of ways:
  - *Internal consistency* is the degree to which items within a PROM relate to one another. This is measured using Cronbach's alpha.
  - *Test-retest reliability* refers to the degree of agreement between repeat measurements by either the same person on different occasions (intra-rater) or different persons (inter-rater). This is typically measured using intra-class correlation coefficients for continuous variables.
- *Responsiveness* is the ability for an instrument to measure change over time in the construct under investigation. This is often evaluated by formulating hypotheses to challenge the instrument. For example, about the magnitude of the expected effect size for an instrument.
- *Interpretability* is the degree to which clinical meaning can be assigned to the instrument. One aspect of this is the estimation of the smallest change in a PROM score over time that can be interpreted as clinically important (the *minimal important change*, MIC); or the smallest difference in a PROM score between two groups that can be interpreted as clinically important (the *minimal important difference*, MID).

3.1.2 Aim

The aims of this review were: (i) to scope the literature to identify PROMS in current use for evaluation of symptoms, health status or quality of life following elective, aseptic revision (or re-revision) KA, and (ii) to identify validated joint-specific PROMs, their measurement properties and quality of evidence.

3.1.3 Methods

This section is structured to follow the COSMIN Handbook [89].

3.1.3.1 Patient and Public Involvement

Patients and the public were involved in the design, or conduct, or reporting, or dissemination plans of our research. This article was motivated by the James Lind Alliance Priority Setting Partnership for rKA [3], particularly the question: *"How should we measure the outcomes following revision knee surgery in a way that is meaningful to patients?"*

3.1.3.2 Part A: Aim and literature search

Step 1: Aims (described above)

Step 2: Study eligibility criteria Randomised and non-randomised studies were eligible for inclusion. Revision knee arthroplasty was defined as any procedure where an arthroplasty component was removed, modified or added. This included isolated liner exchange, secondary patellar resurfacing and re-revision procedures. Studies where the majority of procedures were performed for urgent or non-discretionary indications (such as infection or malignancy) were excluded, as well as amputations and arthrodesis procedures. Since 85% of revisions are for elective, aseptic indications, studies where the indication was not specified were deemed eligible for inclusion. PROMs were required to address one of the following domains:

- Pain (e.g. Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain subscale [95]),
- Function (e.g. WOMAC functional limitation subscale),
- Combined pain and function (e.g. Oxford Knee Score [96]),
- Joint-related health status (e.g. Knee Injury and Osteoarthritis Outcome Score (KOOS) quality of life (QOL) [97]), or
- Patient activity (e.g. Lower Extremity Activity Scale (LEAS [98]).

Collectively, I have termed these 'joint-specific' PROMs. The focus of this study was not to examine generic health-related quality of life instruments (e.g. EQ-5D [51]). However, I did report the use of these instruments in conjunction with a joint-specific PROM. Outcome scores not considered to be patient-centred were excluded; for example, surgeon-completed scores such as the Bristol Knee Score (BKS), Hospital for Special Surgery Knee Score, and the Knee Society Score (KSS). Studies with less than fifty patients were excluded as their sample size would be considered inadequate when applying COSMIN rules for rating of measurement properties and evidence quality [99].

Step 3: Search strategy This is provided in Appendix B. MEDLINE, Embase, AMED and PsycINFO were searched on 1st July 2020 using the Oxford PROM filter [100]. Searches were translated for each database. There were no limitations on language or publication date. The citations of included studies were searched to identify additional articles.

Step 4: Study selection Two authors (SAS and EAH) independently reviewed the title and abstract for all records returned by the search against eligibility criteria. Disagreement was resolved through discussion of the full text publication. Data were extracted using a calibrated form on name and type of PROM, geography, journal, year of publication and number of patients. Data were summarised using counts with percentage frequency for each of the data items collected.

3.1.3.3 Part B: Evaluation of measurement properties of the included PROMs

Steps 5, 6 and 7: Content validity, Internal structure, Reliability and Responsiveness Terminology for measurement properties were described earlier. Each measurement property was evaluated in three separate sub-steps:

Sub-step 1: Evaluation of methodological quality Two authors (SAS and SGFA) independently evaluated the measurement properties in each article against the COSMIN Risk of Bias checklist. A priori hypotheses for construct validity and responsiveness were set. Study quality was assessed separately for each measurement property using a four-point rating system (very good, adequate, doubtful or inadequate). The "worst score counts" principle was used, where the overall rating for each measurement property is given by the lowest rating of any standard in the box [101].

Sub-step 2: Application of criteria for good measurement properties (GMP) Two authors (SAS and SGFA) independently extracted data on: PROM characteristics (intended construct for measurement, measurement properties, method of administration), study sample (number of patients, patient demographics, diagnosis) and study details (setting, country, language). The few disagreements were resolved through discussion. The results from each study on a measurement property were assigned a quality rating as: sufficient (+), insufficient (-) or indeterminate (?).

Sub-step 3: Summary and grading of quality of evidence This section refers to rating the quality of the PROM as a whole. PROMs were qualitatively summarised and assigned a four-point quality rating. A modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (omitting publication bias) was used to assign evidence quality as high, moderate, low or very low [102].

3.1.3.4 Part C: Selecting a PROM

Step 8: Description of interpretability and feasibility Interpretability and feasibility were analysed descriptively as per COSMIN guidance [89].

Step 9: Formulation of recommendations PROMs were categorised into three categories: (A) Sufficient content validity and at least low-quality evidence for internal consistency; (B) Between 'A' and 'C'; and (C) High-quality evidence for an insufficient measurement property. PROMs rated 'A' can be recommended for use. PROMs rated 'B' have potential for recommendation but require further evaluation. PROMs rated 'C' should not be recommended.

Step 10: Reporting of the systematic review The PRISMA flow diagram is provided in Figure 3.1.

3.1.4 Results

Part A

Study selection 1205 unique articles were identified for screening. 66 full text articles were assessed for eligibility. 51 studies were included in the scoping review, reporting on 8 joint-specific PROMs. Four studies met inclusion criteria for PROM validation, describing measurement properties for three PROMs (Figure 3.1).

Characteristics of studies reporting PROM outcomes for rKA Fifty-one studies reported on PROM outcomes (Table 3.2 and Table 3.1) recruiting a median of 104 (range 51 – 1391) patients. Study designs included 1 (2.0%) randomised controlled trial, 14 (27.5%) prospective cohort studies, 29 (56.9%) retrospective cohort studies, 3 (5.9%) reports from national joint registries, 3 (5.9%) cross-sectional surveys and 1 (2.0%) data analysis of routinely-collected secondary care data. Twenty-five studies (49.0%) were from Europe, 19 (37.3%) from North America, 6 (11.8%) from Asia and 1 (2.0%) from Australasia. The joint-specific PROMs reported were the WOMAC Index (25 studies, 49.0%), OKS (19 studies, 37.3%), KOOS (8 studies, 15.7%), Lower Extremity Activity Scale (LEAS, 4 studies, 7.8%), University of California Los Angeles Activity Score (UCLA, 4 studies, 7.8%), Kujala score (2 studies, 3.9%), Lower Extremity Functional Scale (LEFS, 2 studies, 3.9%), and the Lysholm score (1 study, 2.0%). The majority of studies were published within the past five years (27/51 (52.9%) studies) (Figure 3.2).

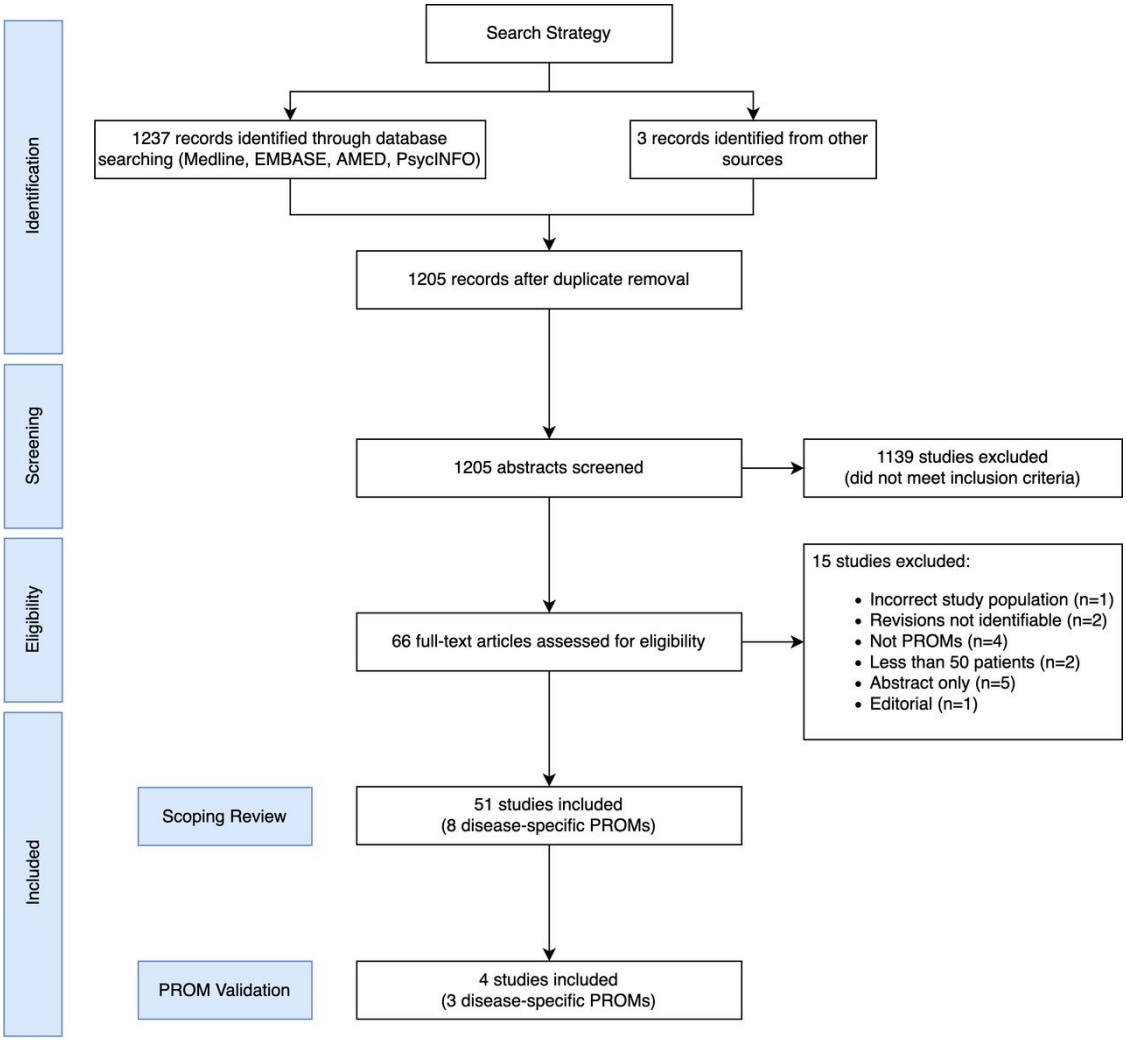

Figure 3.1: PRISMA flow diagram.

Part B

Quality of PROM development studies The quality of PROM development for the 8 disease-specific PROMS identified in Part A is summarised in Table 3.3. The construct to be measured was clear in two studies (25%), with the remainder rated 'inadequate'. One example of a study rated 'inadequate' was the Kujala study [103]. This rating was made because, whilst the score was designed to measure anterior knee symptoms, the specific aspects of these symptoms to be measured were not described (such as pain intensity or pain interference). The Lysholm score [104] was rated 'very good' due to a specific description (defining "the lowest activity level needed during walking, running, or jumping to produce giving way or

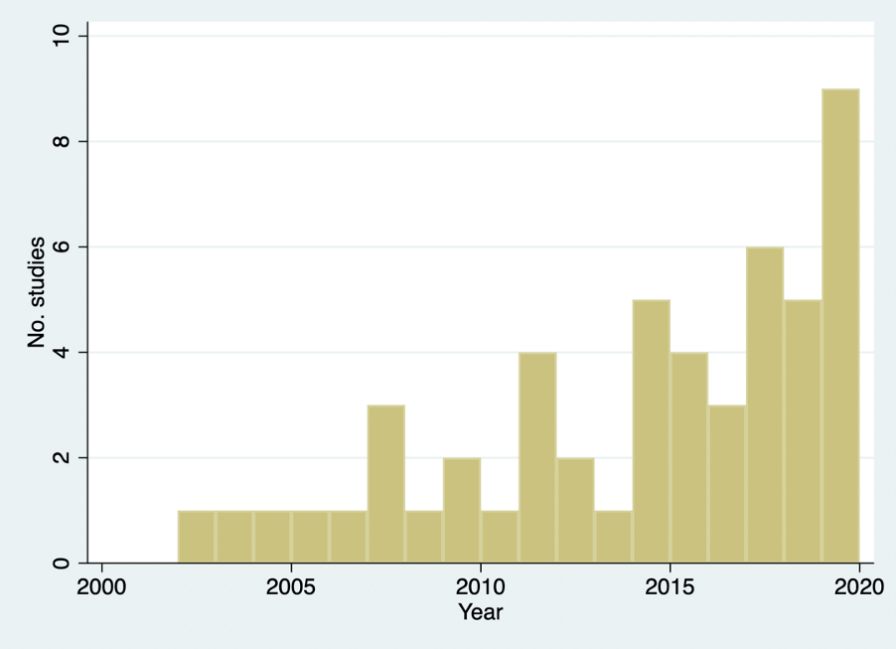

Figure 3.2: Histogram demonstrating increasing numbers of studies reporting on PROMS following rKA over time

Table 3.1: Summary characteristics for studies reporting PROMs following rKA

	Number of studies (%)
No. patients	median 104 (range 51 - 1391)
Continent	
Europe	25 (49%)
North America	19 (37.3%)
Asia	6 (11.8%)
Australasia	1 (2%)
Type of study	
Randomized controlled trial	1 (2%)
Prospective cohort	14 (27.5%)
Retrospective cohort	29 (56.9%)
Joint Registry	3 (5.9%)
Routine data analysis	1 (2%)
Cross-sectional survey	3 (5.9%)
Joint-specific PROMs*	
KOOS	8 (15.7%)
Kujala	2 (3.9%)
LEAS	4 (7.8%)
LEFS	1 (2%)
Lysholm	1 (2%)
OKS	19 (37.3%)
UCLA	4 (7.8%)
WOMAC	25 (49%)
Generic PROMs*	
EQ-5D	7 (13.7%)
SF12	8 (15.7%)
SF36	18 (35.3%)

* KOOS = Knee injury and osteoarthritis outcome score; LEAS = Lower extremity activity scale; LEFS = Lower extremity functional scale; OKS = Oxford Knee Score; SF = Short Form; UCLA = University of California Los Angeles Activity Score; WOMAC = Western Ontario and McMaster Universities Arthritis Index

Table 3.2: Characteristics of studies reporting PROMs for rKA

Authors	Year	Country	Journal	Study design	No. rTKR	Validation Study?	PROM(s) used*
Hartley et al	2002	UK	BJJ	Prospective cohort	60		SF12, WOMAC
Meek et al	2003	Canada	BJJ	Prospective cohort	107		SF12, WOMAC
Meek et al	2004	Canada	JOA	Cross-section	67		OKS, SF12, WOMAC
Saleh et al	2005	US	JBJS(Am)	Prospective cohort	297	Yes	LEAS, WOMAC
Masri et al	2006	Canada	JOA	Retrospective cohort	126		OKS, SF12, WOMAC
Dahm et al	2007	US	JOA	Cross-section	335		UCLA
Ghanem et al	2007	US	CORR	Prospective cohort	80		SF36, WOMAC
Mulhall et al	2007	US	J Knee Surg	Prospective cohort	291		LEAS, SF36, WOMAC
de Groot et al	2008	Netherlands	Health Qual Life	Prospective cohort	54	Yes	KOOS, SF36
Ghomrawi et al	2009	US	JBJS(Am)	Prospective cohort	308	Yes	LEAS, SF36, WOMAC
Kim et al	2009	South Korea	JBJS(Am)	Retrospective cohort	157		WOMAC
Ghanem et al	2010	US	JBJS(Am)	Retrospective cohort	152	Yes	SF36, WOMAC
Greidanus et al	2011	US	JOA	Retrospective cohort	60		OKS, SF12, WOMAC
Hanna et al	2011	UK	CORR	Retrospective cohort	56		OKS
Lavernia et al	2011	US	CORR	Retrospective cohort	132		SF36, WOMAC
Richards et al	2011	Canada	JOA	Cross-section	72		SF12, UCLA, WOMAC
Baker et al	2012	UK	CORR	Joint Registry	797		EQ-5D, OKS
Malviya et al	2012	UK	KSSTA	Prospective cohort	175		SF36, WOMAC
Baier et al	2013	Germany	J Orth Sci	Retrospective cohort	78		WOMAC
Huang et al	2014	US	Orthopedics	Prospective cohort	96		SF36, WOMAC
Kasmire et al	2014	US	The Knee	Retrospective cohort	175		SF36, WOMAC
Luque et al	2014	Spain	Int Orth	Retrospective cohort	125		OKS
Stambough et al	2014	US	BJJ	Retrospective cohort	81		UCLA
Weiss et al	2014	Sweden	Acta Orthop	Retrospective cohort	65		EQ-5D, KOOS
Hitt et al	2015	US	J Knee Surg	Prospective cohort	95		KOOS, LEAS, SF36
Kim et al	2015	South Korea	JOA	Retrospective cohort	228		WOMAC
Konrads et al	2015	Germany	Int Orth	Retrospective cohort	62		Kujala, OKS, SF36
Lunebourg et al	2015	France	JOA	Retrospective cohort	54		KOOS
Grayson et al	2016	US	JOA	Retrospective cohort	177		UCLA
Leta et al	2016	Norway	JBJS(Am)	Joint Registry	1346		EQ-5D, KOOS
Leta et al	2016	Norway	Int Orth	Joint Registry	308		EQ-5D, KOOS
Hamilton et al	2017	UK	JOA	Prospective cohort	53		OKS
Lim et al	2017	Singapore	BJJ	Retrospective cohort	75		OKS, SF36
M-Hernandez et al	2017	Spain	KSSTA	Prospective cohort	134		SF12, WOMAC
Rajgopal et al	2017	India	JOA	Retrospective cohort	98		WOMAC
Sandiford et al	2017	Canada	CORR	Retrospective cohort	450		OKS, SF12, WOMAC
Zhamilov et al	2017	Turkey	JOA	Retrospective cohort	92		LEFS

continued

Table 3.2: Characteristics of studies reporting PROMs for rKA

Authors	Year	Country	Journal	Study design	No. rTKR	Validation Study?	PROM(s) used*
Agarwal et al	2018	UK	The Knee	Prospective cohort	104		EQ-5D, OKS
Boelch et al	2018	Germany	Int Orth	RCT	51		OKS, SF36
Eibich et al	2018	UK	BMJ Open	Routine data	1391		EQ-5D, OKS
Gomez-Vallejo et al	2018	Spain	J Orth Traum	Retrospective cohort	67		SF36, WOMAC
Weber et al	2018	Germany	BioMed RI	Retrospective cohort	68		EQ-5D, WOMAC
Bin Abd Razak et al	2019	Singapore	J Knee Surg	Retrospective cohort	163		OKS, SF36
Konrads et al	2019	Germany	J Knee Surg	Retrospective cohort	135		Kujala, OKS, SF36
Kurmis et al	2019	Australia	JOA	Retrospective cohort	321		OKS, WOMAC
Lim et al	2019	Singapore	The Knee	Retrospective cohort	70		OKS, SF36
Scior et al	2019	Germany	JOA	Prospective cohort	482		OKS
Stockwell et al	2019	Canada	The Knee	Retrospective cohort	234		OKS
Klim et al	2020	Austria	KSSTA	Retrospective cohort	93		SF36, WOMAC
Larsen et al	2020	Denmark	BMC Sports Sci	Retrospective cohort	51		KOOS
Oliver et al	2020	Spain	Orth Surg	Retrospective cohort	89		KOOS, Lysholm

* KOOS = Knee injury and osteoarthritis outcome score; LEAS = Lower extremity activity scale; LEFS = Lower extremity functional scale; OKS = Oxford Knee Score; SF = Short Form; UCLA = University of California Los Angeles Activity Score; WOMAC = Western Ontario and McMaster Universities Arthritis Index

pain and swelling"). The origin of the construct to be measured was clear in only two studies (25.0%). One example of a study rated 'very good' for this property was the LEFS study [105], which referenced the World Health Organization's International Classification of Functioning, Disability and Health (ICF) conceptual framework [106]. The context of use was rated 'very good' for three studies (37.5%). These studies provided at least one clear description of the intended application of the instrument. For example, the OKS was designed to evaluate patients before and after knee arthroplasty surgery [96]. All studies were rated as 'very good' for their description of a clear target population. Whilst many studies provided a very broad description (for example, the LEFS described patients "with lower-extremity orthopaedic conditions" [107]), the COSMIN guidance is permissive for rating this property. However, the PROM development sample was rated 'inadequate' for all studies either because the patient sample was not correspondingly broad or, taking a view on the patient sample of interest in this review, did not recruit a sample representative of elective, aseptic rKA. Whilst the LEAS study did recruit patients

with rKAs for some aspects of PROM development, a surgeon panel was used in lieu of patients for content validity, justifying an 'inadequate' rating [105]. In summary, the total PROM development was rated 'inadequate' for all studies based on the "worst score counts" principle recommended by COSMIN. However, this does not reflect positive ratings for some aspects of PROM development as described above.

Table 3.3: Quality of PROM development

PROM	PROM design[1]							Cognitive interview (CI) study[3]				Total PROM development
	General design							General design				
	Clear construct	Clear origin of construct	Clear target population	Clear context of use	PROM development sample	Concept elicitation[2]	Total PROM design	CI sample	Comprehensibility	Comprehensiveness	Total CI study	
Joint-specific[4]												
KOOS	I	D	VG	D	I		I	Yes				I
Kujala	I	D	VG	D	I		I	No				I
LEAS	I	D	VG	VG	I		I	No				I
LEFS	I	VG	VG	D	I		I	No				I
Lysholm	VG	D	VG	D	I		I	No				I
Oxford Knee Score	I	D	VG	VG	I		I	No				I
WOMAC	VG	VG	VG	VG	I		I	Yes				I
UCLA	I	D	VG	D	I		I	No				I
Generic[5]												
EQ-5D	I	D	VG	VG	I		I					I
SF-36	VG	VG	VG	VG	I		I					I
SF-12	VG	VG	VG	VG	I		I					I

[1] VG = Very good, A = Adequate, D = Doubtful, I = Inadequate, N= Not assessed

[2] Where the PROM was not developed in a sample representing the target population, the concept elicitation was not further rated

[3] Empty cells indicate that a CI study (or part of it) was not performed

[4] KOOS = Knee injury and osteoarthritis outcome score; LEAS = Lower extremity activity scale; UCLA = University of California at Los Angeles; WOMAC = Western Ontario and McMaster Universities Arthritis Index

[5] SF = Short-Form

Characteristics of PROM validation studies Four studies [108; 98; 109; 105] from the scoping review validated three joint-specific PROMs (KOOS, LEAS, WOMAC) (Table 3.4). The mean age of patients in the included studies ranged from 67 to 77 years. Female patients accounted for 50 to 78% of the study populations. The primary objective of the included articles varied from validation of a PROM, validation of another instrument with the PROM as a comparator, development of a new instrument and reporting of clinical outcome after rKA. The characteristics of the PROMs included in the validation studies are described in Table 3.5.

Table 3.4: Characteristics of PROM validation studies

Study[1]	Instrument(s)	Primary objective	Country (Language)	Population (Inclusion/ Exclusion)	Enrolled (n)	LTFU (n)	Final (n)	Age (years)[2]	Female (%)	FU (months)	Indications for revision	
de Groot (2008)	KOOS SF-36 VAS for pain	To validate the Dutch translation of KOOS	Netherlands (Dutch)	Inc: Revision TKR Exc: Unable to understand Dutch written language.	54	7	47	77 (36-89)	78	NR	NR	
Saleh (2005)	LEAS WOMAC	To develop and validate the Lower-Extremity Activity Scale	United States (English)	Inc: First revision TKR capable of completing questionnaires in English and >= 18 years Exc: Re-revision, failed UKR, poly. exchange only, bone tumour, reflex sympathetic dystrophy, unfit for revision TKR, neurological deficit of affected limb, referred pain from spine, declined to participate, concern about compliance, inability to consent, progressive muscular condition of quadriceps, infection delay, stiffness not requiring component revision.	297	12	285	68.6 (r 34 - 85)	55	6	Instability n=82 (28.8%) Tibial osteolysis n=78 (27.4%) Poly. wear n=70 (24.5%) Fem. osteolysis n=64 (22.5%) Tibial loosening n=63 (22.1%)	
Ghomrawi (2009)	LEAS SF-36 WOMAC	To characterise patterns of functional improvement after revision total knee arthroplasty over a two-year period using Lower-Extremity Activity Scale	United States (English)	As per Saleh et al (2005)	308	87	221	68.7 (r 34 - 85)	55	24	Instability 28.9% Poly. wear 24.5% Failed poly. insert 18.1% Malalignment 9.4% Tibial loosening 22.2%	Fem. loosening 14.1% Infection 10.4% Tibial lysis 27.5% Fem. lysis 22.5% Patella lysis 9.4%
Ghanem (2010)	WOMAC SF-36 KSS 4-point Likert	To determine validity and responsiveness of the Knee Society Rating System	United States (English)	Inc: Revision TKR Exc: Infection (n=85), Patella or poly. exchange only (n=35); Conversion of UKR or internal fixation (n=15), Non-prosthetic failure (n=4)	165	13	152	67 (r 36 - 89)	NR	24	Mechanical failure: Aseptic loosening 69.7% Knee instability 30.3%	

[1] KOOS, Knee injury and osteoarthritis outcome score; KSS, Knee Society Rating system; LEAS, Lower extremity activity scale; Lig, Ligamentous; LTFU, Lost to follow-up; NR, Not reported; Poly, polyethylene; SF-36, Short-Form 36; WOMAC, Western Ontario and McMaster Universities Arthritis Index
[2] mean (sd) or range

Table 3.5: Characteristics of the joint-specific PROMs evaluated in validation studies

Instrument[1]	Year	Original language	Target population	Intended construct / Domains	No. questions	Best/ worst score
Symptoms and functional status						
KOOS	1998	English & Swedish	Younger and more active subjects at risk of knee osteoarthritis following knee injury	Pain Symptoms Activities of daily life function Sports and recreation function Knee-related quality of life	42 questions	100/0
WOMAC	1982	English	Patients with OA of the hip or knee	Pain Stiffness Function and daily activities	24 questions	0/96
Activity-level						
LEAS	2005	English	Patients awaiting or had undergone primary or revision lower limb joint arthroplasty	Physical activity	1 question	18/1

[1] KOOS, Knee injury and osteoarthritis outcome score; LEAS, Lower extremity activity scale; WOMAC, Western Ontario and McMaster Universities Arthritis Index

Quality of studies on measurement properties In total, 20 measurement properties for the KOOS, LEAS and WOMAC were evaluated (Table 3.6). There were 40 additional opportunities to evaluate measurement properties that were not attempted. 2 (10.0%) measurement properties were rated 'very good', 5 (25.0%) 'adequate', 3 (15.0%) 'doubtful' and 10 (50.0%) 'inadequate'. For structural validity, de Groot's evaluation for the KOOS was rated 'inadequate' due to an insufficient sample size for factor analysis (less than five times the number of participants). Three out of four (75.0%) studies that reported on responsiveness were rated 'inadequate' due to their construct approach. For example, Saleh et al [105] used an 'inadequate' comparator instrument for development of the LEAS - the measurement properties of the WOMAC are not well enough known for revision. Ghomrawi et al [98] did not set hypotheses for construct validity, and their statistical methodology did not allow these to be evaluated at review. Two studies reported on reliability. These were rated 'adequate' as, whilst they chose an appropriate interval, they did not also ensure patients were stable.

Table 3.6: Quality of studies on measurement properties

PROM[1]	Study	Structural validity[2]	Internal consistency	Cross-cultural validity	Reliability	Measurement error	Criterion validity	Construct validity		Responsiveness			
								Convergent validity	Known groups validity	Comparison with gold standard	Comparison with other instruments	Comparison between sub-groups	Comparison before-after intervention
KOOS	de Groot	I	VG	I	A	A	N	D	N	N	N	N	N
LEAS	Saleh	N	N	N	A	A	N	I	N	N	I	N	A
LEAS	Ghomrawi	N	N	N	N	N	N	N	N	N	I	I	I
WOMAC	Ghanem	N	N	N	N	N	N	D	N	N	D	N	VG
WOMAC	Ghomrawi	N	N	N	N	N	N	N	N	N	I	I	I

[1] KOOS, Knee injury and osteoarthritis outcome score; LEAS, Lower extremity activity scale; WOMAC, Western Ontario and McMaster Universities Arthritis Index
[2] VG = Very good, A = Adequate, D = Doubtful, I = Inadequate, N = Not assessed

Quality of the evidence for measurement properties of the PROMs
The quality of the evidence for measurement properties of the included PROMs is provided in (Table 3.7). 25 out of 27 (92.6%) measurement properties were rated either insufficient, indeterminate, or not assessed. The only measurement property to receive a 'sufficient' rating was reliability for both the KOOS and LEAS, supported by 'low' and 'moderate' quality evidence respectively.

Table 3.7: Quality of the evidence for measurement properties of the PROMs

	KOOS		LEAS		WOMAC	
	OVERALL RATING	QUALITY OF EVIDENCE	OVERALL RATING	QUALITY OF EVIDENCE	OVERALL RATING	QUALITY OF EVIDENCE
Structural validity	-	Very low	N	N	N	N
Internal consistency	?	Moderate	N	N	N	N
Cross-cultural validity	?	Very low	N	N	N	N
Measurement invariance	?	Very low	N	N	N	N
Reliability	+	Low	+	Moderate	N	N
Measurement error	?	Low	?	Very low	N	N
Criterion validity	N	N	N	N	N	N
Construct validity	-	Low	-	Very low	?	Very low
Responsiveness	N	N	?	Very low	?	Very low

[1] KOOS, Knee injury and osteoarthritis outcome score; LEAS, Lower extremity activity scale; WOMAC, Western Ontario and McMaster Universities Arthritis Index
[2] N = not assessed; + = sufficient, - = insufficient, ? = indeterminate

3.1.4.1 Part C

Data on the interpretability of the studies is summarised in Table 3.8. The mode of PROM administration was unclear for all studies except de Groot et al [109]. Missing responses ranged from 25-60%. No study reported on missing items within a PROM instrument. Floor and ceiling effects were not reported, except by Saleh et al [105]. No PROM met criteria either to be recommended or not recommended for use. Each of the validated PROMs (i.e. KOOS, LEAS and WOMAC) were therefore assigned recommendation 'B', indicating that further evidence is needed.

Table 3.8: Interpretability including missing items, response rate and floor/ceiling effects

Instrument and study[1,2]		Administration	Missing responses (%)	Missing items (%)	Overall % achieving lowest possible total score (floor)	Overall percentage achieving highest possible score (ceiling)	Items/ Domains with >15% responses with lowest score (floor)	Items/ Domains with >15% responses with highest score (ceiling)	MIC
Symptoms and functional status									
KOOS	de Groot (2008)	Postal	25	NR	NR	NR	Sports/ Recreation	Nil	NR
WOMAC									
	Ghomrawi (2009)	Unclear	30.5	NR	NR	NR	NR	NR	NR
	Ghanem (2010)	Unclear	NR	NR	NR	NR	NR	NR	NR
	Saleh (2005)	Unclear	NR	NR	NR	NR	NR	NR	NR
Health-related quality of life									
SF-36									
	de Groot (2008)	Postal	NR	NR	NR	NR	NR	NR	NR
	Ghomrawi (2009)	Unclear	30.5	NR					
	Ghanem (2010)	Unclear	NR	NR	NR	NR	NR	NR	NR
Activity-level									
LEAS									
	Ghomrawi (2009)	Unclear	30.5	NR	NR	NR	NR	NR	NR
	Saleh (2005)	Unclear	59.6*	NR	0	0	NR	NR	NR

[1] KOOS, Knee injury and osteoarthritis outcome score; LEAS, Lower extremity activity scale; SF-36, Short-Form 36; WOMAC, Western Ontario and McMaster Universities Arthritis Index
[2] NR = Not reported

3.1.5 Discussion

This review has demonstrated the increasing use of PROMs to evaluate symptoms and functional outcomes following elective, aseptic rKA. The majority of studies were retrospective and observational, with only one randomised controlled trial. Eight different joint-specific PROMs were identified, with the WOMAC index (25 studies, 49.0%) and the OKS (19 studies, 37.3%) the most frequent. Only three joint-specific PROMs were supported by a validation study: KOOS, LEAS and WOMAC. Each of these validation studies had 'low' or 'very low' quality evidence and the majority of measurement properties were either not evaluated or rated 'inadequate' or 'indeterminate'. As such, each of these PROMs requires more evidence in order to be recommended for use.

Musculoskeletal disorders account for one-third of all reviews on the COSMIN database [110]. At least three reviews have evaluated the measurement properties of PROMs following pKA [111; 99; 112]. These studies found that many PROM instruments had limited evidence to support their measurement properties, justifying the need for further research. I am not aware of previous reviews that have examined the measurement properties of PROMs following rKA. Whilst many of the goals from elective, aseptic rKA are shared with pKA, there are important differences in the patient populations and disease processes being treated and the surgical interventions themselves. For example, whilst pKA treats predominantly osteoarthritis, rKA treats many varied disease processes [31]. The revision patient population is also more comorbid and may have different expectations from surgery [113]. As such, the evidence for PROMs developed in pKA cannot necessarily be assumed to be transferable across to rKA.

This study has a number of important strengths, including the use of a broad search strategy based on the Oxford PROM filter [100], and the application of latest COSMIN guidelines. The use of a priori hypotheses by our review team to evaluate construct validity and responsiveness is novel and meant these properties could be considered even when not a focus of the original article. This study was

motivated by the James Lind Alliance Priority Setting Partnership for rKA, which generated the question: "How should we measure the outcomes following revision knee surgery in a way that is meaningful to patients?" [3]. As such, outcome scores that were not patient completed were excluded. I acknowledge that this has restricted the number of eligible studies from North America, where use of the Knee Society Score (KSS) is prevalent. In the future, qualitative studies to explore patients' reasons for choosing surgery and to identify the outcomes that are most important to patients may be needed.

I have not put forward a PROM for recommendation because the quality of the available evidence was low, and data were lacking for many of the measurement properties. However, I can make recommendations to direct future research and to move towards developing a core outcome set for elective, aseptic rKA. First, I wish to highlight that standards for reporting of psychometric studies have changed considerably over the past twenty years [112]. COSMIN tools are not limited to systematic reviews and may be used guide the scope and detail required to develop a new instrument or to evaluate an existing one. Second, this study has highlighted a number of common methodological flaws that result in high risk of bias. For example, when evaluating structural validity, none of the validation studies performed confirmatory factor analysis to understand whether the PROM scores reflected the dimensionality of the construct. For reliability, test conditions were not recorded with sufficient detail to ensure that not only the repeat interval was appropriate, but also that the patient remained stable. For interpretability, none of the studies calculated a minimal important change (MIC) nor comprehensively assessed floor and ceiling effects. Third, I recommend that future studies planning to use an existing joint-specific PROM to evaluate outcomes after revision surgery do so in conjunction with a validated generic health-related quality of life instrument (such as the Short Form-36 (SF36) [50] or EQ-5D [51]). Whilst neither the EQ-5D or SF36 were developed in patients undergoing rKA, their measurement properties have been studied extensively and allow generalisability

between different conditions. This approach will provide valuable information on construct validity and responsiveness in the future.

In conclusion, joint-specific PROMs are increasingly used to report outcomes following rKA, but these instruments have insufficient evidence for validity. Future research is needed to target the deficiencies highlighted by this review in order to inform clinical trials and observational studies evaluating these outcomes.

3.2 Validation of the OKS for elective, aseptic revision knee arthroplasty

3.2.1 Introduction

The Oxford Knee Score (OKS) was developed in 1998 from interviews with patients undergoing pKA [96; 114]. A recent systematic review demonstrated it had good measurement properties and a robust evidence base for use in this population [112]. However, its measurement properties for rKA are less well evaluated and the score was not developed using a rKA cohort. In the previous section, I showed that no validation study is available to support the use of the OKS in rKA. Despite this, the OKS is already used widely in this context. The previous section identified nineteen studies that had used the OKS to report on the outcome of rKA and the OKS is a key component of the NHS PROMs programme in the UK. Since 2009, this programme has routinely collected information on pre- and post-operative joint function and quality of life for NHS-funded patients undergoing elective revision knee arthroplasty.

The aim of this study was to evaluate the measurement properties of the OKS for rKA.

3.2.2 Methods

This was a retrospective cohort study using freely available, de-identified patient data where ethical approval is not required. This study followed guidelines from the COSMIN group for evaluation of internal consistency, construct validity, responsiveness, and interpretability for the OKS in rKA [89]. Supporting Evaluation, Analysis and Reporting of routinely Collected Healthcare Data (SEARCHeD) guidelines were followed to report this study [115].

3.2.2.1 Study dataset

Patient data was obtained from the UK NHS national PROMs programme from 1st April 2013 to 31st March 2019. rKAs were identified from the 'Revision

Flag' field in the PROM dataset [83]. This flag is raised if a PROM is matched to a revision procedure episode in Hospital Episode Statistics (HES) [83]. A list of Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS-4) codes for eligible procedures is provided in Appendix A. This definition encompasses any subsequent procedure to add, remove or modify a joint replacement, and represents those procedures that contribute to publicly available provider reports from NHS Digital on PROM performance in rKA [83]. Patients who withheld informed consent, were unable to complete PROM questionnaires (with or without assistance) and those who subsequently opted out were excluded. Patients undergoing emergency procedures are not included in the NHS PROMs programme.

3.2.2.2 Outcome measures

The OKS is a knee-specific PROM that asks patients about their pain and function over the past 4 weeks [116]. It has 12 Likert items each with five possible responses (0-4), to give a total score from 0 (worst) to 48 (best) [114; 117]. Health-related quality of life is measured using the EQ-5D 3-level score (EQ-5D-3L). This consists of five domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each with three ordinal levels from 1 (no problems) to 3 (extreme problems). The scale is converted to an index ranging from -0.59 (worst) to 1 (best health) using utility values for the UK population. General health is also measured using the EQ "thermometer", a visual-analogue scale (VAS) from 0 (worst) to 100 (best).

Patients complete a pre-operative questionnaire (Q1), which includes these instruments together with additional questions on the need for assistance completing the questionnaire, comorbidities and previous arthroplasty for the affected joint. The mode of questionnaire administration varies between centres, with paper-based and electronic systems in use. A follow-up questionnaire (Q2) is administered at 6 months following surgery. This contains additional questions on patient satisfaction ("How would you describe the results of your operation? Response: Excellent, Very

good, Good, Fair, Poor") and perceived success of surgery ("Overall, how are the problems now in the knee on which you had surgery, compared to before your operation? Response: Much better, A little better, About the same, A little worse, Much worse"). Further information on the dataset and PROMs methodologies is available from NHS Digital [83].

3.2.2.3 Statistical analyses

The study population was described using frequencies, means and standard deviations or medians and ranges, as appropriate. Statistical analyses were performed using Stata (StataCorp. 2019. *Stata Statistical Software: Release 16.* College Station, TX: StataCorp LLC.) and R version 3.6.2.

3.2.2.4 Study size

10,727 rKA procedures with returned pre- and post-operative questionnaires were available for analysis from the national PROMs programme.

3.2.2.5 PROM Participation Rates

Data on PROM participation for rKA was available for 2016-2019 only. Over this period, 14929 rKA procedures were coded on HES, 7432 patients (49.8%) completed a pre-operative questionnaire and 5112 (34.2%) patients returned a post-operative questionnaire.

3.2.2.6 Procedures for handling missing data

Missing data was described for each variable in the dataset. The proportion of returned pre- and post-operative questionnaires with incomplete or erroneous outcome data was reported. Complete case analysis was used throughout, with no imputation for missing values, because the missingness mechanism was unknown. A complete outcome set was defined as a valid response to all items on the pre- and post-operative OKS and EQ-5D instruments, as well as the post-operative success transition question (which was required for calculation of the MIC).

3.2.2.7 Evaluation of internal structure

The internal structure of a PROM refers to how items within an instrument relate to one another. This information is important to determine how items should be combined into a scale. Internal consistency is a measure of the extent to which the items on a scale measure the same concept and was assessed using Cronbach's alpha. The effect of removing each item was also examined. I specified a Cronbach alpha of ≥ 0.7 as acceptable [89].

3.2.2.8 Construct validity

Validity refers to the ability for an instrument to measure the construct it is intended to measure. Since there is no gold-standard instrument for use in this context, a criterion approach could not be used. Instead I calculated construct validity, which is the extent to which a measure relates to other measures, consistent with a priori hypotheses. The construct validity of the OKS was estimated through comparison to the EQ-5D index through calculation of Spearman's correlation coefficients. I formulated hypotheses about the size and direction of relationships between OKS and the EQ-5D (Table 3.9). Our main hypothesis concerned the total score for the OKS having at least moderate correlation with the EQ-5D at each time point. I formulated six further a priori hypotheses for convergent construct validity (Hypotheses 2-7) and one for discriminant construct validity (Hypothesis 8). Each hypothesis was tested against pre- and post-operative scores. The strength of correlation coefficient was interpreted according to thresholds from Munro [118]: little, if any (≥ 0.25), low (0.26-0.49), moderate (0.50-0.69), high (0.70-0.89), and very high (0.90-1.00). The proportion of accepted hypotheses was used to define quality of construct validity: $\geq 75\%$ accepted (good), 50-74% (moderate), $\geq 50\%$ (low).

3.2.2.9 Responsiveness

This is the ability for a PROM to detect change over time in the construct to be measured [89]. Pre- and post-operative scores were compared using paired t-tests.

Table 3.9: Hypotheses for construct validity and responsiveness of the Oxford Knee Score in rKA.

Hypothesis		**Pre-op**	**Post-op**	**Change**
1	The correlation between OKS and EQ-5D for the entire cohort is at least moderate ($r \geq 0.50$)	Accepted	Accepted	Accepted
2	The correlation between OKS and EQ-5D mobility is at least moderate ($r \geq 0.50$)	Rejected	Accepted	Rejected
3	The correlation between OKS and EQ-5D self-care was at least moderate ($r \geq 0.50$)	Accepted	Accepted	Rejected
4	The correlation between OKS and EQ-5D usual activities was at least moderate ($r \geq 0.50$)	Rejected	Accepted	Rejected
5	The correlation between OKS and EQ-5D pain/discomfort was at least moderate ($r \geq 0.50$)	Accepted	Accepted	Accepted
6	The correlation between OKS Pain Component Score and EQ-5D pain/discomfort is at least 0.05 greater than with EQ-5D mobility	Accepted	Accepted	Accepted
7	The correlation between OKS Function Component Score and EQ-5D mobility is at least 0.05 greater than with EQ-5D pain/discomfort	Rejected	Rejected	Rejected
8	The correlation between OKS and EQ-5D anxiety/depression was low (≤ 0.49)	Accepted	Accepted	Accepted
Summary		63% accepted	88% accepted	50% accepted

I also calculated and compared the standardised effect size (SES, which is the mean change score divided by the standard deviation (SD) of the measure at baseline) and standardised response mean (SRM, which is the mean change score, divided by the SD of the change scores for the outcome measure used) [119]. To evaluate construct responsiveness, I evaluated the same hypotheses as for construct validity, but this time applied to the change scores for the OKS and EQ-5D.

3.2.2.10 Meaningful changes in the OKS

The clinically relevant improvement for the *average individual* over a period of time was estimated by calculating the MIC using receiver operator curve (ROC) analysis [120]. The external anchor was the perceived success transition item from the Q2 Questionnaire [121]. Patients who responded to this question to indicate a minimal improvement ('a little better'), were compared to those who responded no improvement ('about the same'). The MIC was also calculated for a *single group* of patients as the mean change in OKS for patients who rated 'a little better'. The minimally important difference (MID) was calculated as the difference in mean change of OKS in patients 'a little better' versus 'about the same'. The minimal detectable change (MDC-90) was calculated to represent the smallest change beyond the measurement error of the instrument. I used the standard

error of the mean (standard deviation x $\sqrt{(1 - reliability)}$), multiplied by $\sqrt{2}$ (to account for measurement on two occasions) multiplied by a z score of 1.65 (to indicate a 90% confidence level).

3.2.2.11 Floor and ceiling effects

The effect of an intervention might be missed for patients who occupy the minimum or maximum scores. I defined floor and ceiling effects as being present if more than 15% of respondents achieved these scores.

3.2.3 Results

3.2.3.1 Study population

A total of 10,727 rKA procedures (49.6% female, 44.3% male, 6.0% gender suppressed) were available for analysis. The most frequent age category was 70-79 years (37.3%).

3.2.3.2 Missing outcome data

For returned questionnaires, 9,219 patients had complete pre- and post-operative outcome data. This is illustrated in Figure 3.3. There were baseline differences for age- and gender between populations with incomplete and complete sets of outcome measures (Table 3.10).

3.2.3.3 Outcome scores

For patients with complete outcome measurements, pre-operative OKS approximated a normal distribution, with a subtle right-sided tail. Post-operative OKS had a left-sided tail, Figure 3.4. Pre-operative OKS was mean 16.7 (sd 8.1) points, post-operative OKS 29.1 (11.4), and change in OKS +12.5 (10.7). The EQ-5D index had a bimodal distribution, Figure 3.5. Pre-operative EQ-5D index was median 0.260 (interquartile range (IQR) 0.055 - 0.691), post-operative EQ-5D index 0.691 (0.516 – 0.796), and change in EQ-5D index +0.240 (0.000 – 0.567); EQ-VAS improvement was mean 3.4% (sd 23.4%). 6955 patients (75.4%) reported improvement on the

Table 3.10: Summary of patient demographics and outcome measures

	Revision Knee Replacement	
	Incomplete outcome measurements	**Complete outcome measurements**
	N=1,508	N=9,219
Age-band		
40 to 49	2 (0.1%)	17 (0.2%)
50 to 59	151 (10.0%)	1,037 (11.2%)
60 to 69	431 (28.6%)	3,115 (33.8%)
70 to 79	602 (39.9%)	3,395 (36.8%)
80 to 89	243 (16.1%)	1,087 (11.8%)
Missing/Suppressed	79 (5.2%)	568 (6.2%)
Gender		
Male	618 (41.0%)	4,142 (44.9%)
Female	811 (53.8%)	4,509 (48.9%)
Not specified	79 (5.2%)	568 (6.2%)
Q1 Oxford Score	15.6 (8.1)	16.7 (8.1)
n	1,327 (88.0%)	N
Q2 Oxford Score	27.7 (11.5)	29.1 (11.4)
n	1,276 (84.6%)	N
Change in Oxford Score	12.0 (10.8)	12.5 (10.7)
n	1,110 (73.6%)	N
Q1 EQ-5D Index	0.195 [-0.003 - 0.620]	0.260 [0.055 - 0.691]
n	820 (54.4%)	N
Q2 EQ-5D Index	0.691 [0.516 0.796]	0.691 [0.516 0.796]
n	949 (62.9%)	N
Change in EQ-5D Index	0.105 [0.000 0.367]	0.240 [0.000 0.567]
n	330 (21.9%)	N
Q1 EQ-VAS	62.2 (22.9)	63.8 (22.0)
n	1,042 (69.1%)	8,569 (92.9%)
Q2 EQ-VAS	64.7 (22.5)	67.3 (21.0)
n	1,251 (83.0%)	8,903 (96.6%)
Change in EQ-VAS	1.7 (25.9)	3.4 (23.4)
n	837 (55.5%)	8,306 (90.1%)
Success Transition		
Much better	711 (47.1%)	4,963 (53.8%)
A little better	282 (18.7%)	1,991 (21.6%)
About the same	141 (9.4%)	931 (10.1%)
A little worse	97 (6.4%)	704 (7.6%)
Much worse	100 (6.6%)	630 (6.8%)
Missing	177 (11.7%)	0 (0.0%)
Patient Satisfaction		
Excellent	215 (14.3%)	1,498 (16.2%)
Very good	363 (24.1%)	2,556 (27.7%)
Good	369 (24.5%)	2,476 (26.9%)
Fair	283 (18.8%)	1,746 (18.9%)
Poor	142 (9.4%)	896 (9.7%)
Missing	136 (9.0%)	47 (0.5%)

* Complete outcome data was defined as patients with fully complete pre- and post-operative Oxford Knee Score, EQ-5D index and Post-operative Success Transition question. A complete EQ-VAS and Post-operative Satisfaction question were not required for our definition as these were not required to test our hypotheses or calculate the minimally important change (MIC). Summary values are presented as mean (SD), median [interquartile range] or count (%). For the incomplete outcome data population, summary measures are provided for fully completed questionnaires within the group.

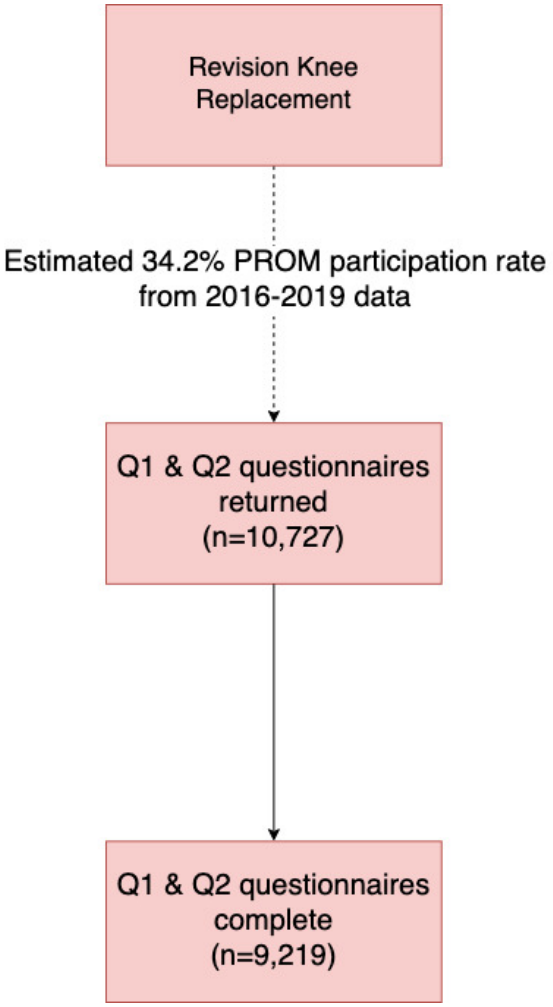

Figure 3.3: NHS PROMs return rate and data attrition

post-operative success transition question. 6530 patients (70.8%) reported post-operative satisfaction of 'Good', 'Very good' or 'Excellent'.

3.2.3.4 Evaluation of internal structure

A high level of internal consistency was found for the OKS with Cronbach's alpha values of 0.88 and 0.94 pre- and post-revision. Alpha values were all very slightly reduced with singular removal of items (observed at three or more decimal places), except for Item 7 'Difficulty with kneeling' for the post-revision measurement only (Tables 3.11 & 3.12).

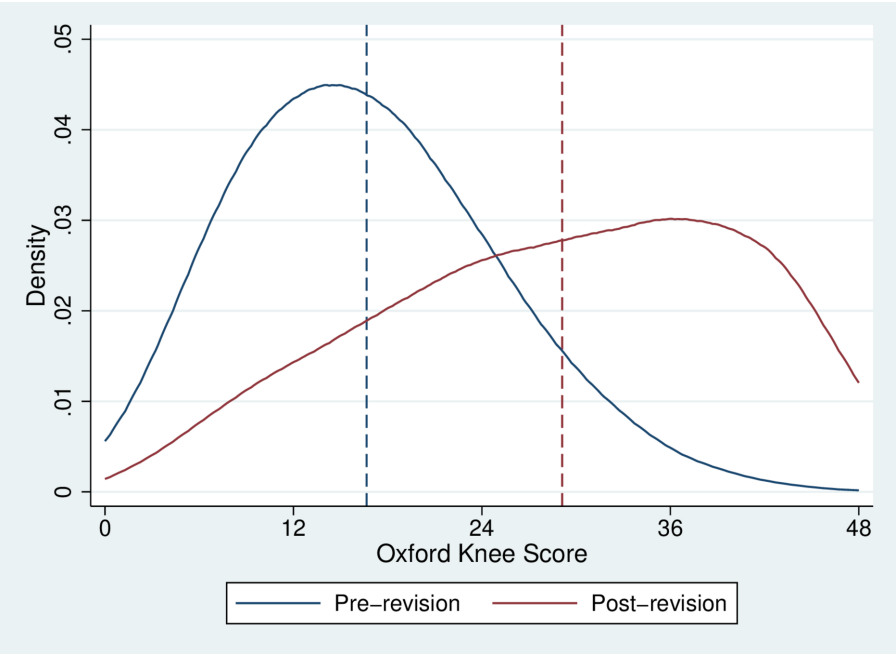

Figure 3.4: Kernel Density Plot of Oxford Knee Score prior to revision and at six months. Dashed lines represent mean OKS for each group.

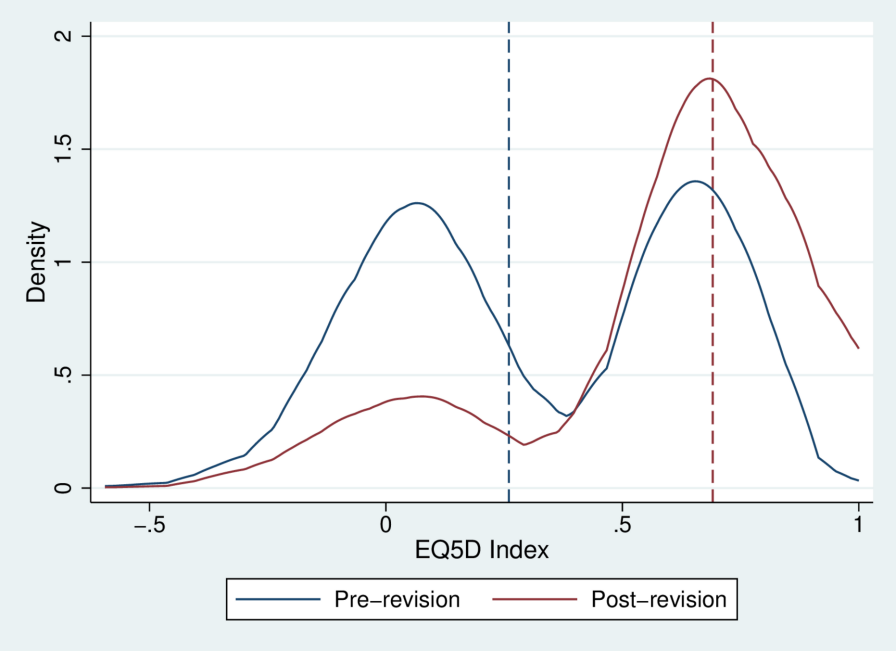

Figure 3.5: Kernel Density Plot of EQ-5D index prior to revision and at six months. Dashed lines represent median EQ-5D index for each group.

Table 3.11: Internal consistency for Oxford Knee Score in rKA (pre-operative score)

Overall Cronbach's Alpha	0.88				
Item	**Mean item score**	**% at floor**	**% at ceiling**	**Item-total correlation**	**Alpha if item removed**
1 Pain	0.58	54	1	0.57	0.88
2 Washing	2.65	2	28	0.65	0.88
3 Transport	1.88	2	5	0.69	0.87
4 Walking time	1.81	19	8	0.68	0.88
5 Standing	1.56	6	2	0.70	0.87
6 Limping	0.78	52	1	0.65	0.88
7 Kneeling	0.40	71	0	0.51	0.88
8 Night pain	1.10	39	6	0.62	0.88
9 Work interference	1.23	23	2	0.79	0.87
10 Instability	1.61	23	8	0.67	0.88
11 Shopping	1.48	31	8	0.76	0.87
12 Stairs	1.58	12	3	0.73	0.87

Table 3.12: Internal consistency for Oxford Knee Score in rKA (post-operative score)

Overall Cronbach's Alpha	0.94				
Item	**Mean item score**	**% at floor**	**% at ceiling**	**Item-total correlation**	**Alpha if item removed**
1 Pain	2.01	11	15	0.80	0.94
2 Washing	3.26	1	55	0.74	0.94
3 Transport	2.65	1	25	0.81	0.94
4 Walking time	2.78	6	37	0.78	0.94
5 Standing	2.57	1	21	0.83	0.94
6 Limping	2.31	16	23	0.83	0.94
7 Kneeling	0.94	54	4	0.62	0.95
8 Night pain	2.29	15	29	0.78	0.94
9 Work interference	2.46	6	23	0.88	0.93
10 Instability	2.96	5	43	0.77	0.94
11 Shopping	2.46	16	34	0.80	0.94
12 Stairs	2.41	7	22	0.79	0.94

3.2.3.5 Construct validity

Pre- and post-revision OKS total score correlated highly (r 0.76, r 0.83, both $p<0.001$) with EQ-5D index, consistent with our prespecified main hypothesis (Table 3.9). For post-revision scores, seven out of eight hypotheses (88%) were accepted for the OKS and its subscales, which COSMIN rate as good [89]. For pre-operative scores, five out of eight hypotheses (63%) were accepted, which is rated moderate. A correlation matrix is provided in Table 3.13 to support these judgements.

Table 3.13: Correlation matrix providing Spearmans rho for OKS versus EQ-5D

		EQ-5D Domain				
Pre-operative measure	**EQ-5D index**	**Mobility**	**Self-Care**	**Usual Activities**	**Pain Discomfort**	**Anxiety Depression**
OKS	0.76	-0.32	-0.52	-0.49	-0.63	-0.36
OKS PCS		-0.29			-0.66	
OKS FCS		-0.33			-0.49	

		EQ-5D Domain				
Post-operative measure	**EQ-5D index**	**Mobility**	**Self-Care**	**Usual Activities**	**Pain Discomfort**	**Anxiety Depression**
OKS	0.83	-0.66	-0.57	-0.69	-0.7	-0.49
OKS PCS		-0.62			-0.71	
OKS FCS		-0.65			-0.61	

		EQ-5D Domain				
Change in measure	**EQ-5D index**	**Mobility**	**Self-Care**	**Usual Activities**	**Pain Discomfort**	**Anxiety Depression**
OKS	0.63	-0.46	-0.34	-0.49	-0.57	-0.31
OKS PCS		-0.44			-0.58	
OKS FCS		-0.44			-0.47	

* OKS, Oxford Knee Score; OKS PCS, Pain Component Subscale; FCS, Function Component Subscale. Spearman rho are presented for pre-operative, post-operative and change in scores for OKS versus EQ5D and their respective subscales/domains. Correlations were performed only for prespecified hypotheses. All $p<0.001$.

3.2.3.6 Responsiveness

Pre- and post-operative OKS and EQ-5D scores were significantly different following knee surgery ($p<0.001$). The OKS measured large mean effect sizes, all of which were greater than corresponding effect sizes for the EQ-5D index. The standardised effect size (SES) of the OKS was 1.54 (90% CI 1.51 – 1.57) and standardised response mean (SRM) 1.16 (1.14 – 1.19). This compared to SES 0.83 (0.81 – 0.86) and SRM 0.76 (0.74 – 0.79) for the EQ-5D index. The change in OKS had moderate correlation with the change in EQ-5D index (r 0.63, $p<0.001$). Overall, exactly half of the hypotheses for responsiveness were accepted, which is rated moderate.

3.2.3.7 Meaningful changes in the OKS

The MIC for an *individual patient* was calculated to be a change in OKS of 7.5 points (95% CI 5.5 to 8.5) based on the optimal cut-off value with specificity 0.72 and sensitivity 0.60, with area under the ROC curve 0.66 (Figure 3.6). The MIC for a *single group* of patients (i.e. the mean COKS for patients who were 'a little better') was calculated to be 9.5 (sd 7.4) points. The mean COKS for patients who were 'about the same' was 4.3 (sd 6.7) points, which indicates a minimal important

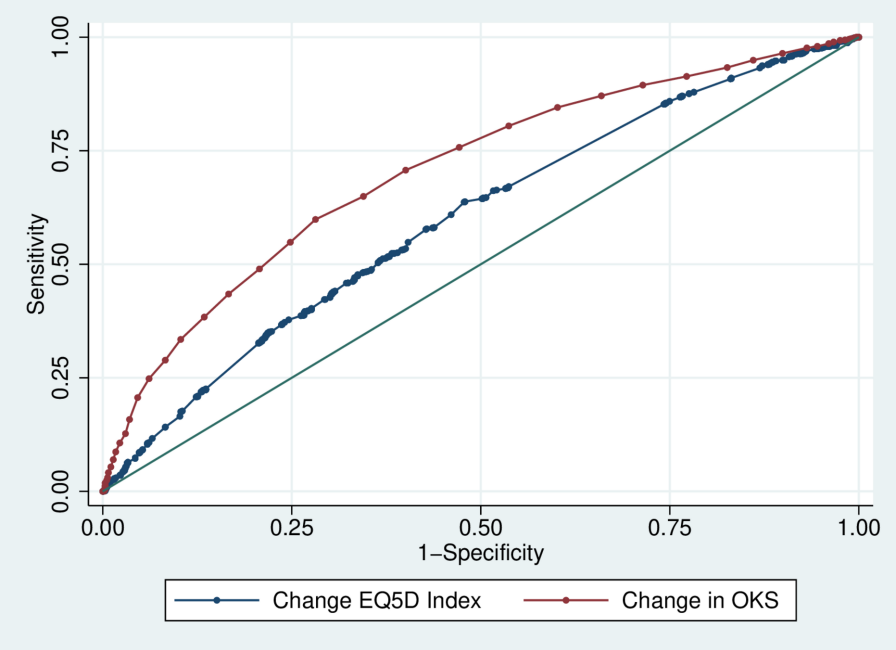

Figure 3.6: Receiver-Operating Characteristic (ROC) Curve for the Oxford Knee Score used in rKA (gold-standard = EQ-5D Index).

difference (MID) of 5.2 points. Patients who reported that they were 'a little worse' were actually a mean of 2.1 points better. The MDC-90 was 3.9 points

3.2.3.8 Floor and ceiling effects

The OKS did not demonstrate significant floor or ceiling effects. The percentages of patients achieving the minimum score were 0.15% and 0.02% pre- and post-revision. The percentages achieving the maximum score were 0.01% and 1.59%, respectively. Floor and ceiling effects are tabulated per item in Tables 3.11 & 3.12.

3.2.4 Discussion

This study demonstrated that the OKS was a responsive instrument for assessment of functional outcome in elective rKA with good measurement properties. At six months post-operation, the OKS was demonstrably more responsive than the EQ-5D index. The anchor-based minimal important change (MIC) was found to be 7.5 points, the minimal important difference (MID) 5.2 points, and the minimal detectable change (MDC-90) 3.9 points. Our work reinforces the paradigm that

extension of a PROM beyond its development population should be accompanied by re-assessment of its measurement properties to ensure that it is valid for use in the new population.

The OKS has been extensively studied in the setting of pKA and has good evidence to support its use [112]. Outside joint replacement, its measurement properties have been investigated for non-operative management of osteoarthritis of the knee [122] and for soft-tissue knee pathology [123]. However, I believe this is the first study to investigate its measurement properties for rKA. I corroborated findings from pKA which showed that the OKS had good psychometric properties: high internal consistency, good convergent and divergent construct validity, and no significant floor or ceiling effects [124; 125; 126]. Our findings disagreed with previous studies which showed that divergent construct validity was unsatisfactory [127]. For the assessment of individual patients, I found an MIC of 7.5 points using an anchor-based method. This metric reflects what the patient considers to be an important *change over time* – the difference between 'a little better' and 'about the same' - rather than statistical inference. In pKA, the MIC for the OKS was similar at 6.5 points [120]. The MID, which reflects the smallest meaningful *difference* in score *between* groups of patients, was the same as for pKA at ~5 points. The MDC-90, which represents the smallest change in score that can be considered beyond the measurement error of the instrument, of ~4 points was the same as a previous study in pKA [120].

This is the first study to evaluate the measurement properties of the OKS in rKA. The study benefits from recruitment of a very large cohort of patients that had completed both the OKS and the EQ-5D, allowing assessment of construct validity. Our methodology is based on latest COSMIN guidance [89] and follows SEARCHeD reporting criteria [115]. The study does have some limitations, and it is important to interpret our findings in the context of the patient sample. Patients are typically enrolled in the NHS national PROMs programme from the outpatient or pre-operative assessment clinic, whilst awaiting elective revision procedures. Patients attending with emergent, non-discretional reasons for revision (such as prosthetic

joint infection, or fracture) are less likely to be enrolled. As such, the measurement properties described are likely to be more applicable to patients with discretional reasons for revision (such as aseptic loosening or prosthesis wear). This study used a de-identified dataset where revision procedures were flagged by Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS-4) codes through central linkage with Hospital Episode Statistics (HES) [83]. Data are entered into HES by trained administrators, with NHS Trusts incentivised to code procedures accurately in order to receive the correct tariff. There is good evidence that HES is a reliable dataset for coding of comorbidities [128; 129], but more evidence is needed to determine to what extent this is true for procedural coding. The wider debate as to which procedures should be considered to be a revision also needs to be addressed. For the purposes of this study, any procedure that contributes to NHS Digital PROMs performance reports for rKA was eligible for inclusion. This included procedures to replace a further compartment of the knee, which do not necessarily represent failure of the primary joint replacement. There may be benefit in the future to examination of a PROM dataset linked to the National Joint Registry (NJR) for England, Wales, Northern Ireland and the Isle of Man, both to investigate the quality of HES procedural coding and to examine the psychometric properties of the OKS for subgroups within the sample. However, data linkage is likely to be associated with heavy attrition of PROM data [78; 79]. Future studies should examine the content validity of the OKS, particularly for non-discretional reasons for revision, where functional benefit may not be the principal objective of surgery.

This study has demonstrated that the OKS is a useful instrument to capture patients' perspectives on pain and function following rKA. A valid score is important not only to interpret outcomes for individual patients, but also to compare across groups of patients and to allow meaningful participation of potential surgical candidates in shared decision-making. In the wider context, valid PROMs are necessary for health economic evaluations [130], for managing healthcare providers [87] and for implementing service reconfigurations that are evidence-based [36].

An outcomes framework to assess rKA is needed and is likely to benefit from the inclusion of PROMs, but must recognise differences in the primary goal of surgery between different revision indications.

In conclusion, this study found that the OKS was a useful and valid instrument for assessment of outcome following rKA. The OKS was responsive to change and demonstrated good measurement properties.

3.2.5 Link to the next chapter

This chapter evaluated PROMs used to evaluate pain and function following rKA. The first part of the chapter scoped the literature to identify eight different joint-specific PROMs in current use for rKA. Only three of these instruments were supported by a validation study: KOOS, LEAS and WOMAC. Each of these instruments was found to require further evidence before recommendation for use. The second part of the chapter addressed the lack of a validation study to support use of the OKS in rKA, despite the instrument being widely used in this context. This found the OKS had good measurement properties and was responsive to change.

Outside the scope of this thesis, I have contributed to work to develop estimates for minimal important changes and differences for primary and revision hip and knee arthroplasties [131] and evaluated the OKS using an item response theory framework [132; 133].

The next chapter will systematically review the literature to characterise the clinical effectiveness of rKA compared to non-operative treatment for the management of patients with aseptic, non-urgent causes for failed knee arthroplasty. This will include summary of pain and joint function using the instruments validated in this chapter, as well as the other domains of patient-relevant outcome described earlier.

4

Patient-relevant outcomes following elective, aseptic revision knee arthroplasty compared to non-operative management

Contents

This chapter has been published:

- *Sabah SA, Hedge EA, von Fritsch L, Xu J, Rajasekaran RB, Hamilton TW, Shearman AD, Alvand A, Beard DJ, Hopewell S, Price AJ. Patient-relevant outcomes following elective, aseptic revision knee arthroplasty: a systematic review. Systematic Reviews. 2023 Aug 1;12(1):133. doi: 10.1186/s13643-023-02290-6*

4.1 Introduction

Around 13% of patients are dissatisfied with their outcome following knee arthroplasty [134] and up to 20% of patients have chronic pain [65]. Whilst many of these patients improve with support, those who do not may look to explore revision surgery. Revision knee arthroplasty (rKA) has been defined earlier, together with some of the common indications for surgery. For some patients, there is an absolute indication for rKA, and alternative treatment options are reserved for those unfit (or unwilling) to undergo surgery. This group can include a variety of diagnoses, but urgent indications (such as prosthetic joint infection [PJI] and certain types of fracture) provide unambiguous examples [135]. Elective, aseptic rKA is more common (>80% cases) [1; 77] and the decision of whether (or when) to undergo rKA follows a shared decision-making process between a patient and their surgeon after discussion of the risks, benefits and alternative treatment options [136]. The goals of surgery in these cases are often similar to primary knee arthroplasty: to reduce pain, improve quality of life and minimise the risk of future complications.

For patients considering elective, aseptic rKA, it follows that full participation in a shared decision-making process requires clear information (supported by high-quality evidence) on the expected outcome should they choose surgery, do nothing or select another type of care [137]. However, the evidence to support these discussions is limited, and has not previously been addressed with a systematic review. As such, the aim of this systematic review was to summarise the evidence for the clinical effectiveness of rKA compared to non-operative treatment for the management of patients with aseptic, non-urgent causes for failed knee arthroplasty.

4.2 Methods

4.2.0.1 Registration and Reporting

The study was prospectively registered with PROSPERO (CRD42020196922) and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 Statement [138].

4.2.0.2 Search strategy

The search strategy (Appendix C) was designed with an experienced information specialist. MEDLINE, Embase, AMED and PsychINFO were searched from inception to 1st December 2020. There was no restriction on language of publication. Reference lists of included studies were examined to identify further relevant publications.

4.2.0.3 Types of study

The literature search was organised into three separate reviews, in anticipation of a large number of studies without a control group that may not be directly synthesised with comparative studies:

- *Review 1:* Randomised and non-randomised studies comparing patient-relevant outcomes of elective, aseptic revision total knee arthroplasty (rKA) to one or more alternative forms of treatment;
- *Review 2*: Uncontrolled studies of patients treated with non-operative management for a failed KA due to an elective, aseptic indication (for example, cohort studies investigating patients on the waiting list for rKA, or patients offered rKA who chose non-operative management); and
- *Review 3:* Uncontrolled studies of patients treated with elective, aseptic rKA.

Randomised studies of any size were eligible for inclusion. Non-randomised studies with fewer than 100 patients were excluded. The chosen sample size threshold was arbitrary, intended to filter out small, low-quality case series which would not be expected to make an important contribution to the review.

4.2.0.4 Population, Interventions, Comparisons and Outcomes (PICO)

The PICO framework for this study is illustrated in Figure 4.1 and described below.

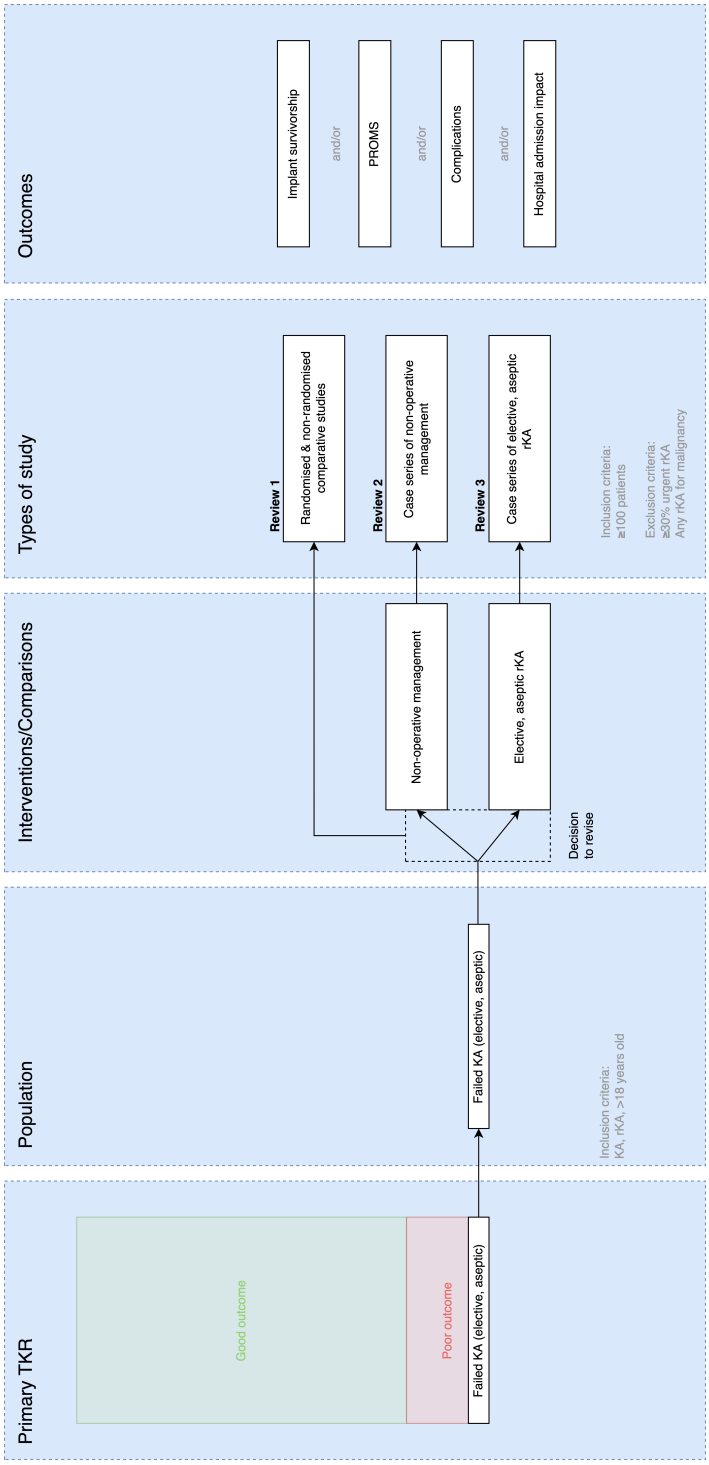

Figure 4.1: A diagram to illustrate the study population, interventions and comparisons, types of study and patient-relevant outcomes for each of the reviews

4. A systematic review of patient-relevant outcomes following elective, aseptic rKA

Population Patients aged 18 years or older with a failed KA were eligible for inclusion. A *failed* KA was defined when patients were explicitly stated to be candidates for rKA. It was anticipated that this definition may haved failed to identify some studies reporting on suitable patients receiving non-operative management. However, I considered it important to be able differentiate this patient group from the larger population with a poor outcome after KA, where revision surgery is often not discussed or offered. I did not consider patient-report outcome measures (PROMs) to be suitable to define failure, since no clear threshold has been defined and current evidence suggests this is likely to vary widely between patients and surgeons [139].

Interventions and Comparators *Revision knee arthroplasty* (rKA) was defined as any procedure following primary knee arthroplasty where a component of an arthroplasty was removed, modified, or added [1]. This included isolated exchange of a polyethylene insert, secondary patella resurfacing after total knee arthroplasty, arthroplasty of a further compartment of the knee after partial knee arthroplasty and re-revision surgery. Studies with any procedures for malignancy were excluded. Studies with up to 30% of procedures for urgent indications (infection or fracture) were included. This threshold was chosen to maximise inclusion of the available literature, without compromising the population of interest. Approximately, 20% of all rKA are performed for 'urgent' indications [1; 77]. The pilot work for this review found that studies often poorly reported whether their populations were undergoing first or re-revision surgery. As such, I did not exclude studies which reported on re-revision procedures. Non-operative management was defined as any intervention to the joint arthroplasty other than revision arthroplasty (including no treatment).

Outcomes The time-points of interest (unless otherwise stated) were defined as: *immediate* ("in-hospital" or up to 30 days), *early* (up to 1 year); *medium-term*

(1-5 years); and *longer-term* (over 5 years). Studies were required to report on one or more of the following outcomes:

1. *Implant survivorship*

The primary outcome of interest was all-cause re-revision surgery (which included both elective, aseptic and non-elective, aseptic reasons for re-revision). Studies were required to report implant survivorship using the Kaplan-Meier method. The time-points of interest were 1, 5, 10 and 15 years. Studies reporting implant survivorship at other time points were rounded down to the nearest of these milestones. A further analysis was performed based on the calculation of person-time incidence rates (PTIRs).

2. *Patient-reported outcome measures (PROMs)*

'Joint-specific' PROMs were defined as instruments addressing one of the following domains: pain, function, combined pain and function, joint-related health status, or patient activity. These instruments were required to be supported by a validation study in a rKA population and to have at least 'potential for recommendation' as defined by the COnsensus-based Standards for the selection of health status Measurement INstruments (COSMIN) initiative [89]. The Knee Injury and Osteoarthritis Outcome Score (KOOS) [97], Lower Extremity Activity Scale (LEAS) [105], Oxford Knee Score (OKS) [96; 140], and Western Ontario and McMaster Universities Arthritis Index (WOMAC) [95] instruments met these criteria. A clinically meaningful change following elective, aseptic rKA has only been defined for the OKS (where the $\text{MIC}_{\text{group}} = 9.5$ points) [140; 131]. For health-related quality of life (QoL), anxiety or depression instruments were not required to have been validated specifically for elective, aseptic rKA.

3. *Acquired comorbidity (including mortality)*

4. A systematic review of patient-relevant outcomes following elective, aseptic rKA

Acquired comorbidity following rKA was recorded for immediate and early follow-up. The following adverse events were recorded: death, allogeneic blood transfusion, cardiac complications, central nervous system complications, deep vein thrombosis, pulmonary embolism, genitourinary complications, renal complications, respiratory complications, post-operative infection (such as deep surgical site infection or sepsis) and wound dehiscence. I also recorded the incidence of 'any complication' where reported as such in a study. This system was chosen based on prior knowledge of World Health Organisation (WHO) International Classification of Disease (ICD) codes, which it was anticipated that many studies would use [141].

4. *Hospital admission impact*

Hospital admission impact was evaluated according to length of stay, requirement for high-dependency or intensive care, and hospital re-admission.

4.2.0.5 Data extraction and management

All citations were imported to the web application Rayyan [142]. De-duplication and abstract screening was performed by two review authors (SS and JX/LF). The full-text of each study potentially meeting inclusion criteria was screened by two reviewers (SS and AS/EH/RB/TH). Disagreements were resolved through discussion. A standardised data collection form was created using the Research Electronic Data Capture (REDCap) data management platform [143]. Data were extracted on study design, dates of study, number of sites and location, and study setting. Participant enrolment and withdrawals were recorded, together with demographic information (age, gender, comorbidities and revision diagnosis). The funding source and notable declarations of interest for trial authors were recorded. Data were extracted from figures at the discretion of the lead author.

4.2.0.6 Data analysis

Meta-analysis was performed for implant survivorship at 1, 5, 10, and 15 years following assessment of clinical and methodological homogeneity. The included

studies were required to report survivorship using Kaplan-Meier estimates, under the assumption that these estimates approximated risk. The Stata package *metan* was used for analysis. A random effects model was used to account for variability among the included studies (for example, due to different characteristics of the patient groups). Statistical heterogeneity was assessed by visual inspection of the forest plot for obvious differences in results between the studies, and by using the Iš and Chiš statistical tests. Where studies did not report a 95% confidence interval around the Kaplan-Meier estimate, simple imputation was performed to impute the mean standard error calculated from the other studies reporting at that time point. A sensitivity analysis was performed to examine the effect of excluding studies with imputed data. Since not all studies reported Kaplan-Meier estimates, an additional analysis was performed for studies that provided data where person time incidence rates (PTIRs) could be calculated. The denominator for rate was calculated by multiplying the number of patients with the mean follow-up. The numerator was calculated by totalling the number of first re-revisions over the study follow-up. The PTIR was then expressed as the number of re-revisions per 100 patient years at risk (which corresponds with current NJR methodology) [144]. Secondary outcome measures (patient reported outcome measures, acquired comorbidity, and hospital admission impact) were evaluated using narrative synthesis with results organised into tables.

4.2.0.7 Quality assessment

Two authors (SS and EH/RB) independently assessed study quality according to the checklist proposed by Wylde et al [145], which was designed for studies on joint arthroplasty. The tool evaluates bias due to patient selection (two items), missing data (one item) and confounding (one item). Each item is rated either 'adequate' or 'inadequate' and reported individually, rather than as a summary score. An adequate rating is given to: (i) recruitment of consecutive patients, (ii) recruitment of patients from multiple centres, (iii) follow-up of more than 80% of patients, and (iv) use of a multivariable model.

4.2.0.8 Missing data

I did not contact investigators or study sponsors to obtain missing outcome data.

4.2.0.9 Software

Statistical analyses were performed using Stata (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC.)

4.3 Results

After deduplication, the titles and abstracts were screened for 4,297 articles. 149 full-text articles were assessed for eligibility. The PRISMA flow diagram is provided in Figure 4.2.

4.3.0.1 Review 1: Elective, aseptic rKA versus non-operative management

No randomised or non-randomised studies were identified that reported on patient-relevant outcomes following elective, aseptic rKA compared to another form of care.

4.3.0.2 Review 2: Non-operative management for failed KA

No studies were identified that reported on patient-relevant outcomes following non-operative management for failed KA.

4.3.0.3 Review 3: Elective, aseptic rKA

Forty non-randomised, uncontrolled studies (434,434 rKA) [146; 147; 148; 149; 150; 151; 152; 153; 154; 155; 156; 157; 158; 159; 160; 161; 162; 163; 164; 165; 166; 167; 168; 169; 170; 171; 172; 173; 12; 174; 31; 175; 176; 177; 178; 179; 180; 181; 182; 183] reported on patient-relevant outcomes following elective, aseptic rKA and were included in this review (Table 4.1).

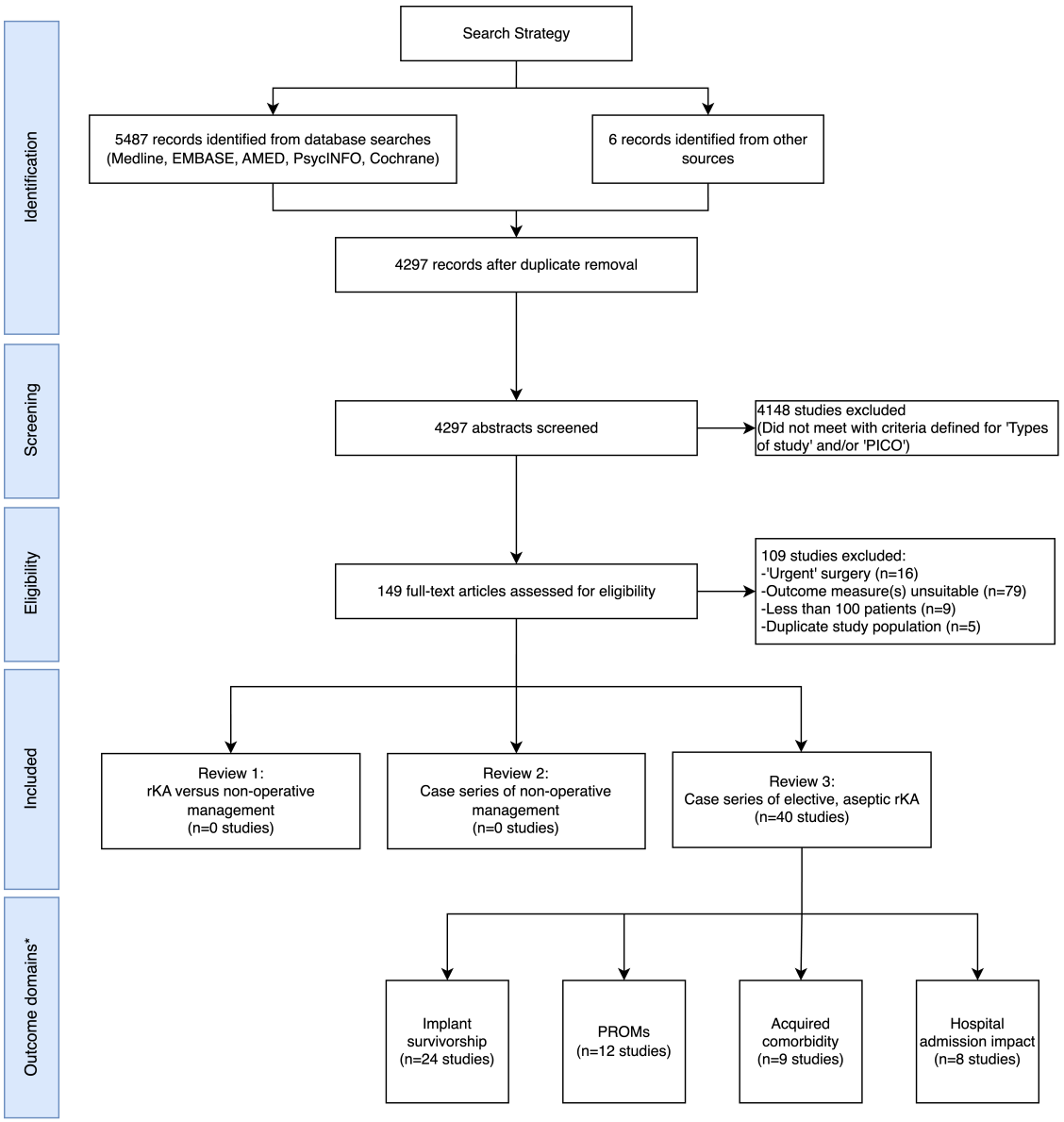

Figure 4.2: PRISMA flow diagram

Table 4.1: Overview of included studies

Study	Study Design	Brief aim (To investigate)	No. rKA	Female (%)	Age in years (mean (sd))	Patient-relevant outcomes			
						Implant survivorship	PROMs	Acquired comorbidity	Hospital admission impact
Bloch et al (2020) [146]	Retrospective observational (single centre)	Implant survivorship of metaphyseal sleeves	316	52	70 (10)	Yes			
Dai et al (2020) [147]	Retrospective observational (NIS)	Immediate complications of rKA	5187	51	66 (NS)			Yes	
Martin et al (2020) [148]	Retrospective observational (single centre)	Implant survivorship following rKA for aseptic loosening tibia	164	62	median 64 (IQR 59-71)	Yes			
Piuzzi et al (2020) [149]	Prospective cohort (OME)	Joint function after aseptic rKA	246	57	65 (10)		Yes		
Bin Abd Razak et al (2019) [150]	Retrospective observational (single centre)	Joint function after rKA	163	77	68 (NS)	Yes	Yes		Yes
Edmiston et al (2019) [151]	Retrospective observational (CCAE/MDCR)	Impact of patient comorbidity on surgical site infection	14486	58	66 (11)			Yes	
Sachdeva et al (2019) [152]	Retrospective observational (single centre)	Implant survivorship and joint function after aseptic rKA	100	64	64 (NS)	Yes			
Stevens et al (2019) [153]	Retrospective observational (single centre)	Implant survivorship and joint function after rKA	100	58	70 (10)	Yes	Yes		
Stockwell et al (2019) [154]	Retrospective observational (single centre)	Implant survivorship and joint function after rKA	170	57	68 (NS)	Yes	Yes		
Turnbull et al (2019) [155]	Retrospective observational (single centre)	Joint function after rKA	112	44	71 (10)	Yes	Yes		
Yao et al (2019) [156]	Retrospective observational (single centre)	Mortality after rKA	3138	53	68 (11)			Yes	
Boddapati et al (2018) [157]	Retrospective, observational (NSQIP)	Immediate complications and hospital admission impact of rKA (aseptic versus PJI)	10584	60	NS			Yes	Yes
Lombardi et al (2018) [158]	Retrospective observational (single centre)	Implant survivorship following rKA for failed unicompartmental KA	193	60	64 (NS)	Yes			
Boylan et al (2017) [159]	Retrospective observational (SPARCS)	Venous thromboembolism after rKA	16630	61	66 (NS)			Yes	
Burnett et al (2017) [160]	Retrospective observational (Humana)	Blood transfusion after rKA	12493	61	NS			Yes	
Crawford et al (2017) [161]	Retrospective observational (single centre)	Implant survivorship after aseptic rKA usaing modular system	278	60	67 (NS)	Yes			
Kim et al (2017) [162]	Retrospective observational (multicentre)	Clinical outcomes following mobile-bearing rKA	280	58	66 (NS)	Yes			
Liang et al (2017) [163]	Retrospective observational (single centre)	Implant survivorship and mode of failure for rKA	258	92	66 (10)	Yes			
Martin-Hernandez et al (2017) [164]	Prospective cohort (single centre)	Joint function after rKA using metaphyseal sleeves	134	61	median 75 (range 51-88)		Yes		
Siqueira et al (2017) [165]	Retrospective observational (single centre)	Implant survivorship of varus-valgus constrained aseptic rKA	315	59	66 (12)	Yes			
Bini et al (2016) [166]	Retrospective observational (TJRR)	Implant survivorship of aseptic rKA	1154	61	65 (10)	Yes			
Leta et al (2016) [167]	Retrospective observational (NAR)	Implant survivorship and joint function following secondary patella resurfacing	308	73	NS	Yes	Yes		
Nichols et al (2016) [168]	Retrospective, observational (MarketScan)	Immediate complications of rKA	25354	58	63 (11)			Yes	Yes
Graichen et al (2015) [169]	Retrospective observational (single centre)	Implant survivorship after aseptic rKA using metaphyseal sleeves	121	69	74 (9)	Yes			
Kim et al (2015) [170]	Retrospective observational (single centre)	Clinical outcomes after condylar constrained rKA	228	87	65 (10)	Yes	Yes		Yes
Kasmire et al (2014) [171]	Retrospective observational (single centre)	Joint function after aseptic rKA	175	63	66 (NS)		Yes		Yes
Kremers et al (2014) [172]	Retrospective observational (single centre)	The effect of obesity on medical costs in KA	1654	53	NS			Yes	Yes
Schairer et al (2014) [173]	Retrospective observational (single centre)	Hospital readmission after rKA	262	56	62 (13)				Yes
Sierra et al (2013) [12]	Retrospective observational (multicentre)	Implant survivorship following rKA for failed unicompartmental KA	175	52	66 (NS)	Yes			
Venkataramanan et al (2013) [174]	Retrospective observational (multicentre)	Patient-reported outcomes after rKA	145	54	69 (10)		Yes		
Baker et al (2012) [31]	Retrospective observational (NJR-PROMs)	Patient-reported outcomes by diagnosis after aseptic rKA	797	53	68 (10)		Yes		
Engh et al (2012) [175]	Retrospective observational (single centre)	Implant survivorship after rKA for polyethylene wear	119	45	68 (NS)	Yes			
Hardeman et al (2012) [176]	Retrospective observational (single centre)	Implant survivorship after rKA	146	NS	68 (NS)	Yes			
Malviya et al (2012) [177]	Retrospective observational (single centre)	Joint function after rKA	120	53	69 (NS)		Yes		
Ong et al (2010) [178]	Retrospective observational (Medicare)	Implant survivorship after rKA	1599	63	72 (5)	Yes			
Wood et al (2009) [179]	Retrospective observational (single centre)	Implant survivorship after rKA using press-fit stem	135	56	71 (NS)	Yes			
Memtsoudis et al (2008) [180]	Retrospective, observational (NHDS)	Immediate complications of rKA	334155	58	68 (NS)			Yes	Yes
Suarez et al (2008) [181]	Retrospective observational (single centre)	Implant survivorship after rKA	443	NS	66 (NS)	Yes			
Sheng et al (2006) [182]	Retrospective observational (FAR)	Implant survivorship after first rKA	1874	NS	69 (NS)	Yes			
Bugbee et al (2001) [183]	Retrospective observational (single centre)	Implant survivorship after rKA	123	NS	NS	Yes			

4.3.0.4 Outcome measures

1. *Implant survivorship*

Fifteen studies [146; 182; 152; 154; 165; 178; 176; 163; 167; 175; 153; 170; 179; 181; 166] reported all-cause implant survivorship for 7,227 rKA (Figure 4.3 and Table 4.2). Seven studies (5,524 rKA) reported survivorship at 1-year, thirteen studies (5,754 rKA) at 5-years, nine studies (2,188 rKA) at 10-years and two studies (452 rKA) at 15-years. Pooled analysis of data found all-cause implant survivorship of 95.5% (95% CI 93.2-97.7%) at 1-year, 90.8% (95% CI 87.6-94.0%) at 5-years, 87.4% (95% CI 81.7-93.1%) at 10-years, and 83.2% (95% CI 76.7-89.7%) at 15-years. These estimates changed little when studies that did not report confidence intervals for survivorship estimates were excluded (Figure 4.4). Eighteen studies (3,205 rKA) [146; 152; 154; 176; 163; 175; 153; 170; 179; 148; 169; 155; 162; 161; 158; 12; 183; 150] provided data from which person-time incidence rates could be calculated. These are provided as a further sensitivity analysis in Table 4.3.

2. *Patient-reported outcome measures (PROMs)*

Twelve studies [167; 31; 154; 150; 153; 164; 177; 171; 174; 170; 155; 149] reported on the outcome of 2,382 rKA with one or more returned PROM questionnaires (Table 4.4). The instruments used to report joint function were: KOOS (2 studies), OKS (5 studies), and WOMAC (5 studies). The instruments used to report QoL were: EQ-5D (2 studies), SF-12 (2 studies) and SF-36 (3 studies). None of the included studies measured anxiety or depression using dedicated instruments, although these domains were assessed within some of PROMs listed above. Ten of the twelve studies (83.3%) reporting on joint-function and six of the seven studies (85.7%) reporting on QoL provided both pre-operative and post-operative summary statistics. Each of these studies reported improvement in joint-function and QoL following elective, aseptic rKA. Indeed, the two studies that reported mean change in score using the OKS [31; 150], both found that improvement in joint function exceeded the MIC_{group} estimate of 9.5 points at all post-operative timepoints.

Table 4.2: Studies reporting implant survivorship following rKA using Kaplan-Meier estimates

		Implant survivorship		
Study	No. knees[1]	Estimate (%)	Lower confidence interval (%)	Upper confidence interval (%)
1 year				
Bloch et al (2020)	316	99.7	97.8	100
Sheng et al (2006)[3]	1874	95	94	96
Sachdeva et al (2019)[3]	100	87	NS	NS
Stockwell et al (2019)	234	99.6	97.3	99.9
Siqueira et al (2017)[2]	247	92.8	NS	NS
Ong et al (2010)[2]	1599	94.1	92.7	95.1
Bini et al (2016)[3]	1154	97.1	95.7	98.1
5 years				
Bloch et al (2020)	316	98.7	96.5	99.5
Sheng et al (2006)	1874	89	88	90
Stockwell et al (2019)	234	92.3	87.9	95.2
Hardeman et al (2011)	146	90	NS	NS
Liang et al (2017)	258	97.8	97.1	99.1
Leta et al (2016)	308	91	87	94
Engh et al (2012)	119	87	81	93
Stevens et al (2019)	100	89	87.3	90.7
Ong et al (2010)[2]	1599	87.4	85.2	89.3
Siqueira et al (2017)[2]	247	81.3	NS	NS
Kim et al (2015)	194	100	94.3	100
Wood et al (2009)	135	95	NS	NS
Bini et al (2016)	1154	80	76	84
10 years				
Bloch et al (2020)	316	97.8	94.2	99.2
Sheng et al (2006)	1874	79	78	81
Siqueira et al (2017)	247	75.8	70.4	81.7
Kim et al (2015)	194	97.8	92.5	99
Suarez et al (2008)[4]	443	85	79	91
Hardeman et al (2011)	146	84.6	NS	NS
Liang et al (2017)	258	91.4	89.3	94.3
Leta et al (2016)	308	87	82	91
Wood et al (2009)[4]	135	87	NS	NS
15 years				
Kim et al (2015)[5]	194	87.3	81.3	96.4
Liang et al (2017)	258	80.5	76.6	85.6

NS, Not specified;
[1] The number of knees enrolled at the beginning of each study are presented, since few studies reported the number of participants at-risk at each follow-up timepoint;
[2] Estimate extracted from figure;
[3] Follow-up rounded down to timepoint from 2-year estimate
[4] Follow-up rounded down to timepoint from 12-year estimate;
[5] Follow-up rounded down to timepoint from 16-year estimate;

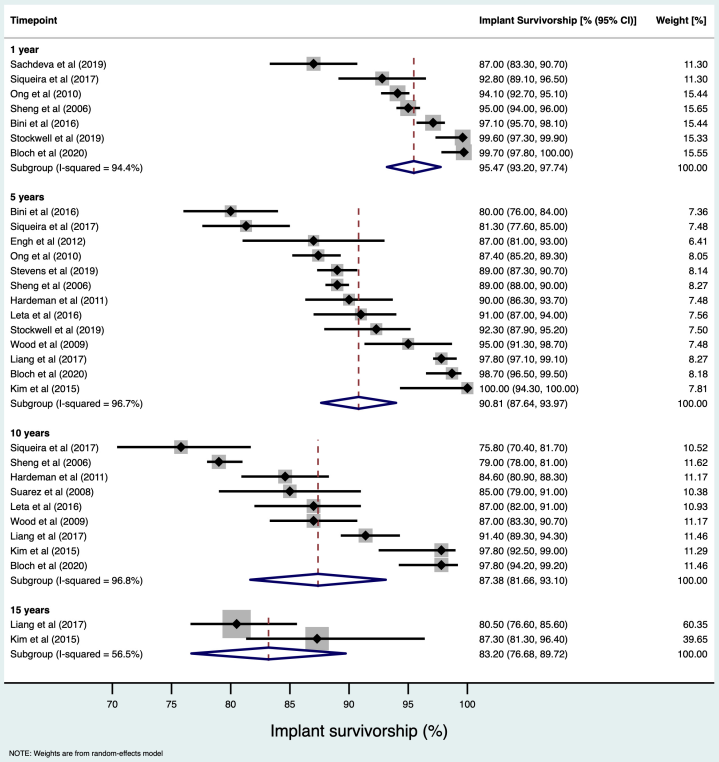

Figure 4.3: Forest plot of estimates for implant survivorship following elective, aseptic rKA

Table 4.3: Studies reporting implant survivorship for rKA expressed as person-time incidence rates (PTIR)

Study[1]	Time period[2]	Mean follow-up (years)	No. knees	No. revisions	PTIR[3]
Martin et al (2020)	Medium term	3.5	164	12	2.1
Graichen et al (2015)	Medium term	3.6	121	14	3.2
Turnbull et al (2019)	Medium term	3.9	112	16	3.7
Sachdeva et al (2019)	Medium term	4.3	100	13	3.0
Engh et al (2012)	Medium term	4.6	119	17	3.1
Hardeman et al (2011)	Medium term	4.8	146	13	1.9
Stockwell et al (2019)	Medium term	4.9	234	16	1.4
Kim et al (2017)	Medium term	4.9	280	29	2.1
Wood et al (2009)	Medium term	5.0	135	6	0.9
Crawford et al (2017)	Long term	6.0	278	25	1.5
Lombardi et al (2018)	Long term	6.1	193	13	1.1
Sierra et al (2013)	Long term	6.3	175	9	0.8
Bugbee et al (2001)	Long term	7.0	123	20	2.3
Stevens et al (2019)	Long term	7.2	100	12	1.7
Bloch et al (2020)	Long term	7.6	316	5	0.2
Bin et al (2019)	Long term	8.4	163	1	0.1
Liang et al (2017)	Long term	9.8	258	21	0.8
Kim et al (2015)	Long term	14.6	194	18	0.6

[1] Sorted by mean follow-up time from revision KA;
[2] Medium term defined as 1-5 years; Long-term defined as >5 years;
[3] PTIR, Person time incidence rate of re-revision KA per 100 person-years

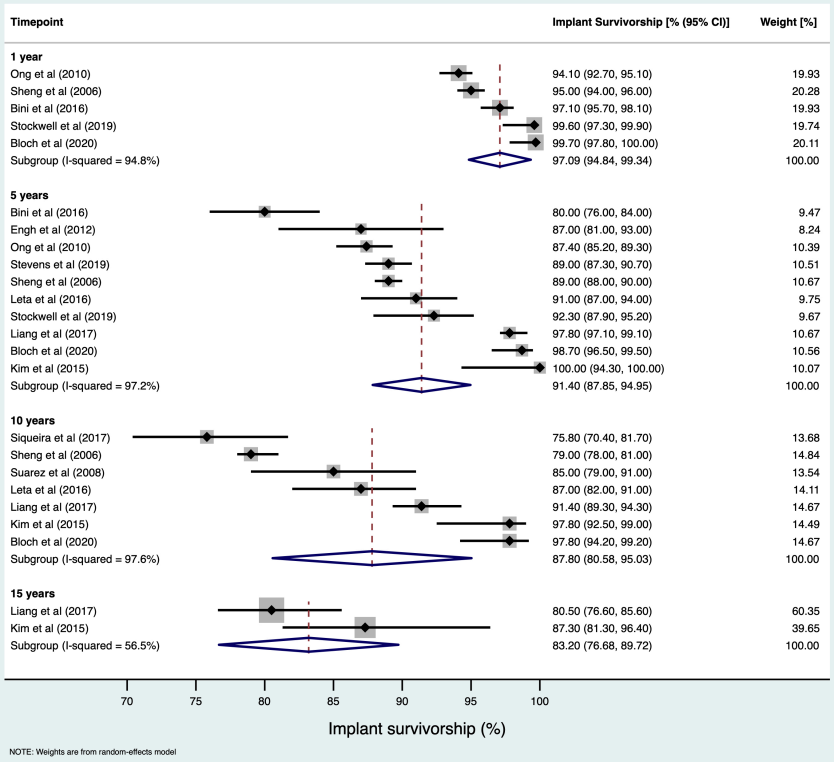

Figure 4.4: Sensitivity analysis: Forest plot of estimates for implant survivorship following elective, aseptic rKA. Studies not reporting confidence intervals excluded.

Table 4.4: Studies reporting on PROM instruments

Instrument	Subscale	Study[1]	Study Design	Timepoint	No. rKA[2]	Scale (Best-worst)	Pre-op. score (mean [sd])	Post-op. score (mean [sd])	Change score (mean [sd])
Joint-specific KOOS									
	ADL	Leta (2016) [167]	Retrospective (NAR)	≥ 1 yr	114	100 to 0	NS	52 [24]	NS
	Pain	Piuzzi (2020) [149]	Prospective (OME)	1 yr	246	100 to 0	39.9 [19.9][3]	NS	30.3 [24.5]
	Pain	Leta (2016) [167]	Retrospective (NAR)	≥ 1 yr	114	100 to 0	NS	55 [25]	NS
	PS	Piuzzi (2020) [149]	Prospective (OME)	1 yr	246	100 to 0	45.9 [17.8][3]	NS	19.2 [22.5]
	QoL	Piuzzi (2020) [149]	Prospective (OME)	1 yr	246	100 to 0	18.5 [18.8][3]	NS	29.7 [28.0]
	QoL	Leta (2016) [167]	Retrospective (NAR)	≥ 1 yr	114	100 to 0	NS	38 [26]	NS
	Symptoms	Leta (2016) [167]	Retrospective (NAR)	≥ 1 yr	114	100 to 0	NS	64 [20]	NS
	Sports Rec.	Leta (2016) [167]	Retrospective (NAR)	≥ 1 yr	114	100 to 0	NS	17 [22]	NS
OKS									
		Baker (2012) [31]	Retrospective (NJR-PROMs)	6 mo	797	48 to 0	16.2 [8.6]	26.6 [11.5]	10.4 [10.1]
		Stockwell (2019) [154]	Retrospective (single centre)	1 yr	209	48 to 0	18.8 [NS]	31.7 [NS]	NS
		Stockwell (2019) [154]	Retrospective (single centre)	2 yr	170	48 to 0	18.8 [NS]	30.7 [NS]	NS
		Bin Abd Razak (2019)[4] [150]	Retrospective (single centre)	2 yr	163	48 to 0	21 [NS]	36 [NS]	15 [NS]
		Stockwell (2019) [154]	Retrospective (single centre)	Last fu (mean 5.1 yr)	139	48 to 0	18.8 [NS]	30.6 [NS]	NS
		Turnbull (2019) [155]	Retrospective (single centre)	Last fu (mean 3.9 yr)	112	48 to 0	15 [8.8]	27 [11.1]	NS
		Bin Abd Razak (2019)[4] [150]	Retrospective (single centre)	5 yr	163	48 to 0	21 [NS]	38 [NS]	17 [NS]
		Stevens (2019) [153]	Retrospective (single centre)	min 5 yr, med 7.2 yr	45	48 to 0	NS	27 [11.9]	NS
WOMAC									

Table 4.4: Studies reporting on PROM instruments *(continued)*

Instrument	Subscale	Study[1]	Study Design	Timepoint	No. rKA[2]	Scale (Best-worst)	Pre-op. score (mean [sd])	Post-op. score (mean [sd])	Change score (mean [sd])
	Pain	Martin-Hernandez (2017)[4] [164]	Prospective (single centre)	3 mo	134	100 to 0	40 [NS]	55 [NS]	NS
	Pain	Martin-Hernandez (2017)[4] [164]	Prospective (single centre)	1 yr	134	100 to 0	40 [NS]	75 [NS]	NS
	Pain	Malviya (2012) [177]	Retrospective (single centre)	1 yr	120	100 to 0	34.5 [14.9]	61.9 [19.1]	NS
	Pain	Kasmire (2014)[4] [171]	Retrospective (single centre)	2 yr	175	100 to 0	48.5 [NS]	74 [NS]	NS
	Pain	Venkataramanan (2013) [174]	Retrospective (multi-centre)	2 yr	145	100 to 0	46.5 [19.8]	71.3 [24.4]	NS
	Pain	Martin-Hernandez (2017)[4] [164]	Prospective (single centre)	Last fu (med 72 mo)	134	100 to 0	40 [NS]	80 [NS]	NS
	Stiffness	Martin-Hernandez (2017)[4] [164]	Prospective (single centre)	3 mo	134	100 to 0	37.5 [NS]	62.5 [NS]	NS
	Stiffness	Martin-Hernandez (2017)[4] [164]	Prospective (single centre)	1 yr	134	100 to 0	37.5 [NS]	75 [NS]	NS
	Stiffness	Malviya (2012) [177]	Retrospective (single centre)	1 yr	120	100 to 0	40.4 [17.1]	59.7 [18.7]	NS
	Stiffness	Kasmire (2014)[4] [171]	Retrospective (single centre)	2 yr	175	100 to 0	47.5 [NS]	68.8 [NS]	NS
	Stiffness	Martin-Hernandez (2017)[4] [164]	Prospective (single centre)	Last fu (med 72 mo)	134	100 to 0	37.5 [NS]	75 [NS]	NS
	Function	Martin-Hernandez (2017)[4] [164]	Prospective (single centre)	3 mo	134	100 to 0	33.8 [NS]	51.5 [NS]	NS
	Function	Martin-Hernandez (2017)[4] [164]	Prospective (single centre)	1 yr	134	100 to 0	33.8 [NS]	73.5 [NS]	NS
	Function	Malviya (2012) [177]	Retrospective (single centre)	1 yr	120	100 to 0	32.1 [16.6]	54.6 [20.1]	NS
	Function	Kasmire (2014)[4] [171]	Retrospective (single centre)	2 yr	175	100 to 0	49.7 [NS]	70.0 [NS]	NS
	Function	Venkataramanan (2013) [174]	Retrospective (multi-centre)	2 yr	145	100 to 0	45.5 [20]	65.8 [22.3]	NS
	Function	Martin-Hernandez (2017)[4] [164]	Prospective (single centre)	Last fu (med 72 mo)	134	100 to 0	33.8 [NS]	79.4 [NS]	NS
	Total	Kim (2015)[4] [170]	Retrospective (single centre)	1 yr	192	100 to 0	8.3 [NS]	74.0 [NS]	NS
	Total	Kim (2015)[4] [170]	Retrospective (single centre)	5 yr	183	100 to 0	8.3 [NS]	75.0 [NS]	NS

Table 4.4: Studies reporting on PROM instruments *(continued)*

Instrument	Subscale	Study[1]	Study Design	Timepoint	No. rKA[2]	Scale (Best-worst)	Pre-op. score (mean [sd])	Post-op. score (mean [sd])	Change score (mean [sd])
	Total	Kim (2015)[4] [170]	Retrospective (single centre)	10 yr	183	100 to 0	8.3 [NS]	76.0 [NS]	NS
	Total	Kim (2015)[4] [170]	Retrospective (single centre)	15 yr	183	100 to 0	8.3 [NS]	74.0 [NS]	NS
Generic									
EQ-5D									
		Baker (2012)[5] [31]	Retrospective (NJR-PROMs)	6 mo	797	1.00 to -0.59	0.310 [0.346]	0.541 [0.382]	0.231 [0.338]
		Leta (2016) [167]	Retrospective (NAR)	$\geq$ 1 yr	114	1.00 to -0.59	0.41 [0.21]	0.56 [0.25]	NS
SF-12									
	PCS	Martin-Hernandez (2017) [164]	Prospective (single centre)	3 mo	134	100 to 0	27 [NS]	37 [NS]	NS
	PCS	Martin-Hernandez (2017) [164]	Prospective (single centre)	1 yr	134	100 to 0	27 [NS]	41 [NS]	NS
	PCS	Martin-Hernandez (2017) [164]	Prospective (single centre)	Last fu (med 72 mo)	134	100 to 0	27 [NS]	44 [NS]	NS
	PCS	Stevens (2019) [153]	Retrospective (single centre)	min 5 yr, med 7.2 yr	45	100 to 0	NS	40.6 [17.6]	NS
	MCS	Martin-Hernandez (2017) [164]	Prospective (single centre)	3 mo	134	100 to 0	43 [NS]	48 [NS]	NS
	MCS	Martin-Hernandez (2017) [164]	Prospective (single centre)	1 yr	134	100 to 0	43 [NS]	51 [NS]	NS
	MCS	Martin-Hernandez (2017) [164]	Prospective (single centre)	Last fu (med 72 mo)	134	100 to 0	43 [NS]	54 [NS]	NS
	MCS	Stevens (2019) [153]	Retrospective (single centre)	min 5 yr, med 7.2 yr	45	100 to 0	NS	48.3 [15.5]	NS
SF-36									
	PCS	Kasmire (2014) [171]	Retrospective (single centre)	2 yr	175	100 to 0	40.7 [NS]	55.5 [NS]	NS
	PCS	Bin Abd Razak (2019) [150]	Retrospective (single centre)	2 yr	163	100 to 0	28 [NS]	45 [NS]	17 [NS]
	PCS	Bin Abd Razak (2019) [150]	Retrospective (single centre)	5 yr	163	100 to 0	28 [NS]	46 [NS]	18 [NS]
	MCS	Kasmire (2014) [171]	Retrospective (single centre)	2 yr	175	100 to 0	60.3 [NS]	70.2 [NS]	NS

Table 4.4: Studies reporting on PROM instruments *(continued)*

Instrument	Subscale	Study[1]	Study Design	Timepoint	No. rKA[2]	Scale (Best-worst)	Pre-op. score (mean [sd])	Post-op. score (mean [sd])	Change score (mean [sd])
	MCS	Bin Abd Razak (2019) [150]	Retrospective (single centre)	2 yr	163	100 to 0	49 [NS]	52 [NS]	3 [NS]
	MCS	Venkataramanan (2013) [174]	Retrospective (multi-centre)	2 yr	145	100 to 0	51.9 [11.5]	54.6 [9.7]	NS
	MCS	Bin Abd Razak (2019) [150]	Retrospective (single centre)	5 yr	163	100 to 0	49 [NS]	53 [NS]	4 [NS]

ADL, Activities of daily living; KOOS, Knee Injury and Osteoarthritis Outcome Score ; MCS, Mental component score; NAR, Norwegian Arthroplasty Register; NJR, National Joint Registry; NS, Not specified; OKS, Oxford Knee Score; OME, Orthopaedic Minimal Data Set Episode of Care database; PCS, Physical component score; PROMs, NHS Patient Reported Outcome Measures; PS, KOOS Physical Function Short Form; QoL, Quality of life; SF, Short form; WOMAC, Western Ontario and McMaster Universities Arthritis Index;

[1] Sorted by PROM instrument, subscale, timepoint then study size ;

[2] rKA who responded to PROM questionnaire ;

[3] Cohort with 1-year PROM available ;

[4] Reported scores transformed to the scale indicated ;

[5] Standard deviations calculated from 95% confidence intervals ;

Table 4.5: Studies reporting on mortality after rKA

Study [1]	Study Design	Timepoint	No. rKA	No. Deaths	Mortality rate
Memtsoudis et al (2008) [180]	Retrospective observational (NHDS)	Immediate (in hospital)	334155	560	0.2%
Dai et al (2020) [147]	Retrospective observational (NIS)	Immediate (in hospital)	5187	14	0.3%
Boddapati et al (2017) [157]	Retrospective observational (NSQIP)	Immediate (within 30 days)	10584	NS	0.16%
Yao et al (2018) [156]	Retrospective observational (single centre)	Early (within 1 year)	3138	NS	1-2% [2]

NS, not specified; NHDS, National Hospital Discharge Survey; NIS, Nationwide Inpatient Sample; NSQIP, American College of Surgeons National Surgical Quality Improvement Program; rKA, revision total knee arthroplasty
[1] Sorted by timepoint of assessment, then study size;
[2] For indications other than fracture and infection;

3. *Acquired comorbidity*

a. *Mortality*

Four studies (353,064 rKA) reported mortality rates after rKA [180; 147; 157; 156] (Table 4.5). Three studies reported on *immediate-term* mortality [180; 147; 157] with estimates ranging from 0.16% to 0.30%. Yao et al [156] reported an *early* (1-year) mortality rate of 1-2% for indications other than fracture and infection from a single tertiary centre in the United States between 1985-2015.

b. *Blood transfusion*

Four studies [147; 157; 168; 160] (53,618 rKA) reported on the need for blood transfusion following rKA (Table 4.6. All studies were based in the United States and the rate of blood transfusion ranged from 8.4% [168] to 18.4% [147]. Nichols et al [168] analysed the Marketscan administrative claims dataset and reported a rate of allogeneic blood transfusion of 7.9% during the index hospitalisation, with a further 0.5% requiring autologous blood transfusion. Dai et al [147] reported a transfusion rate of 18.4% during the index hospitalisation from 5187 patients within the US Nationwide Inpatient Sample (NIS). Burnett et al [160] analysed the Humana Inc. administrative claims database where 11.9% of patients required blood transfusion within 3 days of rKA between 2007-2015. Most transfusions (92.0%) were with allogeneic packed red blood cells and they found a 72% reduction in requirement for blood transfusion from 2007 (15.9% rKA) to 2015 (4.5% rKA). Boddapati et al [157] analysed data from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) where they found a transfusion rate of 11.9% within 30-days of aseptic rKA.

Table 4.6: Studies reporting on blood transfusion after rKA

Study [1]	Study Design	Timepoint	No. rKA	Transfused
Nichols et al (2016) [168] [3]	Retrospective observational (MarketScan)	Early (within 90 days)	25354	2130 (8.4%)
Burnett et al (2017) [160]	Retrospective observational (Humana Inc)	Immediate (within 3 days)	12493	1482 (11.9%)
Boddapati et al (2017) [157]	Retrospective observational (NSQIP)	Immediate (within 30 days)	10584	1256 (11.9%)
Dai et al (2020) [147]	Retrospective observational (NIS)	Immediate (""in-hospital"")	5187	955 (18.4%)

NIS, Nationwide Inpatient Sample; NSQIP, American College of Surgeons National Surgical Quality Improvement Program; rKA, revision total knee arthroplasty
[1] Sorted by study size;

c. *Complications*

Seven studies [180; 147; 157; 168; 159; 151; 172] (408,050 rKA) reported on complications after rKA (Table 4.7). Three studies reported *immediate* complications [180; 147; 157] and four studies reported *early* complications [168; 159; 151; 172]. The rate of any complication at up to 90 days ranged from 9.1% [172] to 37.2% [168]. The reported rate of surgical site infection ranged from 15.6% [151] to 24.1% [168] in the two studies reporting *early* complications. Studies reporting *immediate* complications all reported lower rates of post-operative infection (<1%). The specific complication of wound dehiscence was identified in 0.3% [180] to 1.7% [168] rKA. Medical complications included: deep vein thrombosis (0.2% [147] to 1.7% [159] rKA), pulmonary embolism (0.1% [168] to 0.6% [159] rKA), cardiac complications (0.3% [168] to 0.9% [180] rKA) and central nervous system complications (0.1% [180; 157] rKA).

Table 4.7: Early complications after rKA

Study [1]	Study Design	Timepoint	No. rKA	Any complication[2]	Cardiac[2]	Central nervous system[2]	Deep vein thrombosis[2]	Pulmonary embolism[2]	Genitourinary[2]	Renal[2]	Respiratory[2]	Post-operative infection[2]	Wound dehiscence[2]
Memtsoudis et al (2008) [180]	Retrospective observational (NHDS)	Immediate (in hospital)	334155	29007 (8.7%)	3141 (0.9%)	308 (0.1%)	NS	NS	3020 (1%)	NS	4393 (1.3%)	2241 (0.7%)	854 (0.3%)
Dai et al (2020) [147]	Retrospective observational (NIS)	Immediate (in hospital)	5187	1025 (19.8%)	41 (0.8%)	NS	10 (0.2%)	12 (0.2%)	32 (0.6%)	NS	37 (0.7%)	43 (0.8%)	27 (0.5%)
Boddapati et al (2017) [157] [3]	Retrospective observational (NSQIP)	Immediate (within 30 days)	10584	4.7%	0.4%	0.1%	0.9%	NS	0.9%	0.3%	0.6%	(0.6%)[4]	40 (0.4%)
Nichols et al (2016) [168] [3]	Retrospective observational (MarketScan)	Early (within 90 days)	25354	37.2%	0.3%	NS	NS	0.1%	NS	0.2%	1.3%	24.1%	1.7%
Boylan et al (2017) [159]	Retrospective observational (SPARCS)	Early (within 90 days)	16630	NS	NS	NS	276 (1.7%)	105 (0.6%)	NS	NS	NS	NS	NS
Edmiston et al (2019) [151]	Retrospective observational (CCAE MDCR)	Early (within 90 days)	14486	NS	NS	NS	NS	NS	NS	NS	NS	2259 (15.6%)	NS
Kremers et al (2014) [172]	Retrospective observational (single centre)	Early (within 90 days)	1654	151 (9.1%)	NS	NS	NS	NS	NS	NS	NS	NS	NS

CCAE, IBM Market Scan Commercial Claims and Encounters; MDCR, Medicare Supplemental and Coordination of Benefits; NHDS, National Hospital Discharge Survey; NIS, Nationwide Inpatient Sample; NS, not specified; NSQIP, American College of Surgeons National Surgical Quality Improvement Program; rKA, revision knee arthroplasty; SPARCS, New York Statewide Planning and Research Cooperative System database

[1] Sorted by timepoint of assessment, then study size;

[2] n (%);

[3] Study reported percentage frequency experiencing outcome only;

[4] Coded separately as deep surgical site infection or sepsis after rKA for aseptic indications

Table 4.8: Studies reporting on length of stay (LOS) after rKA

Study[1]	Study Design	No. rKA	Mean LOS (days)	SD LOS (days)
Memtsoudis et al (2008) [180]	Retrospective observational (NHDS)	334155	5.4	NS
Nichols et al (2016) [168]	Retrospective observational (MarketScan)	25354	5.6	7.2
Boddapati et al (2017) [157]	Retrospective observational (NSQIP)	10584	3.4	3.3
Kremers et al (2014) [172]	Retrospective observational (single centre)	1654	5.3	3.1
Schairer et al (2014) [173]	Retrospective observational (single centre)	262	4.6	2.5
Kim et al (2015) [170]	Retrospective observational (single centre)	228	16.0	NS
Kasmire et al (2014) [171]	Retrospective observational (single centre)	175	4.3	NS
Bin Abd Razak et al (2019) [150]	Retrospective observational (single centre)	163	7.7	NS

NHDS, National Hospital Discharge Survey; NS, Not specified; NSQIP, American College of Surgeons National Surgical Quality Improvement Program; rKA, revision total knee arthroplasty
[1] Sorted by study size;

4. *Hospital admission impact*

a. *Length of stay (LOS)*

Eight studies [180; 157; 168; 172; 173; 170; 171; 150] (372575 rKA) reported on LOS after rKA (Table 4.8). Among the studies based in the United States mean LOS ranged from 3.4 days [157] to 5.6 days [168]. Bin Abd Razak et al [150] reported a mean LOS of 7.7 days at a single tertiary centre in Singapore. Whilst Kim et al [170] reported a mean LOS of 16 days following rKA in the Republic of Korea from a single surgeon series.

b. *High-dependency care*

None of the included studies provided information on high-dependency care utilisation after rKA.

c. *Hospital re-admission*

Three studies (36,200 rKA), all from the United States, reported on hospital re-admission after rKA [157; 168; 173] (Table 4.9). Boddapati et al [157] analysed data from 10584 aseptic rKA within ACS-NSQIP between 2005-2015 where they identified a readmission rate of 6% at 30-days. Nichols et al [168] reported a 23% re-admission rate at 90-days based on data from 25,354 rKA registered with the Truven MarketScan database in North America from 2009-2013. Schairer et al [173] reported a 13% re-admission rate at 90-days using a hospital administrative claims database of 262 rKA from 2005-2011.

Table 4.9: Studies reporting on hospital re-admission after rKA

Study[1]	Study Design	Timepoint	No. rKA	Readmissions
Boddapati et al (2017) [157]	Retrospective observational (NSQIP)	Immediate (within 30 days)	10584	581 (5.5%)
Nichols et al (2016) [168]	Retrospective observational (MarketScan)	Early (within 90 days)	25354	5857 (23.1%)
Schairer et al (2014) [173]	Retrospective observational (single centre)	Early (within 90 days)	262	34 (13.0%)

NSQIP, American College of Surgeons National Surgical Quality Improvement Program; rKA, revision total knee arthroplasty
[1] Sorted by timepoint of assessment, then study size;

4.3.0.5 Quality assessment

Among the 40 studies, 21 studies (53%) recruited consecutive patients, 15 studies (38%) were multicentre, 31 studies (78%) had adequate patient follow-up and 20 studies (50%) included a multivariable regression model (Table 4.10).

4.4 Discussion

This study has summarised patient-relevant outcomes (PROs) following elective, aseptic revision knee arthroplasty (rKA). The quality of the included studies was low, comprising uncontrolled observational series. I did not find any studies comparing PROs following revision surgery to non-operative management or no treatment at all. I have addressed the question: "*How long is an elective, aseptic rKA expected to last?*". I found rKA survivorship ~96% at 1 year, ~91% at 5 years, ~87% at 10 years and ~83% at 15 years. All studies reporting on joint function and quality-of-life showed large improvements at early timepoints following rKA. The study has also reported the rate of complications following elective, aseptic rKA. These estimates may be useful to support the process of informed consent. The risk of death in the immediate post-operative period was low, with reported rates of 0.16% to 0.30%. Only one study reported mortality at one-year, with a rate of 2%. The rate of any complication was highly variable (from 9.1% to 37.2% at up to 90 days following surgery). This is likely to reflect the heterogeneity of both patients undergoing elective, aseptic rKA and the procedures themselves. Post-operative infection (which is a set of administrative codes incorporating both systemic sepsis and surgical site infections) was one of the most common complications. There were large differences between studies reporting rates at *immediate* timepoints (<1% *"in-hospital"* or within 30 days) compared to those reporting at *early* timepoints (15.6%

Table 4.10: Assessment of the methodological quality of the included studies using the checklist developed by Wylde et al for studies on joint arthroplasty

Author	Consecutive patients	Representativeness[1]	Follow-up[2]	Minimisation of confounding[3]
Baker et al (2012)	-	+	-	-
Bin Abd Razak et al (2019)	+	-	-	-
Bini et al (2016)	-	+	+	+
Bloch et al (2020)	-	-	+	-
Boddapati et al (2018)	-	+	+	+
Boylan et al (2017)	-	+	+	+
Bugbee et al (2001)	+	-	+	-
Burnett et al (2017)	-	+	+	-
Crawford et al (2017)	+	-	-	-
Dai et al (2020)	-	+	+	+
Edmiston et al (2019)	-	+	+	+
Engh et al (2012)	-	-	+	-
Graichen et al (2015)	+	-	+	-
Hardeman et al (2012)	+	-	+	-
Kasmire et al (2014)	-	-	+	+
Kim et al (2017)	+	+	+	-
Kim et al (2015)	-	-	+	-
Kremers et al (2014)	-	-	+	+
Leta et al (2016)	-	+	-	+
Liang et al (2017)	+	-	-	+
Lombardi et al (2018)	+	-	+	-
Malviya et al (2012)	+	-	+	+
Martin et al (2020)	+	-	-	-
Martin-Hernandez et al (2017)	+	-	+	-
Memtsoudis et al (2008)	+	+	+	+
Nichols et al (2016)	-	+	+	+
Ong et al (2010)	-	+	+	+
Piuzzi et al (2020)	-	-	-	+
Sachdeva et al (2019)	-	-	+	-
Schairer et al (2014)	+	-	+	+
Sheng et al (2006)	+	+	+	+
Sierra et al (2013)	+	+	+	-
Siqueira et al (2017)	+	-	+	+
Stevens et al (2019)	+	-	+	-
Stockwell et al (2019)	+	-	+	-
Suarez et al (2008)	+	-	+	-
Turnbull et al (2019)	-	-	-	+
Venkataramanan et al (2013)	-	+	-	+
Wood et al (2009)	+	-	+	-
Yao et al (2019)	+	-	+	+

+ (adequate); - (inadequate);
[1] Multicentre studies rated +;
[2] A follow-up rate greater than 80% rated +;
[3] Use of multivariate analysis rated +;

to 24.1% within 90 days). Cardiac, central nervous system, genitourinary, renal and respiratory complications were all rare (~1% or less at 90-days). The rate of deep vein thrombosis ranged from 0.2% to 1.7%, while the rate of pulmonary embolism ranged from 0.1% to 0.6% at 90-days. With respect to the hospital admission, the mean length of stay (LOS) in the United States ranged from 3.4 days to 5.6 days. The two studies included from Singapore and Korea both reported longer mean LOS. I have not explored the reasons for this. The rate of re-admission to

hospital ranged from 13% to 23% within the first 90-days. Patients undergoing elective, aseptic rKA were at high risk for blood transfusion, with rates of 8.4% to 18.4% reported.

A number of relevant studies have been published since the literature search for this review was completed. Deere et al [45] reported on implant survivorship following first and multiple rKA procedures using data from the National Joint Registry (NJR) for England, Wales, Northern Ireland, the Isle of Man and the States of Guernsey. They reported Kaplan Meier survivorship estimates for first rKA procedures of 96.4% at 1-year, 87.4% at 5-years and 82.9% at 10-years. The reported re-revision rates at 5- and 10-years were higher than in the present study, which may be due to the inclusion of 'urgent' rKA procedures. They found that male gender and younger age were risk factors for multiple revisions. A recent study from our group reported on mortality and complication rates following 30,826 elective rKA procedures recorded in Hospital Episode Statistics (HES) in the UK [135]. This found a 90-day mortality rate of 0.44%, which is comparable to the estimates reported in this review, and similar to primary KA (0.46%). Of note, the early mortality rate following infected rKA appears to be greater (2.04% at 90-days) [135]. A further study from our group reported on patient-reported outcome measures following elective, aseptic rKA in 10,727 patients from the NHS PROMs dataset [139]. This found that two-thirds of patients experienced a meaningful improvement in joint function after rTKA, 69.4% were satisfied with the procedure and 74.1% felt that surgery was a success [139]. However, the rate of early patient-reported complications was very high (46.0% at 6 months) – which is much higher than reported in administrative datasets, as confirmed by the current review – and this finding requires further exploration.

A major strength of this study is that it has reported domains of outcomes following surgery that patients themselves have identified to be important [41]. Whilst the quality of the included studies was low, this was predicted with the design of the review. Due to the preponderance of small, low-quality studies reporting on elective, aseptic rKA, one inclusion criterion enforced was to exclude studies with fewer

than one hundred participants. This has resulted in bias towards larger studies (such as those reporting data from joint registries and other routine healthcare datasets). On the one hand, these studies have enabled us to capture data on rare outcomes (such as mortality and a range of different complications). However, the limitations of administrative data coding and the restricted perspective of these datasets must also be understood. For example, whilst many studies reported the diagnosis of a complication, this was not always paired with information on the treatment that the patient subsequently went on to receive. Re-operations not classified as re-revisions were poorly reported and so were not summarised. I recognise that elective, aseptic rKA is an 'umbrella term' with heterogeneity in patients, indications for surgery, severity of the disease, and the types of procedure. In the future, estimates for clinical outcomes should be tailored to these different groups. To aid future systematic reviews and meta-analyses, studies reporting on rKA would benefit from consensus on how cause of failure should be categorised. In the meantime, use of a hierarchical system may be beneficial [184].

In conclusion, higher-quality evidence is needed to support patients with the decision of whether to undergo elective, aseptic rKA. This should include studies comparing operative and non-operative management. Implant survivorship following elective, aseptic rKA was ~96% at 1 year, ~91% at 5 years and ~87% at 10 years, with most studies identifying large improvements in pain and joint function. Early complications were common after elective, aseptic rKA and the rates summarised here can be shared with patients during informed consent.

4.5 Link to the next chapter

This chapter has summarised patient-relevant outcomes following aseptic, elective rKA. The estimates produced may be useful to guide conversations around informed consent prior to rKA. However, the quality of the included studies was low and insufficient to support more precise estimates for subgroups within this population.

The next chapter will attempt to address this unmet need by evaluating patient-relevant outcomes for different indications for first rKA using routinely-collected data from the NJR, HES APC, ONS and NHS PROMS.

5

Patient-relevant outcomes by diagnosis for revision knee arthroplasty: An analysis using routinely collected data from the NJR, HES, NHS PROMs and Civil Registrations of Deaths

Contents

This chapter has been published:

- *Sabah SA, Knight R, Alvand A, Palmer AJ, Middleton R, Abram SG, Hopewell S, Petrou S, Beard DJ, Price AJ. Patient-relevant outcomes following first revision total knee arthroplasty, by diagnosis: an analysis of implant survivorship, mortality, serious medical complications, and patient-reported outcome measures utilizing the National Joint Registry data set. JBJS. 2023 Oct*

18;105(20):1611-21. doi: 10.2106/JBJS.23.00251

5.1 Introduction

Revision knee arthroplasty (rKA) describes a heterogeneous set of procedures, with different indications [29] (as described earlier). In general, rKA surgery produces less improvement in joint function and HRQoL compared to pKA [131; 139]. Previous work has highlighted clinically important differences in rKA outcomes between different indications for surgery [31; 135]. rKA for urgent or infective indications has been shown to incur greater costs and higher rates of complications than aseptic, elective rKA [157; 135; 32; 33]. Fewer than half of patients undergoing rKA for stiffness are satisfied with their outcome from surgery, compared to more than two-thirds of patients undergoing surgery for a worn component [31].

A previous study identified the domains of outcome important to patients undergoing joint replacement: survival of the implant, joint function, HRQoL, medical complications and the impact of the hospital admission [41]. These domains are commonly considered individually, rather than presented together. For first rKA, information on these outcomes for different indications for surgery is lacking and is needed to support shared decision-making with patients before surgery.

The aim of this study was to investigate patient-relevant outcomes following first rKA for different indications using routinely collected national data from the UK. The study investigated the rate of further revision surgery (re-revision) at 2 and 5 years; mortality and serious medical complications up to 90 days; patient-reported outcomes at six months; and the length of the index hospital admission.

5.2 Methods

This study is reported according to the RECORD checklist [69]. Ethical approval was obtained from the London-Bromley Research Ethics Committee (20/LO/0428). Data access approvals were obtained from the National Joint Registry (NJR) for England, Wales, Northern Ireland, the Isle of Man and the States of Guernsey

(RSC2017/26) and NHS Digital (DARS-NIC-380650-K4F6X). Datasets were linked after approval from the Confidentiality Advisory Group (20/CAG/0044) supported by Section 251 of the National Health Service Act 2006. Data for patients who opted out of the NJR audit or data collection by NHS Digital were not included.

5.2.0.1 Study datasets

Routinely-collected national data were obtained from the following sources: NJR; Hospital Episode Statistics Admitted Patient Care (HES APC); NHS Patient-Reported Outcome Measures (PROMs); and Civil Registrations (Mortality).

NJR: The NJR is a prospective register of rKA procedures in England, Wales, Northern Ireland, the Isle of Man and the States of Guernsey. Data collection started in 2003 and is now mandatory for both public and private healthcare providers [185]. rKA procedures are submitted using Minimum Data Set (MDS) K2 forms, which include fields for patient, procedure and surgeon characteristics. The NJR originally defined rKA as any *"operation performed to remove and replace one or more components of a total joint prosthesis, for whatever reason"* [70]. The instructions on procedures to be reported changed over the study period, with the addition of: (i) secondary patella resurfacing procedures (from 01/12/2013) and (ii) Debridement, Antibiotics and Implant Retention (DAIR) procedures with or without modular exchange (from 25/06/2018) [186].

HES APC: HES APC includes NHS-funded secondary care episodes in England. Data are entered by trained clerks and submission is mandatory for healthcare providers to receive financial remuneration. Diagnoses are coded using World Health Organization International Classification of Diseases, 10th revision (ICD-10) codes [187]. Procedures are coded using Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS-4) codes [188].

PROMs: The NHS PROMs programme started in 2009 and recruits patients undergoing primary and revision hip and knee arthroplasty procedures. Patients complete a questionnaire pre-operatively (Q1) and at six months following surgery (Q2) [83]. Further information on PROM instruments is provided below.

5. Patient-relevant outcomes by diagnosis following rKA

Mortality: This dataset records date and cause of death and is populated by data from death certificates.

5.2.0.2 Inclusion and exclusion criteria

Patients undergoing first rKA between 1st January 2009 and 30th June 2019 were included in our dataset. All cases were censored on 31st December 2019 (or earlier if an event was observed). These dates were selected to coincide with the start of the NHS PROMs programme and to exclude early NJR data, which had poor compliance [78; 79]. Procedures during the Covid-19 pandemic were excluded under the hypothesis provision of care was not representative of usual practice. Adult patients ($\geq$ 18 years) were eligible for inclusion if they had a *first-linked rKA* procedure recorded on the NJR. This meant that rKA procedures with no pKA recorded on the NJR were excluded, since one could not determine the sequence of events. Where a patient underwent rKA on both knees, only the first procedure was included (or the procedure with the lowest *revision_procedure_id* if simultaneous) to fulfil the assumption of independence of observations. For the analysis of medical complications and length of hospital stay, *first-linked rKA* procedures were joined to a corresponding procedure on HES APC using the methods described below. For the analysis of PROMs, pre-operative PROM questionnaires could be submitted up to a maximum of 90 days prior to revision surgery and post-operative PROM questionnaires needed to be submitted at least 180 days to a maximum of 1-year following revision surgery.

5.2.0.3 Data cleaning and linkage

Statistical code for data preparation and analysis is available as a repository on the lead author's GitHub page. For HES APC, much of the data preparation followed the principles set out in the *HES Pipeline R* from the Health Foundation [189]. Briefly, records in each dataset were de-duplicated and variables were checked for out of range, missing and invalid entries.

For record-linkage, the NJR was used as the master dataset. The *NNNid* field from the NJR dataset was assigned the *study_id* and represented one patient.

Table 5.1: Diagnosis hierarchy for rKA

Rank	NJR diagnosis	Minimum Data Set (MDS) K2 indicators
1	Infection	Infection
2	Malalignment	Malalignment
3	Aseptic loosening & Component wear	Aseptic loosening, Lysis, Wear of polyethylene component, Implant fracture
4	Instability	Instability, Component dissociation, Dislocation / Subluxation
5	Fracture	Peri-prosthetic fracture
6	Progressive arthritis	Progressive arthritis remaining knee
7	Stiffness	Stiffness
8	Unexplained pain	Unexplained pain
9	Other	Other

Patient identifiers stored within the NJR dataset (NHS number, family name, given name, gender, date of birth, postcode) were supplied to NHS Digital to create a HES patient cohort. The data access request was for patient-level linkages where the variable *match_rank* was 4 or less, which indicated *an exact match on NHS number and gender and at least a partial match on date of birth* or better. For the analysis of mortality, NJR records were joined to to Civil Registrations (Mortality) on *study_id* where available. For the analysis of complications and length of stay, the index NJR procedure was required to be joined to HES APC on *study_id* and date of surgery (with a tolerance of +/- 7 days). For the analysis of PROMs, direct linkage of NJR to NHS PROMs was not possible. Instead, HES APC:PROMs linkage was performed by NHS Digital using a four-stage procedure (*patient*, *provider*, *date* and *tie-breaker* matching). Matched PROM records were assigned an identifier (*epikey*) and an indicator of the *closeness* of match (*episode_match_rank*) [83]. PROM records were linked on *epikey* (after sorting to prioritise better matches in the case of duplicates using the *episode_match_rank* field).

5.2.0.4 Groups

Each procedure was assigned a single, dominant indication (*infection/ malalignment/ aseptic loosening/ instability/ fracture/ progressive arthritis/ stiffness/ unexplained pain/ other*) by putting binary indicators on the NJR MDS K2 form into a hierarchy of importance [2; 184] (Table 5.1). Each of the outcome measures below was summarised for each group. While this thesis is focussed on aseptic, elective indications for rKA, urgent indications were included to provide contrast.

5.2.0.5 Outcome measures

Implant survivorship The primary outcome was the cumulative incidence of re-revision surgery at 2 years. A secondary outcome was the cumulative incidence of re-revision surgery at 5 years.

Mortality and serious medical complications recorded in hospital within 90 days of surgery Deaths at up to 90 days following rKA were identified from the Civil Registrations (Mortality) dataset. The following serious medical complications requiring hospital admission were recorded using primary and subsequent diagnosis fields within HES APC: *acute kidney injury (AKI), lower respiratory tract infection (LRTI), myocardial infarction (MI), deep vein thrombosis (DVT), pulmonary embolism (PE), stroke (CVA) and urinary tract infection (UTI).* A list of corresponding ICD-10 codes can be found in the supplementary statistical code.

Patient reported outcome measures

(i) *Post-operative joint function.* Recorded using the Oxford Knee Score (OKS) [96]. The OKS is a 12-Likert item instrument that has been found to have good measurement properties for the assessment of pain and function following rKA [140; 136]. For each item, the best response scores four points, whilst the worst response scores zero points. The scale ranges from 0 points (worst) to 48 points (best) [114].

(ii) *Responder analysis.* Patients were dichotomised into *responders* (if the post-operative OKS score minus the pre-operative OKS score was $\geq$ 6-points, which has been defined as a minimal important change [MIC] for rKA), or *non-responders* [131];

(iii) *Post-operative HRQoL.* This was measured using the EQ-5D-3L [51]. Each permutation of responses to the measure's health status classification system was converted to a utility score scaled for the UK population from -0.594 (worst) to 1 (best). A utility score of zero is considered to represent a health state equivalent to being dead;

5. Patient-relevant outcomes by diagnosis following rKA

(iv) *Satisfaction.* Patients were asked: *"How would you describe the results of your operation?" 'Excellent', 'Very good', 'Good', 'Fair' or 'Poor'.* Responses were analysed as counts with percentage frequency. Patients who responded 'Good' or better were considered to be *satisfied* with the results of their operation.

(v) *Perceived success.* Patients were asked: *"Overall, how are the problems now in the hip/knee on which you had surgery, compared to before your operation?" 'Much better', 'A little better', 'About the same', 'A little worse' or 'Much worse'.* Responses were analysed as counts with percentage frequency. Patients who responded 'Much better' or 'A little better' were deemed to have considered surgery to have been a *success.*

Length of stay (LOS) To calculate length of stay of the index hospital admission for *first rKA*, the duration in days of the single *Continuous Inpatient Spell (CIPS)* on HES APC that corresponded most closely with the date of *first rKA* on the NJR was used. One CIPS refers to one uninterrupted period within NHS secondary care. This may be under the care of many consultants or hospital providers. CIPS were constructed following the methodology described within *HES Pipeline R* [189]. Supplementary analyses were performed for *Finished Consultant Episodes (FCEs)* and *provider spells.* Further detail of different LOS definitions can be found elsewhere [190].

5.2.0.6 Statistical analysis

Patient characteristics (*age, gender, American Society of Anesthesiologists Physical Status Classification, modified Charlson comorbidity index [Summary Hospital-level Mortality Indicator Specification; derived with maximum 5-year diagnosis code look-back][84], index of multiple deprivation, ethnicity, year of surgery*) and the outcome measures defined above were summarised for each revision indication. Continuous variables were described using means and standard deviations (SDs) or medians and interquartile ranges (IQRs) as appropriate, after visual inspection

of data distributions. Binary and categorical data were described using counts with percentages. The cumulative incidence of re-revision surgery was calculated from the complement of net implant survival (1 minus Kaplan-Meier function). All procedures were censored at date of death or end of the study period (31st December 2019). Kaplan-Meier survival curves with 95% confidence intervals and risk tables were constructed. Mortality and serious complications were presented as percentage frequency, with 95% confidence intervals calculated assuming a normal approximation to the Poisson distribution. The PROM linkage rate was defined as the number of knees with a Q1 questionnaire linked to a rKA on the NJR divided by the total number of rKAs on the NJR. Missing data were summarised descriptively for each variable in the dataset. Since the missingness mechanism was unknown, data were assumed to be missing not at random and therefore imputation was not performed, that is all analyses were performed using available data only. Statistical analyses were performed using R version 4.2.1.

5.3 Results

32483 *first-linked rKAs* were recorded on the NJR over the study period. A flowchart to illustrate cleaning and linkage of study records is provided in Figure 5.1. A Shiny application is available at https://shiraz-sabah.shinyapps.io/rKA-app/ to interact with the study results. Baseline patient characteristics are summarised in Table 5.2. The average age at rKA was 68 years (SD 10). More rKAs were performed in females than males overall (17808/32483 [55%]) and for all indications, except infection (2188/5194 [42%] female) and stiffness (655/1360 [48%] female). In patients undergoing rKA to treat fracture, 840/1078 [78%] were female. Patients undergoing rKA for fracture and infection were, on average, older and more comorbid (measured by the proportion ASA Class 3 or more), compared to patients undergoing rKA for other diagnoses. 517/1078 [48%] patients undergoing rKA for fracture and 2037/5194 [39%] undergoing rKA for infection had an American Society of Anesthesiologists (ASA) Class 3 or more, compared with approximately 20% of patients undergoing rKA for other indications.

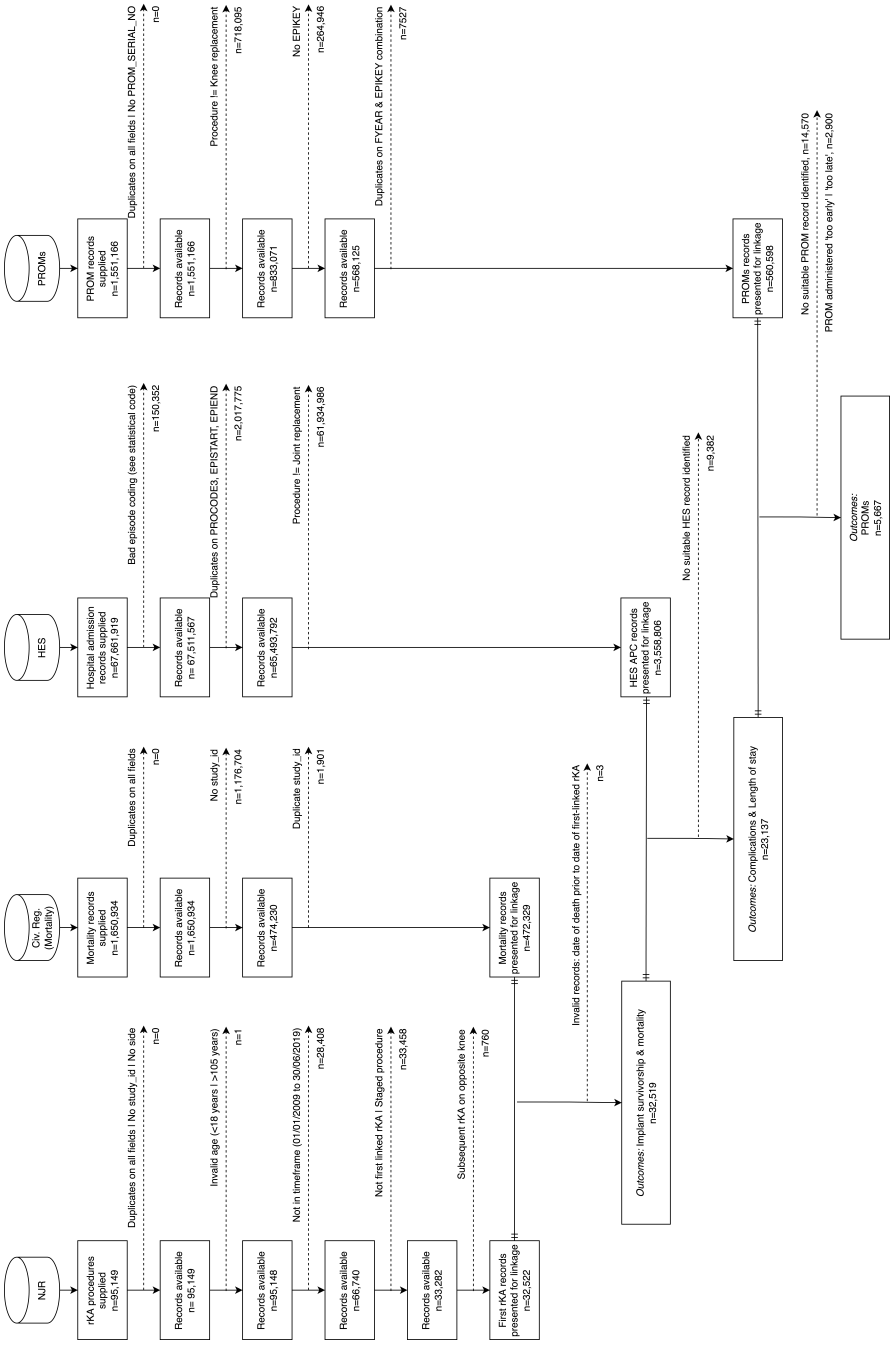

Figure 5.1: Flowchart to demonstrate the attrition of study records during data preparation and record linkage. Where two tables are joined, the attrition of records is reported for the upper left table only (NJR records).

Table 5.2: Baseline characteristics of patients undergoing first rKA by indication

Characteristic	Overall, N = 32,483	Infection, N = 5,194	Malalignment, N = 728	Loosening/Lysis, N = 6,583	Instability, N = 4,677	Fracture, N = 1,078	Progressive Arthritis, N = 4,614	Stiffness, N = 1,360	Unexplained pain, N = 4,669	Other, N = 3,580
Age at rKA (years)										
Mean (SD)	68 (10)	70 (10)	67 (10)	68 (9)	67 (10)	75 (11)	68 (10)	66 (10)	66 (10)	68 (10)
N missing (% missing)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Gender										
Female	17,808 (55%)	2,188 (42%)	476 (65%)	3,430 (52%)	2,677 (57%)	840 (78%)	2,856 (62%)	655 (48%)	2,606 (56%)	2,080 (58%)
Male	14,675 (45%)	3,006 (58%)	252 (35%)	3,153 (48%)	2,000 (43%)	238 (22%)	1,758 (38%)	705 (52%)	2,063 (44%)	1,500 (42%)
ASA grade										
ASA 1	2,475 (7.6%)	211 (4.1%)	60 (8.2%)	506 (7.7%)	410 (8.8%)	29 (2.7%)	374 (8.1%)	130 (9.6%)	437 (9.4%)	318 (8.9%)
ASA 2	21,845 (67%)	2,946 (57%)	514 (71%)	4,589 (70%)	3,140 (67%)	532 (49%)	3,352 (73%)	948 (70%)	3,331 (71%)	2,493 (70%)
ASA 3+	8,163 (25%)	2,037 (39%)	154 (21%)	1,488 (23%)	1,127 (24%)	517 (48%)	888 (19%)	282 (21%)	901 (19%)	769 (21%)
Charlson comorbidity index										
0	11,131 (34%)	1,092 (21%)	288 (40%)	2,554 (39%)	1,718 (37%)	239 (22%)	1,706 (37%)	545 (40%)	1,776 (38%)	1,213 (34%)
1+	11,659 (36%)	1,768 (34%)	292 (40%)	2,466 (37%)	1,675 (36%)	356 (33%)	1,673 (36%)	500 (37%)	1,739 (37%)	1,190 (33%)
Not specified	9,693 (30%)	2,334 (45%)	148 (20%)	1,563 (24%)	1,284 (27%)	483 (45%)	1,235 (27%)	315 (23%)	1,154 (25%)	1,177 (33%)
Body mass index										
Mean (SD)	31.4 (5.9)	31.2 (6.4)	31.5 (6.1)	31.9 (5.9)	31.6 (5.9)	31.1 (7.2)	31.3 (5.4)	31.2 (5.3)	31.5 (5.6)	31.0 (5.8)
N missing (% missing)	11,259 (35%)	2,609 (50%)	213 (29%)	2,042 (31%)	1,486 (32%)	553 (51%)	1,105 (24%)	409 (30%)	1,555 (33%)	1,287 (36%)
Ethnicity										
Asian/Asian British	502 (1.5%)	85 (1.6%)	11 (1.5%)	106 (1.6%)	88 (1.9%)	5 (0.5%)	68 (1.5%)	19 (1.4%)	74 (1.6%)	46 (1.3%)
Black/Black British	303 (0.9%)	38 (0.7%)	7 (1.0%)	114 (1.7%)	62 (1.3%)	7 (0.6%)	13 (0.3%)	19 (1.4%)	24 (0.5%)	19 (0.5%)
Chinese/Other	106 (0.3%)	14 (0.3%)	3 (0.4%)	24 (0.4%)	20 (0.4%)	2 (0.2%)	14 (0.3%)	8 (0.6%)	14 (0.3%)	7 (0.2%)
Mixed	73 (0.2%)	11 (0.2%)	2 (0.3%)	18 (0.3%)	14 (0.3%)	0 (0%)	6 (0.1%)	7 (0.5%)	8 (0.2%)	7 (0.2%)
White	20,368 (63%)	2,550 (49%)	512 (70%)	4,467 (68%)	2,983 (64%)	548 (51%)	3,037 (66%)	916 (67%)	3,192 (68%)	2,163 (60%)
Not specified	11,131 (34%)	2,496 (48%)	193 (27%)	1,854 (28%)	1,510 (32%)	516 (48%)	1,476 (32%)	391 (29%)	1,357 (29%)	1,338 (37%)
Index of multiple deprivation										
Most deprived 20%	4,128 (13%)	540 (10%)	106 (15%)	883 (13%)	626 (13%)	111 (10%)	581 (13%)	192 (14%)	671 (14%)	418 (12%)
More deprived 20-40%	4,249 (13%)	500 (9.6%)	118 (16%)	885 (13%)	624 (13%)	107 (9.9%)	608 (13%)	216 (16%)	715 (15%)	476 (13%)
Middle group	4,424 (14%)	552 (11%)	105 (14%)	1,006 (15%)	662 (14%)	116 (11%)	621 (13%)	210 (15%)	696 (15%)	456 (13%)
Less deprived 20-40%	4,936 (15%)	648 (12%)	113 (16%)	1,150 (17%)	736 (16%)	128 (12%)	737 (16%)	210 (15%)	739 (16%)	475 (13%)
Least deprived 20%	4,713 (15%)	589 (11%)	127 (17%)	1,027 (16%)	675 (14%)	119 (11%)	784 (17%)	193 (14%)	657 (14%)	542 (15%)
Not specified	10,033 (31%)	2,365 (46%)	159 (22%)	1,632 (25%)	1,354 (29%)	497 (46%)	1,283 (28%)	339 (25%)	1,191 (26%)	1,213 (34%)
Year of surgery										
2009	1,884 (5.8%)	270 (5.2%)	55 (7.6%)	404 (6.1%)	256 (5.5%)	40 (3.7%)	55 (1.2%)	80 (5.9%)	389 (8.3%)	335 (9.4%)
2010	2,228 (6.9%)	353 (6.8%)	63 (8.7%)	470 (7.1%)	300 (6.4%)	48 (4.5%)	138 (3.0%)	72 (5.3%)	466 (10.0%)	318 (8.9%)
2011	2,341 (7.2%)	373 (7.2%)	58 (8.0%)	495 (7.5%)	306 (6.5%)	39 (3.6%)	221 (4.8%)	97 (7.1%)	463 (9.9%)	289 (8.1%)
2012	2,958 (9.1%)	447 (8.6%)	69 (9.5%)	592 (9.0%)	415 (8.9%)	66 (6.1%)	324 (7.0%)	119 (8.8%)	561 (12%)	365 (10%)
2013	2,797 (8.6%)	424 (8.2%)	72 (9.9%)	565 (8.6%)	436 (9.3%)	63 (5.8%)	328 (7.1%)	126 (9.3%)	491 (11%)	292 (8.2%)
2014	3,165 (9.7%)	521 (10%)	72 (9.9%)	598 (9.1%)	444 (9.5%)	107 (9.9%)	447 (9.7%)	118 (8.7%)	491 (11%)	367 (10%)
2015	3,476 (11%)	553 (11%)	90 (12%)	675 (10%)	482 (10%)	135 (13%)	576 (12%)	136 (10%)	418 (9.0%)	411 (11%)
2016	3,703 (11%)	586 (11%)	60 (8.2%)	789 (12%)	494 (11%)	152 (14%)	674 (15%)	149 (11%)	429 (9.2%)	370 (10%)
2017	3,877 (12%)	638 (12%)	82 (11%)	782 (12%)	586 (13%)	144 (13%)	712 (15%)	171 (13%)	407 (8.7%)	355 (9.9%)
2018	3,990 (12%)	681 (13%)	58 (8.0%)	815 (12%)	600 (13%)	189 (18%)	756 (16%)	210 (15%)	368 (7.9%)	313 (8.7%)
2019	2,064 (6.4%)	348 (6.7%)	49 (6.7%)	398 (6.0%)	358 (7.7%)	95 (8.8%)	383 (8.3%)	82 (6.0%)	186 (4.0%)	165 (4.6%)

5.3.0.1 Implant survivorship

Overall, the cumulative incidence of re-revision surgery was 7.1% (95% CI: 6.8-7.4%) at 2 years and 12.5% (95% CI: 12.0-12.9%) at 5 years. The cumulative incidence of re-revision surgery is presented for all indications in Figure 5.2. Survival plots with 95% confidence intervals and risk tables are presented for each indication individually in Figures 5.3-5.11. First rKA for infection (one- or two-stage) had the highest cumulative incidence of re-revision at 2 years (16.0% [95% CI: 14.9-17.0%]) and 5 years (22.3% [95% CI: 21.0-23.6%]). First rKA for progressive arthritis had the lowest cumulative incidence of re-revision at 2 years (2.9% [95% CI: 2.4-3.4%]) and 5 years (6.6% [95% CI: 5.6-7.5%]).

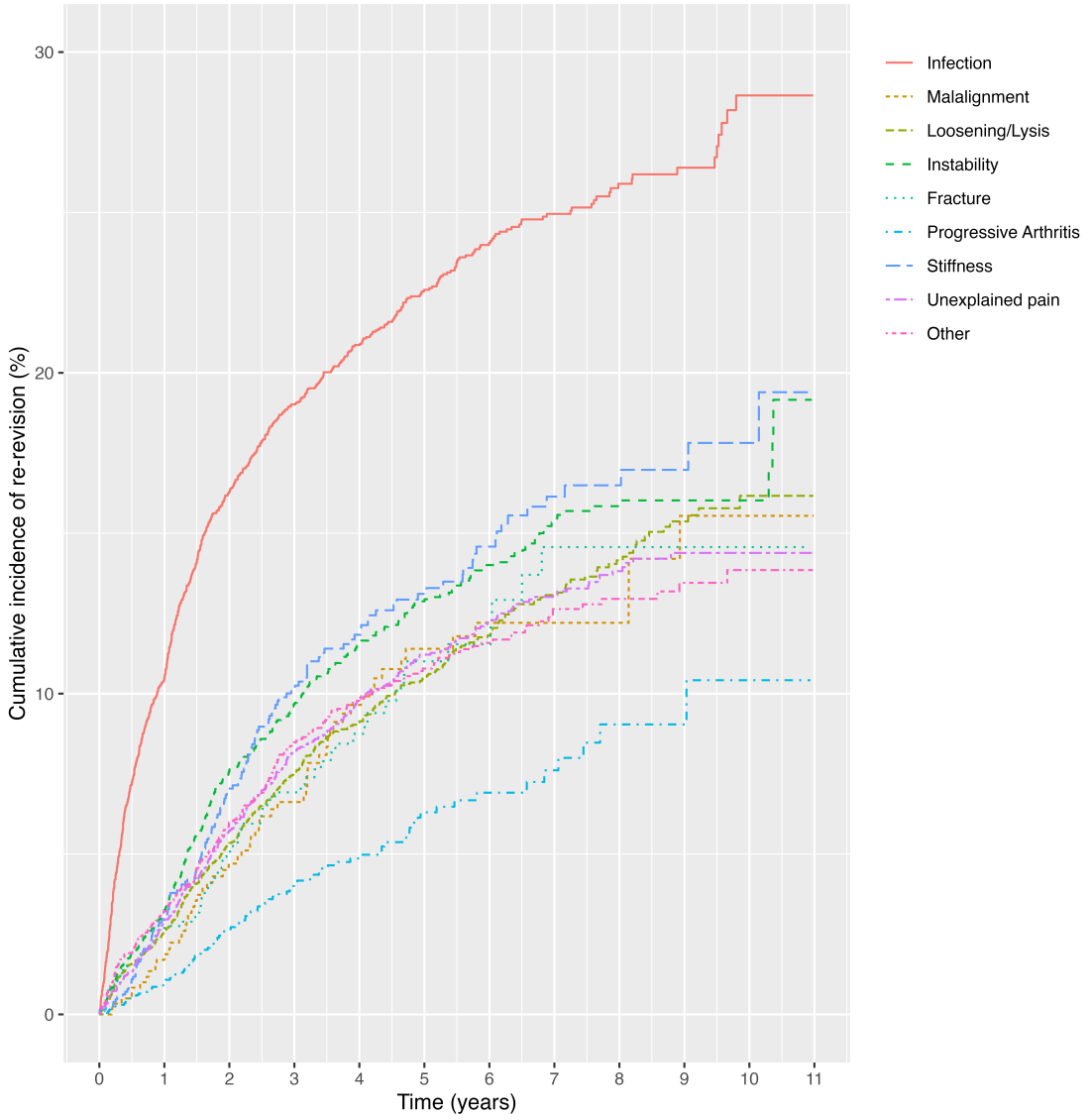

Figure 5.2: Cumulative incidence of re-revision knee arthroplasty by indication for first-linked rKA. Risk tables and confidence intervals are provided separately for each diagnosis.

5.3.0.2 Mortality and serious medical complications

Mortality and serious medical complications requiring hospital admission are summarised in Table 5.3. Overall, 187/32,483 patients died within 90 days of rKA (0.6% [0.5 to 0.7%]). The highest mortality rates were observed in patients undergoing rKA to treat fracture (3.2% [2.3 to 4.5%]) and infection (1.8% [1.4 to 2.2%]). Among the remaining diagnoses, the point estimates for mortality ranged from 0.0 - 0.4%.

5. Patient-relevant outcomes by diagnosis following rKA

Overall, serious medical complications requiring hospital admission were common, with 1,518/22,790 patients (6.7% [95% CI: 6.3-7.0%]) developing one or more complications within 90 days of rKA. Patients undergoing rKA for fracture (19.8% [95% CI: 16.4-23.7%]) and infection (12.2% [95% CI: 10.9-13.5%]) had the highest rates of complications. Acute kidney injury was the most frequent individual complication, observed in 533/22,790 patients (2.3% [95% CI: 2.1-2.5%]). Lower respiratory tract infection was the second most frequent complication, observed in 512/22,790 patients (2.2% [95% CI: 2.1-2.4%]).

Table 5.3: Multi-modal outcomes following rKA by indication

Characteristic	Overall	Infection	Malalignment	Loosening/Lysis	Instability	Fracture	Progressive Arthritis	Stiffness	Unexplained pain	Other
Cumulative incidence re-revision										
2 years / % (95% CI)	7.1 [6.8,7.4]	16 [14.9,17]	5 [3.3,6.6]	5.4 [4.9,6]	8.1 [7.2,8.9]	4.8 [3.3,6.2]	2.9 [2.4,3.4]	7.1 [5.6,8.5]	5.4 [4.7,6]	5.4 [4.6,6.2]
5 years / % (95% CI)	12.5 [12,12.9]	22.3 [21,23.6]	11.6 [8.8,14.2]	10.5 [9.6,11.3]	13.5 [12.4,14.7]	10.4 [7.8,13]	6.6 [5.6,7.5]	13.4 [11.3,15.5]	11 [10,12]	10.4 [9.2,11.5]
Death within 90 days										
n/N (% [95% CI])	187/32,483 (0.6% [0.5,0.7%])	91/5,194 (1.8% [1.4,2.2%])	2/728 (0.3% [0.0,1.0%])	22/6,583 (0.3% [0.2,0.5%])	17/4,677 (0.4% [0.2,0.6%])	35/1,078 (3.2% [2.3,4.5%])	6/4,614 (0.1% [0.0,0.3%])	0/1,360 (0.0% [0.0,0.3%])	6/4,669 (0.1% [0.0,0.3%])	8/3,580 (0.2% [0.1,0.4%])
Complications										
Any medical complication										
n/N (% [95% CI])	1,518/22,790 (6.7% [6.3,7.0%])	348/2,860 (12.2% [10.9,13.5%])	32/580 (5.5% [3.8,7.8%])	313/5,020 (6.2% [5.6,7.0%])	219/3,393 (6.5% [5.6,7.4%])	118/595 (19.8% [16.4,23.7%])	150/3,379 (4.4% [3.8,5.2%])	46/1,045 (4.4% [3.2,5.9%])	175/3,515 (5.0% [4.3,5.8%])	117/2,403 (4.9% [4.0,5.8%])
Acute kidney injury										
n/N (% [95% CI])	533/22,790 (2.3% [2.1,2.5%])	176/2,860 (6.2% [5.3,7.1%])	9/580 (1.6% [0.7,2.9%])	101/5,020 (2.0% [1.6,2.4%])	65/3,393 (1.9% [1.5,2.4%])	38/595 (6.4% [4.5,8.8%])	51/3,379 (1.5% [1.1,2.0%])	9/1,045 (0.9% [0.4,1.6%])	49/3,515 (1.4% [1.0,1.8%])	35/2,403 (1.5% [1.0,2.0%])
Deep vein thrombosis										
n/N (% [95% CI])	112/22,790 (0.5% [0.4,0.6%])	22/2,860 (0.8% [0.5,1.2%])	2/580 (0.3% [0.0,1.2%])	24/5,020 (0.5% [0.3,0.7%])	12/3,393 (0.4% [0.2,0.6%])	6/595 (1.0% [0.4,2.2%])	12/3,379 (0.4% [0.2,0.6%])	9/1,045 (0.9% [0.4,1.6%])	18/3,515 (0.5% [0.3,0.8%])	7/2,403 (0.3% [0.1,0.6%])
Lower respiratory tract infection										
n/N (% [95% CI])	512/22,790 (2.2% [2.1,2.4%])	96/2,860 (3.4% [2.7,4.1%])	10/580 (1.7% [0.8,3.2%])	110/5,020 (2.2% [1.8,2.6%])	76/3,393 (2.2% [1.8,2.8%])	50/595 (8.4% [6.2,11.1%])	51/3,379 (1.5% [1.1,2.0%])	12/1,045 (1.1% [0.6,2.0%])	64/3,515 (1.8% [1.4,2.3%])	43/2,403 (1.8% [1.3,2.4%])
Myocardial infarction										
n/N (% [95% CI])	51/22,790 (0.2% [0.2,0.3%])	10/2,860 (0.3% [0.2,0.6%])	0/580 (0.0% [0.0,0.6%])	18/5,020 (0.4% [0.2,0.6%])	4/3,393 (0.1% [0.0,0.3%])	2/595 (0.3% [0.0,1.2%])	9/3,379 (0.3% [0.1,0.5%])	0/1,045 (0.0% [0.0,0.4%])	4/3,515 (0.1% [0.0,0.3%])	4/2,403 (0.2% [0.0,0.4%])
Pulmonary embolism										
n/N (% [95% CI])	165/22,790 (0.7% [0.6,0.8%])	33/2,860 (1.2% [0.8,1.6%])	3/580 (0.5% [0.1,1.5%])	36/5,020 (0.7% [0.5,1.0%])	26/3,393 (0.8% [0.5,1.1%])	18/595 (3.0% [1.8,4.8%])	9/3,379 (0.3% [0.1,0.5%])	8/1,045 (0.8% [0.3,1.5%])	19/3,515 (0.5% [0.3,0.8%])	13/2,403 (0.5% [0.3,0.9%])
Stroke										
n/N (% [95% CI])	47/22,790 (0.2% [0.2,0.3%])	10/2,860 (0.3% [0.2,0.6%])	1/580 (0.2% [0.0,1.0%])	8/5,020 (0.2% [0.1,0.3%])	5/3,393 (0.1% [0.0,0.3%])	3/595 (0.5% [0.1,1.5%])	6/3,379 (0.2% [0.1,0.4%])	3/1,045 (0.3% [0.1,0.8%])	9/3,515 (0.3% [0.1,0.5%])	2/2,403 (0.1% [0.0,0.3%])
Urinary tract infection										
n/N (% [95% CI])	427/22,790 (1.9% [1.7,2.1%])	94/2,860 (3.3% [2.7,4.0%])	8/580 (1.4% [0.6,2.7%])	74/5,020 (1.5% [1.2,1.9%])	75/3,393 (2.2% [1.7,2.8%])	54/595 (9.1% [6.8,11.8%])	40/3,379 (1.2% [0.8,1.6%])	13/1,045 (1.2% [0.7,2.1%])	36/3,515 (1.0% [0.7,1.4%])	33/2,403 (1.4% [0.9,1.9%])
Hospital admission										
Length of stay (days) / median (Q1,Q3)	4 [3,7]	12 [7,20]	4 [3,7]	4 [3,7]	4 [3,7]	8 [4,17]	3 [2,5]	5 [3,7]	4 [3,6]	4 [3,6]

5.3.0.3 Patient reported outcome measures (PROMs)

Overall, 5,490/32,483 (17%) rKA had PROM data available for analysis. The indications with the lowest proportion of linked PROMs were the *urgent* indications, infection and fracture, (9% rKA). The indications with the highest proportion of linked PROMs were malalignment and aseptic loosening (22% rKA). The results of pre- and post-operative PROM questionnaires are summarised in Table 5.4. Patients revised for infection (mean OKS 15 [SD 8]) and fracture (mean OKS 15 [SD 9]) had the poorest pre-operative joint function, whilst patients with progressive arthritis had the highest pre-operative joint function (mean OKS 18 [SD 7]). At six months post-revision, patients with progressive arthritis had the best function (mean OKS 32 [SD 10]), while patients revised for malalignment (mean OKS 24 [SD 10]), stiffness (mean OKS 24 [SD 11]) and unexplained pain (mean OKS 25 [SD 11]) had the poorest function. The group with the highest proportion of patients whose joint function improved by a clinically meaningful amount (i.e. *responders*) was rKA for fracture (73/95 patients, 77% [95% CI: 67-84%]). The groups with the lowest proportion of responders were rKA for stiffness (127/264 patients, 48% [95% CI: 42-54%]]) and unexplained pain (467/858 patients, 54% [95% CI 51-58%]]). Prior to rKA, patients with fracture, malalignment and unexplained pain reported the poorest HRQoL (median EQ-5D utility ~0.16), while patients undergoing rKA for progressive arthritis reported the highest HRQoL (median EQ-5D utility 0.52 [0.09 - 0.69, Q1 - Q3]). At six months post-operation, the EQ-5D utility score improved for all subgroups. Patients revised for infection, malalignment, stiffness and unexplained pain reported the poorest HRQoL (median EQ-5D utility ~0.62). The proportion of patients who were satisfied with their surgical result was highest for fracture (78/95 patients, 82% [95% CI: 73-89%]) and lowest for stiffness (134/264 patients, 51% [95% CI: 45-57%]) and unexplained pain (453/858 patients, 53% [95% CI: 49-56%]). For all indications, a greater proportion of patients perceived their operation to have been a success than those who were satisfied with the outcome following surgery.

Table 5.4: Patient-reported outcomes following first rKA by indication for surgery

Characteristic	Overall	Infection	Malalignment	Loosening/Lysis	Instability	Fracture	Progressive Arthritis	Stiffness	Unexplained pain	Other
PROM records linked	5,490/32,483 (17%)	454/5,194 (8.7%)	161/728 (22%)	1,480/6,583 (22%)	862/4,677 (18%)	95/1,078 (8.8%)	811/4,614 (18%)	264/1,360 (19%)	858/4,669 (18%)	505/3,580 (14%)
Pre-operative OKS										
Mean (SD)	17 (8)	15 (8)	16 (7)	17 (8)	17 (8)	15 (9)	18 (7)	17 (8)	16 (7)	18 (8)
N missing (% missing)	79 (1.4%)	8 (1.8%)	1 (0.6%)	27 (1.8%)	15 (1.7%)	2 (2.1%)	9 (1.1%)	1 (0.4%)	10 (1.2%)	6 (1.2%)
Post-operative OKS										
Mean (SD)	28 (11)	26 (12)	24 (10)	30 (11)	27 (11)	30 (12)	32 (10)	24 (11)	25 (11)	29 (11)
N missing (% missing)	113 (2.1%)	11 (2.4%)	0 (0%)	28 (1.9%)	16 (1.9%)	2 (2.1%)	16 (2.0%)	9 (3.4%)	19 (2.2%)	12 (2.4%)
Change in OKS										
Mean (SD)	11 (11)	11 (11)	8 (9)	13 (10)	11 (10)	15 (11)	13 (10)	8 (10)	9 (10)	11 (11)
N missing (% missing)	179 (3.3%)	19 (4.2%)	1 (0.6%)	48 (3.2%)	27 (3.1%)	3 (3.2%)	25 (3.1%)	10 (3.8%)	28 (3.3%)	18 (3.6%)
Responder, n (%)										
Yes	3,621 (66%)	301 (66%)	97 (60%)	1,061 (72%)	567 (66%)	73 (77%)	602 (74%)	127 (48%)	467 (54%)	326 (65%)
No	1,652 (30%)	127 (28%)	60 (37%)	364 (25%)	262 (30%)	19 (20%)	178 (22%)	127 (48%)	357 (42%)	158 (31%)
(Missing)	217 (4.0%)	26 (5.7%)	4 (2.5%)	55 (3.7%)	33 (3.8%)	3 (3.2%)	31 (3.8%)	10 (3.8%)	34 (4.0%)	21 (4.2%)
Pre-op. EQ-5D utility										
Median (Q1, Q3)	0.23 (0.06, 0.69)	0.19 (0.00, 0.62)	0.16 (0.06, 0.62)	0.20 (0.06, 0.69)	0.29 (0.06, 0.66)	0.16 (-0.02, 0.59)	0.52 (0.09, 0.69)	0.29 (0.02, 0.62)	0.16 (0.00, 0.62)	0.26 (0.06, 0.69)
N missing (% missing)	338 (6.2%)	26 (5.7%)	10 (6.2%)	76 (5.1%)	59 (6.8%)	7 (7.4%)	62 (7.6%)	11 (4.2%)	47 (5.5%)	40 (7.9%)
Post-op. EQ-5D utility										
Median (Q1, Q3)	0.69 (0.52, 0.78)	0.62 (0.49, 0.76)	0.62 (0.16, 0.69)	0.69 (0.59, 0.80)	0.66 (0.52, 0.76)	0.69 (0.57, 0.73)	0.69 (0.59, 0.80)	0.62 (0.29, 0.72)	0.62 (0.19, 0.73)	0.69 (0.52, 0.80)
N missing (% missing)	297 (5.4%)	23 (5.1%)	5 (3.1%)	87 (5.9%)	57 (6.6%)	7 (7.4%)	31 (3.8%)	17 (6.4%)	44 (5.1%)	26 (5.1%)
Change in EQ-5D utility										
Median (Q1, Q3)	0.19 (0.00, 0.53)	0.26 (0.00, 0.53)	0.06 (0.00, 0.48)	0.26 (0.00, 0.59)	0.17 (0.00, 0.53)	0.42 (0.10, 0.62)	0.24 (0.00, 0.53)	0.10 (0.00, 0.53)	0.11 (0.00, 0.53)	0.16 (0.00, 0.53)
N missing (% missing)	602 (11%)	47 (10%)	15 (9.3%)	155 (10%)	107 (12%)	13 (14%)	88 (11%)	26 (9.8%)	87 (10%)	64 (13%)
Satisfaction, n (%)										
Excellent	705 (13%)	47 (10%)	15 (9.3%)	208 (14%)	117 (14%)	15 (16%)	125 (15%)	28 (11%)	68 (7.9%)	82 (16%)
Very Good	1,428 (26%)	106 (23%)	32 (20%)	447 (30%)	209 (24%)	27 (28%)	265 (33%)	50 (19%)	173 (20%)	119 (24%)
Good	1,435 (26%)	137 (30%)	41 (25%)	428 (29%)	219 (25%)	36 (38%)	193 (24%)	56 (21%)	212 (25%)	113 (22%)
Fair	1,196 (22%)	96 (21%)	50 (31%)	247 (17%)	207 (24%)	10 (11%)	153 (19%)	67 (25%)	245 (29%)	121 (24%)
Poor	632 (12%)	57 (13%)	21 (13%)	126 (8.5%)	98 (11%)	6 (6.3%)	59 (7.3%)	56 (21%)	146 (17%)	63 (12%)
(Missing)	94 (1.7%)	11 (2.4%)	2 (1.2%)	24 (1.6%)	12 (1.4%)	1 (1.1%)	16 (2.0%)	7 (2.7%)	14 (1.6%)	7 (1.4%)
Perceived success, n (%)										
Much better	2,642 (48%)	214 (47%)	58 (36%)	827 (56%)	392 (45%)	56 (59%)	455 (56%)	94 (36%)	317 (37%)	229 (45%)
A little better	1,252 (23%)	92 (20%)	47 (29%)	315 (21%)	201 (23%)	20 (21%)	185 (23%)	60 (23%)	206 (24%)	126 (25%)
About the same	602 (11%)	34 (7.5%)	22 (14%)	123 (8.3%)	109 (13%)	10 (11%)	68 (8.4%)	45 (17%)	132 (15%)	59 (12%)
A little worse	482 (8.8%)	57 (13%)	18 (11%)	116 (7.8%)	76 (8.8%)	6 (6.3%)	53 (6.5%)	22 (8.3%)	96 (11%)	38 (7.5%)
Much worse	421 (7.7%)	45 (9.9%)	13 (8.1%)	80 (5.4%)	71 (8.2%)	2 (2.1%)	36 (4.4%)	38 (14%)	93 (11%)	43 (8.5%)
(Missing)	91 (1.7%)	12 (2.6%)	3 (1.9%)	19 (1.3%)	13 (1.5%)	1 (1.1%)	14 (1.7%)	5 (1.9%)	14 (1.6%)	10 (2.0%)

5.3.0.4 Length of stay (LOS)

LOS is summarised as CIPS in Table 5.3. Further data on FCEs and provider spells are provided in Table 5.5. Overall, the median LOS was 4 days (3-7, Q1-Q3). Patients undergoing first rKA for infection had the longest LOS (median 12 days [7-20, Q1-Q3]) followed by fracture (median 8 days [4-17, Q1-Q3]).

Table 5.5: Length of hospital stay by indication for surgery

Length of stay (days)	Infection	Malalignment	Loosening/Lysis	Instability	Fracture	Progressive Arthritis	Stiffness	Unexplained pain	Other
Finished consultant episodes									
median	11	4	4	4	7	3	5	4	4
mean	15	6	6	6	11	4	6	5	5
max	155	49	156	187	112	69	81	112	115
q1	7	3	3	3	4	2	3	3	3
q3	18	6	7	7	13	5	7	6	6
Provider spells									
median	12	4	4	4	7	3	5	4	4
mean	16	6	6	6	10	4	7	5	5
max	155	49	156	187	112	69	81	72	115
q1	7	3	3	3	4	2	3	3	3
q3	18	6	7	7	13	5	7	6	6
Continuous inpatient spells									
median	12	4	4	4	8	3	5	4	4
mean	18	6	6	7	14	4	7	5	5
max	217	49	339	294	214	234	325	252	224
q1	7	3	3	3	4	2	3	3	3
q3	20	7	7	7	17	5	7	6	6

5.4 Discussion

Patients undergoing rKA for infection were at high risk of re-revision surgery (one in six at 2 years; one in four at 5 years). For other diagnoses, the rate of re-revision surgery was much lower (ranging from one in 12 [instability] to one in 34 [progressive arthritis] at 2 years). The risk of death within 90 days was high for patients undergoing surgery for fracture (one in 31) and infection (one in 56), but less than one in 250 for all other diagnoses. The highest rates of serious medical complications requiring admission to hospital were in patients undergoing surgery for fracture (one in five) and infection (one in eight). For all other indications, the rate of serious medical complications was approximately one in 20. Acute kidney injury (one in 43) and lower respiratory tract infection (one in 45) were the most frequently observed complications overall, with much higher rates in patients undergoing rKA for fracture and infection. There were large differences in patient-relevant outcomes following first rKA between different indications for surgery.

Deere et al [45] recently investigated implant survivorship for first and re-revision rKA using the NJR dataset. They reported similar rates of further surgery following first rKA (~7% at 2 years and ~12% at 5 years). In addition, they demonstrated high rates of further surgery following second and third revision procedures. A recent study reported that *elective* indications for first rKA had comparable mortality and serious complication rates to pKA, while *urgent* indications for rKA (such as infection and fracture) had poorer outcomes [135]. The present study has reproduced these findings using more contemporary data, describing patient subgroups in greater detail using surgeon-coded diagnoses recorded on the NJR, and has included further domains of outcome (joint function, quality of life) through record linkage to NHS PROMs. This approach has revealed differences in outcome within elective, aseptic indications for rKA. For example, only half of patients revised for stiffness (48%) and unexplained pain (54%) reported a clinically meaningful improvement in joint function, compared to 74% of patients treated for progressive arthritis.

This study analysed routinely collected data from NHS and private providers of rKA in the UK over the past decade. The NJR is a mature registry, and has been shown to have excellent data quality [78; 79], whilst HES APC and Civil Registrations (Mortality) provide near universal coverage of emergency hospital admissions and deaths in the UK. The large size of our study population is likely to mean that our estimates provide both an accurate and precise reflection of real world practice.

There are limitations. This study stratified rKA by indication for surgery, but has not controlled for confounding by indication. As such, the outcomes reported may be due to differences in patient characteristics other than the indication for surgery itself. The rates of serious medical complications are an underestimate of the true rate, since they represent only those patients who required admission to secondary care. There may be large discrepancies for conditions commonly managed in primary care or outpatient departments. Finally, the outcomes presented may not be due to surgery and one does not know the outcome had patients been managed non-operatively. There is no gold-standard method for estimating post-operative complications, but several recent studies used similar methodology to report complications following orthopaedic surgery [63; 62]. For the analysis of PROMs, there was a very high rate of record attrition when linking study datasets, such that only one in six rKAs contributed data. This attrition is likely to have been exacerbated by the requirement to link PROMs indirectly to the NJR via HES APC. Less record attrition may be possible in the future when the Master Person Service identifier is available from NHS Digital [191]. The rate of PROM attrition was particularly high for infection and fracture. While returned PROM questionnaires for these diagnoses demonstrated a high proportion of responders and large improvements in HRQoL, there is clear selection bias: those who died within six months of surgery would not have returned a PROM and perhaps also those who experienced a serious complication, of which there were a greater proportion.

5. Patient-relevant outcomes by diagnosis following rKA

This study has investigated multiple, patient-relevant domains of outcome following first rKA. The information reported is likely to prove valuable for informed consent of patients undergoing rKA in the future. Patients with infection and fracture experienced a high rate of adverse events (re-revision surgery, death and serious medical complications). A priority for future research is to investigate whether there are risk factors that can be modified to improve outcomes for patients. The data analysed here predate extension of the Best Practice Tariff to include distal femoral and periprosthetic fractures [192]. Patients with stiffness and unexplained pain accounted for approximately one-fifth of first rKA performed over the study period. However, for a large proportion of patients, the observed improvement in PROMs was small and clinically unimportant. For example, in terms of joint function, only 48% patients with stiffness and 54% of patients with unexplained pain were responders. There is an unmet need for research to predict which patients benefit most from rKA for stiffness and unexplained pain, especially since the risk of serious medical complications is similar to other elective, aseptic indications (one in 20). From the perspective of the NHS, it is important to establish for which patient groups these procedures are (or are not) cost-effective. Recent evidence suggests that more attention may need to be given to non-operative treatment. For example, the Support and Treatment After Replacement [STAR] care pathway was found to be more clinically and cost-effective than usual care for patients with persistent pain at 3 months following pKA [193]. The natural history of pain after pKA also appears to be one of improvement over time, with two-thirds of patients recovering over the first four years [194]. As such, one might caution against early rKA for unexplained pain.

In conclusion, this study found large differences in patient-relevant outcomes between different indications for first rKA. This information can be used to support informed consent of patients undergoing first rKA.

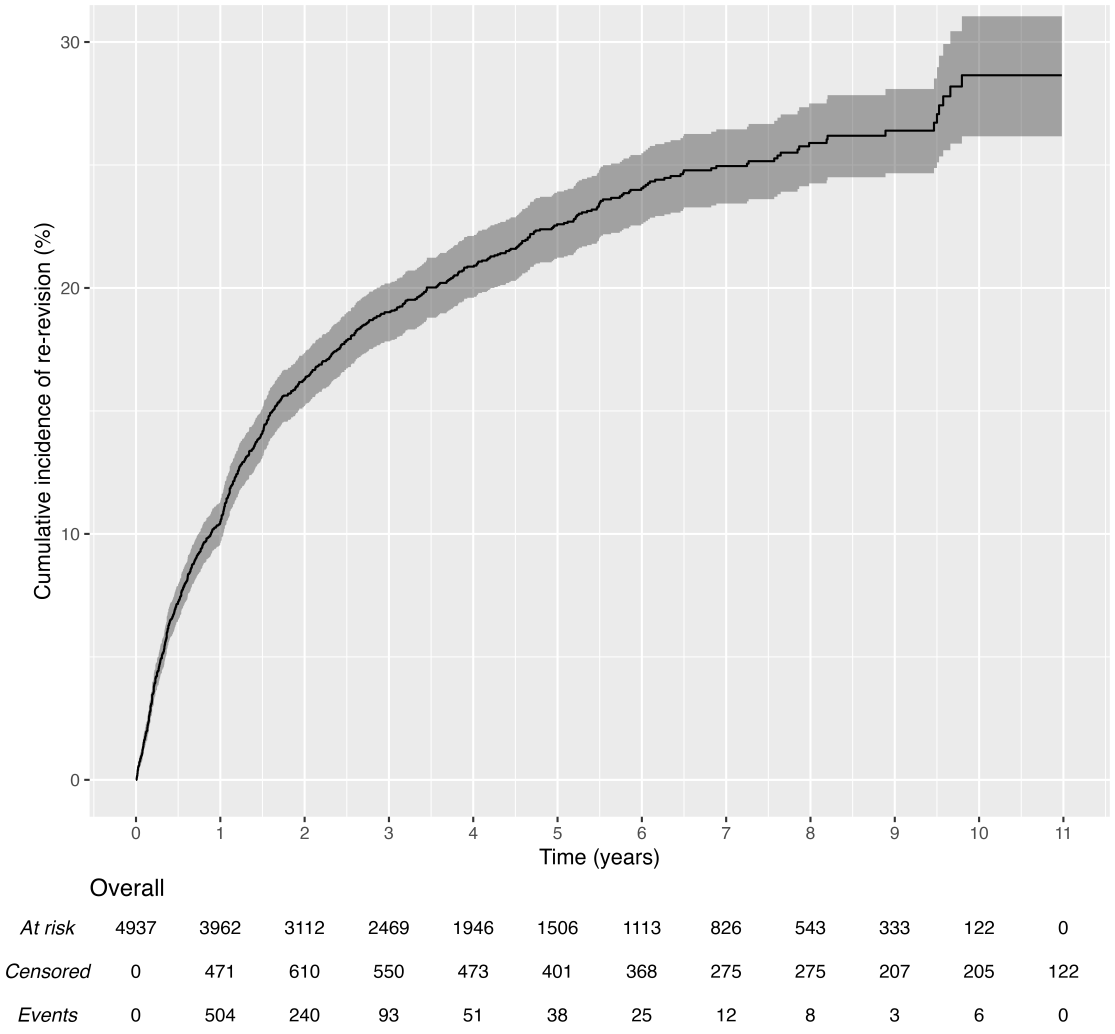

Figure 5.3: Cumulative incidence of re-revision surgery over time following first rKA for infection

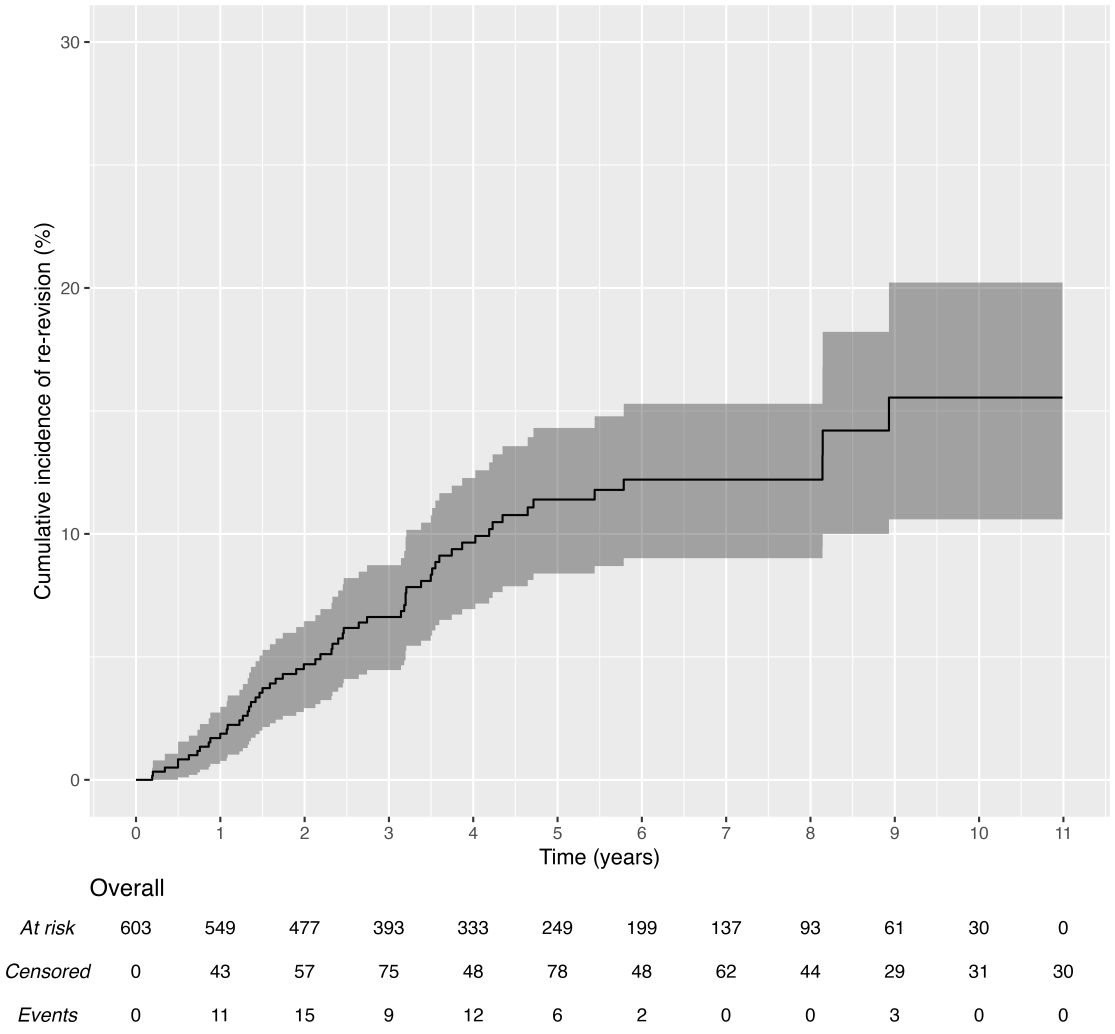

Figure 5.4: Cumulative incidence of re-revision surgery over time following first rKA for malalignment

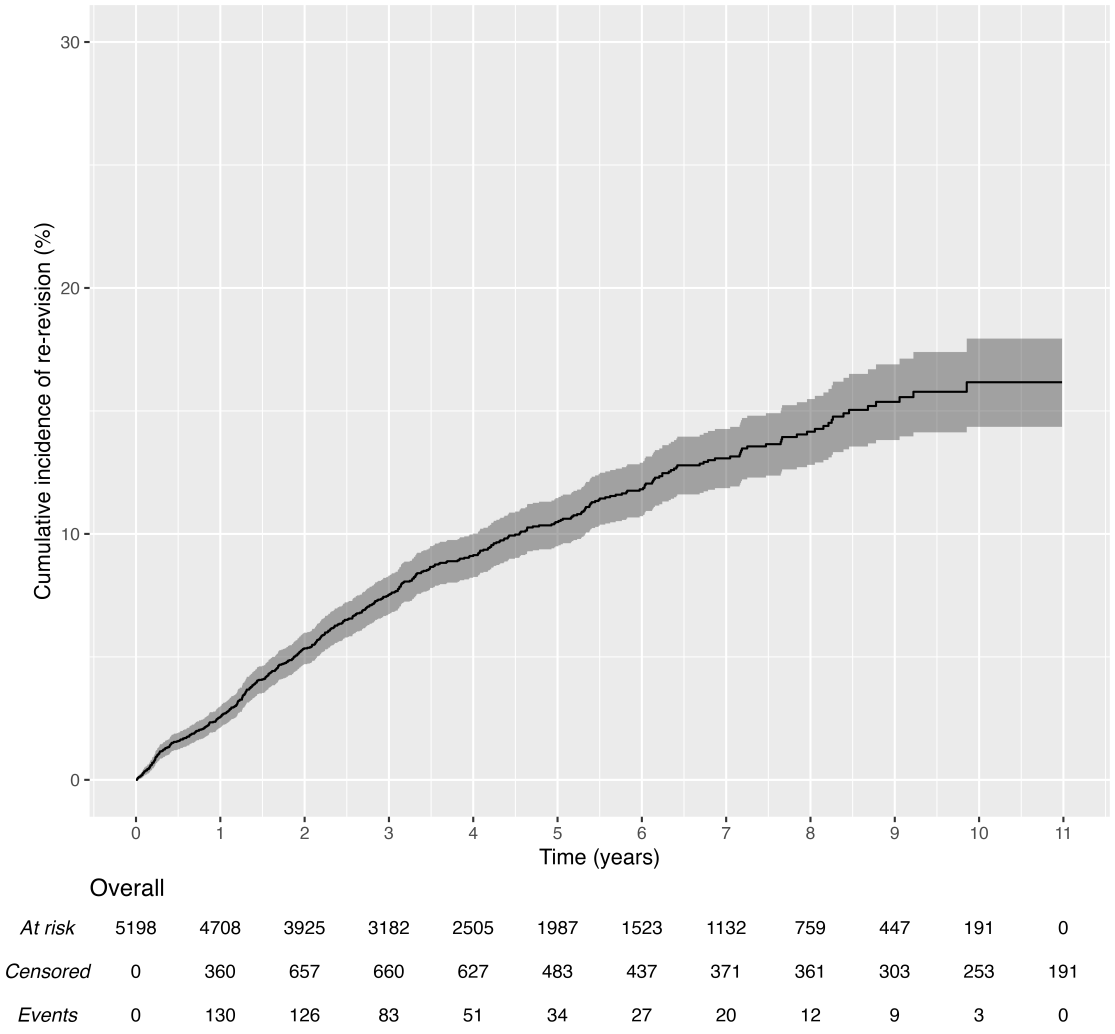

Figure 5.5: Cumulative incidence of re-revision surgery over time following first rKA for loosening/lysis

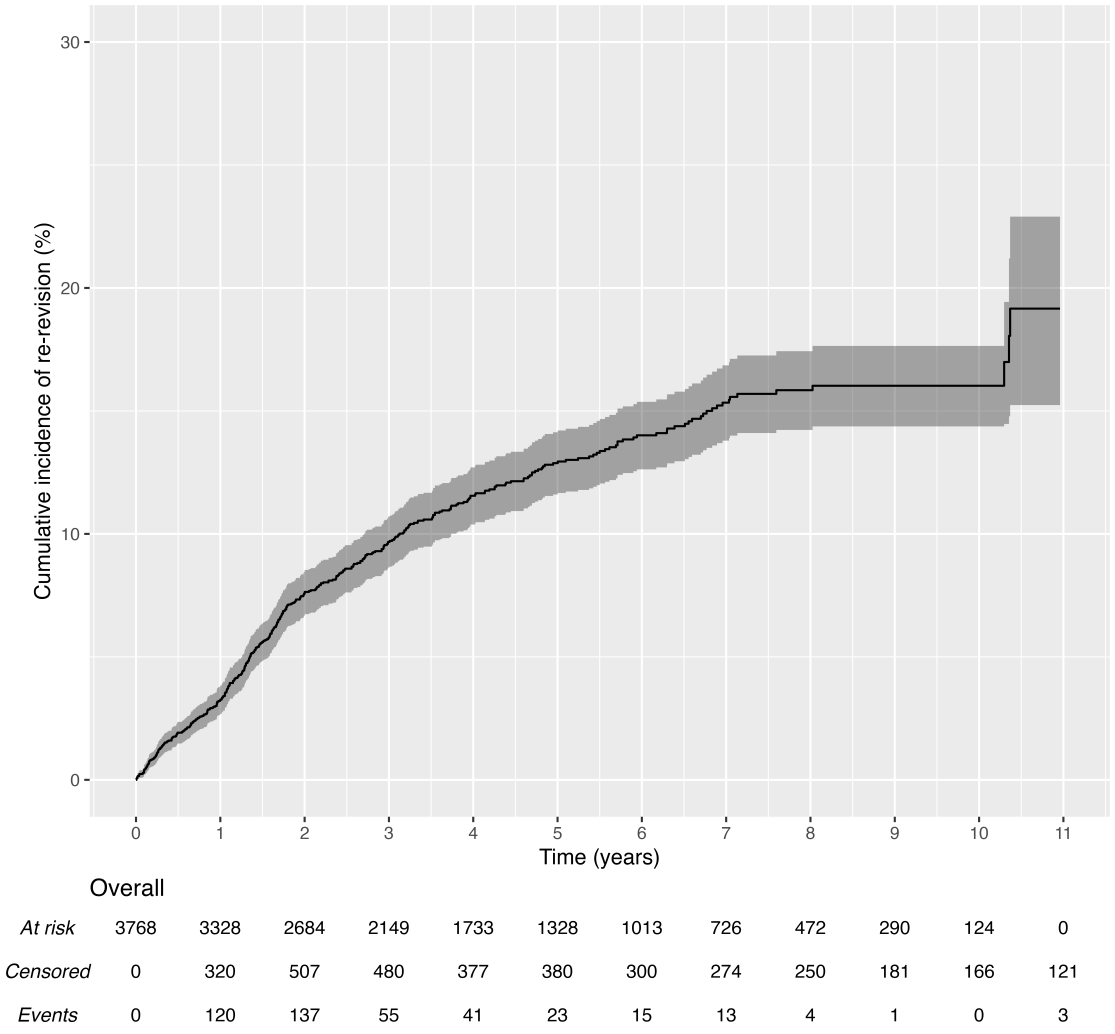

Figure 5.6: Cumulative incidence of re-revision surgery over time following first rKA for instability

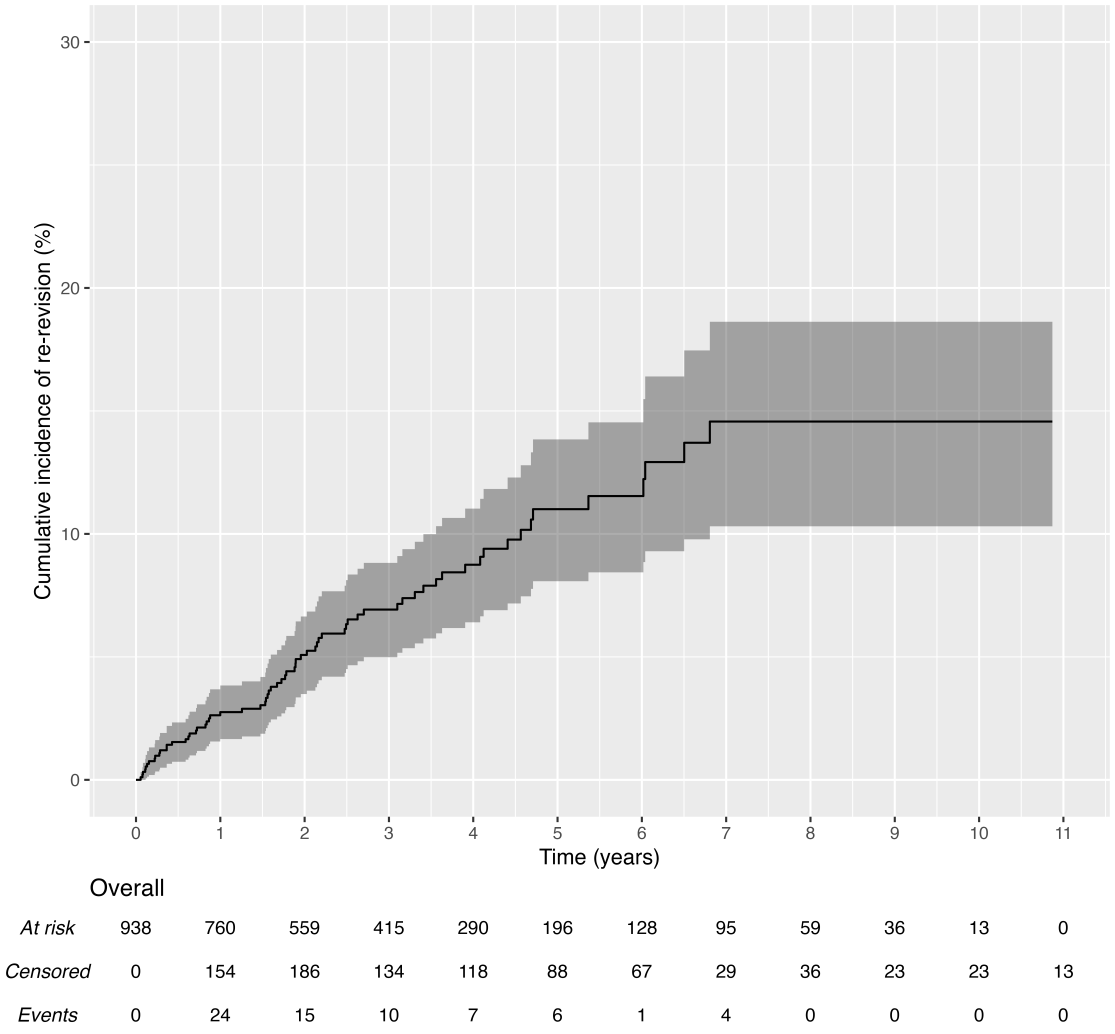

Figure 5.7: Cumulative incidence of re-revision surgery over time following first rKA for fracture

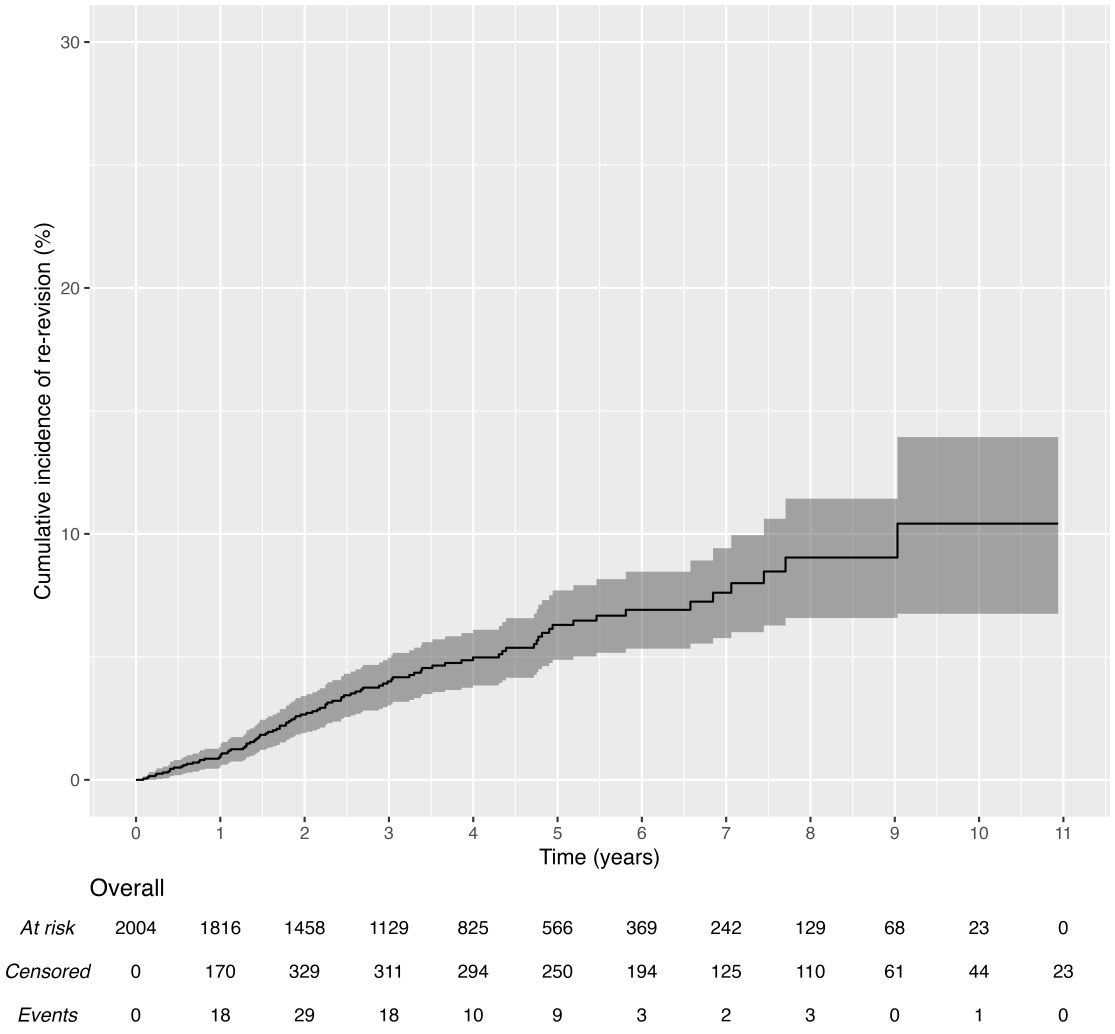

Figure 5.8: Cumulative incidence of re-revision surgery over time following first rKA for progressive arthritis

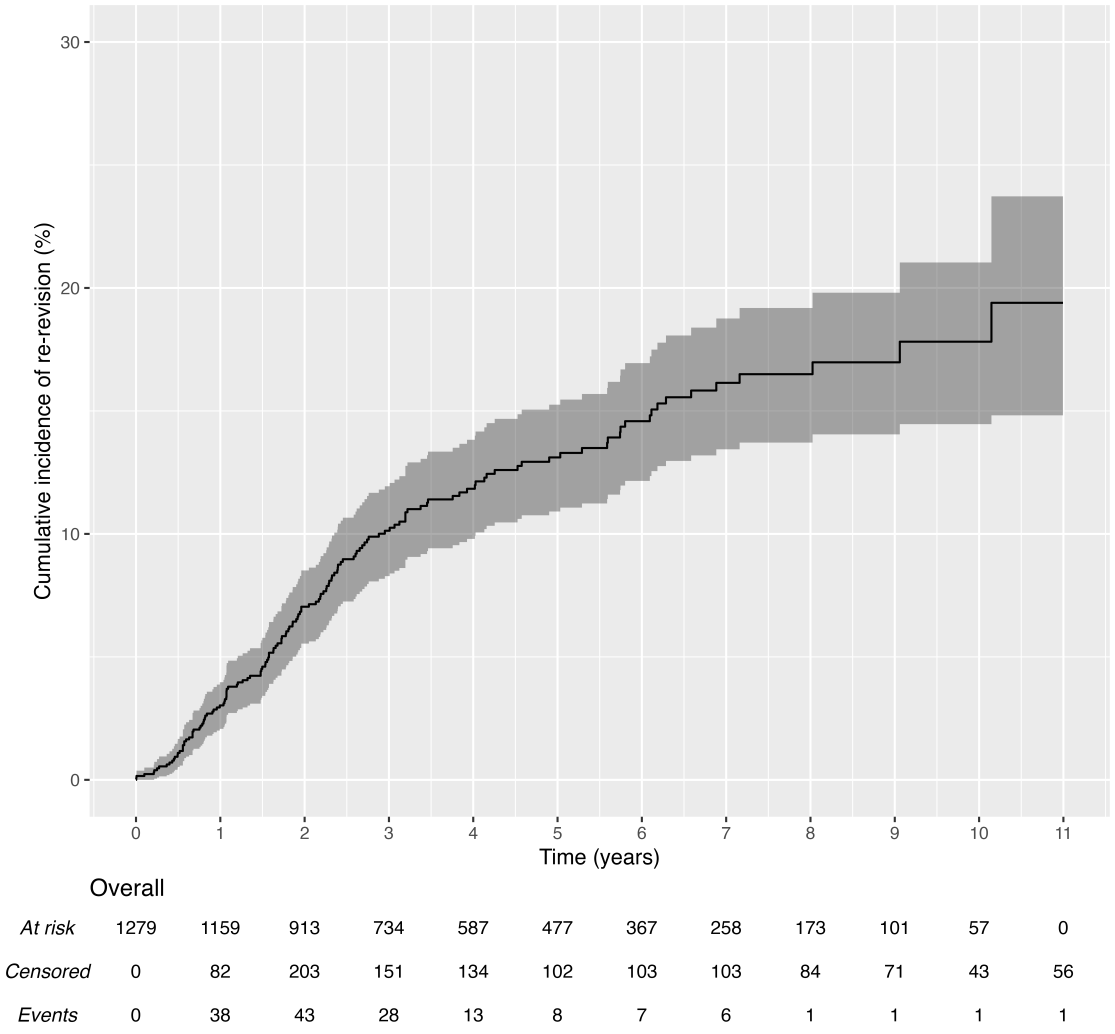

Figure 5.9: Cumulative incidence of re-revision surgery over time following first rKA for stiffness

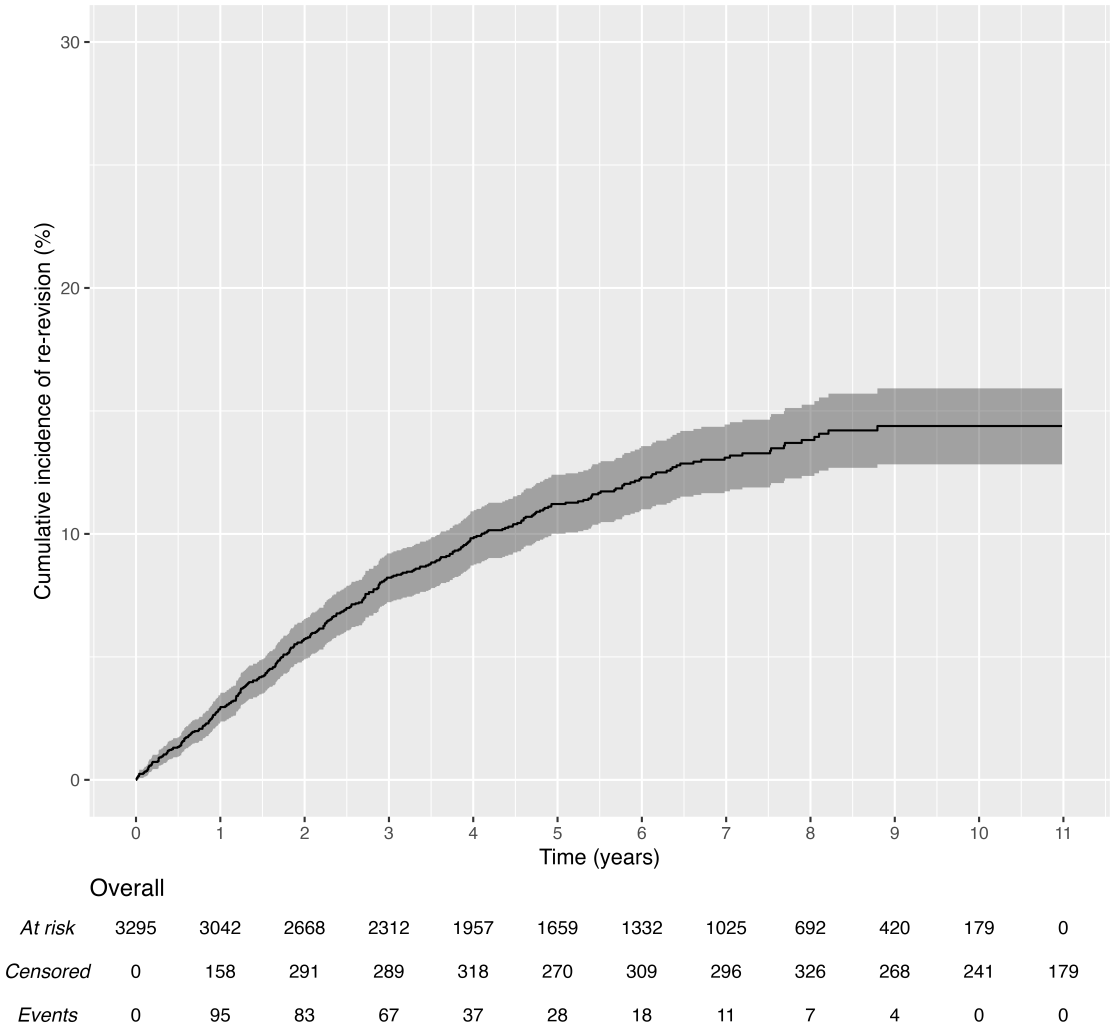

Figure 5.10: Cumulative incidence of re-revision surgery over time following first rKA for unexplained pain

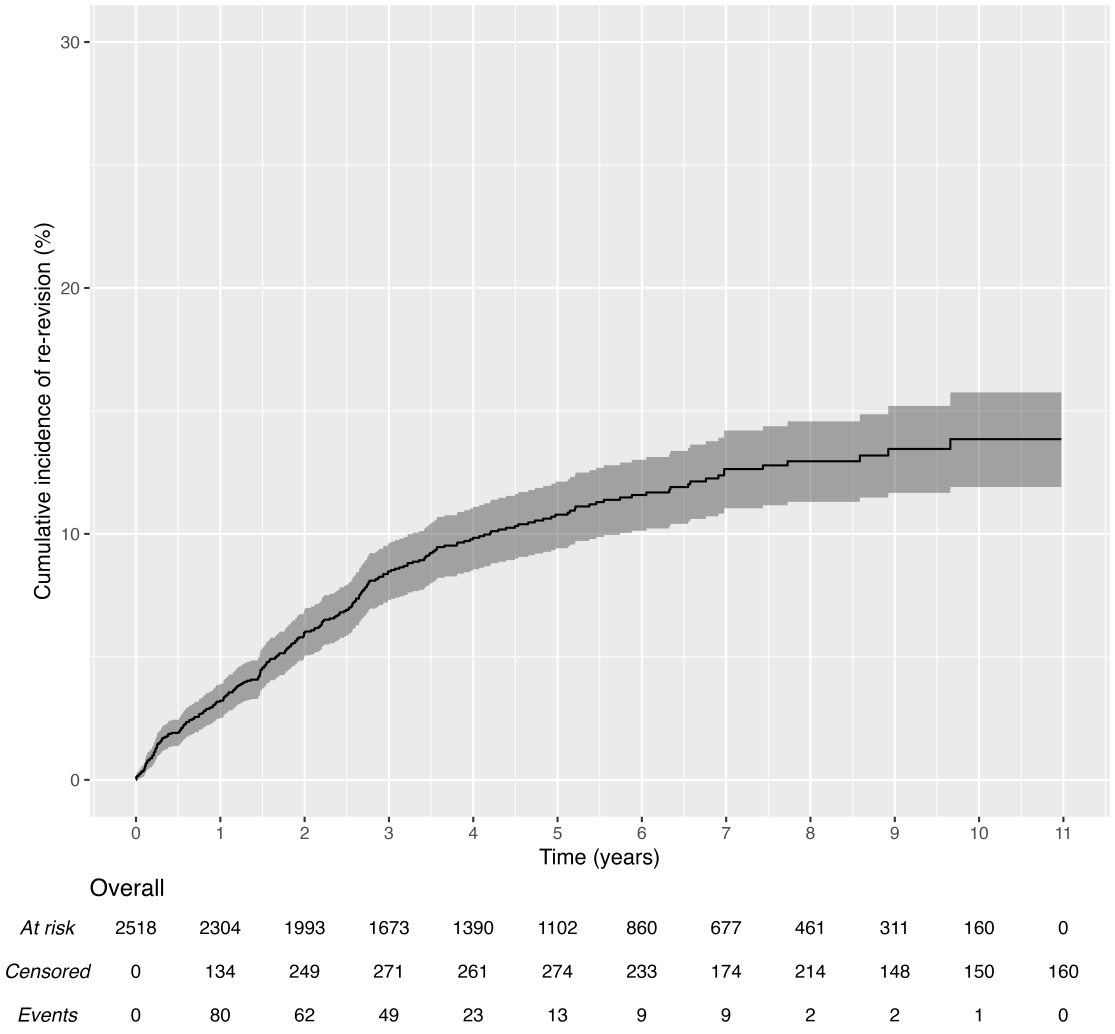

Figure 5.11: Cumulative incidence of re-revision surgery over time following first rKA where the indication was specified as 'Other'

5.5 Link to the next chapter

This chapter has investigated patient-relevant outcomes for different indications for rKA using routinely collected data from the NJR, HES APC, ONS and NHS PROMs datasets. The greatest contrast in the rate of serious medical complications and mortality was evident for rKA performed for urgent compared to aseptic, elective indications. Within aseptic, elective indications for rKA the rate of serious medical complications and mortality was relatively similar. However, there were

large differences in joint function, patient satisfaction and perceived success. rKA for progressive arthritis had excellent PROMs (74% responders, 72% satisfied, 79% perceived success) while rKA for unexplained pain had less predictable outcomes (54% responders, 53% satisfied, 61% perceived success). As discussed earlier, there is uncertainty as to how best to manage this latter group of patients. The next chapter aims to better understand this clinical dilemma, and describes a qualitative study to understand the experience of consultant knee surgeons treating patients with unexplained pain after knee replacement.

6

The experience of surgeons treating unexplained pain after knee arthroplasty: a reflexive thematic analysis

Contents

This chapter has been published:

- *Sabah SA, Nicolson PJA, Hedge EA, Davies L, Beard DJ, Price AJ, Toye, F. The experience of surgeons treating unexplained pain after knee arthroplasty-A reflexive thematic analysis. Bone & Joint Open. 2025. In Press*

6.1 Introduction

Pain from osteoarthritis has a profound impact on patients' lives [195]. For patients with knee osteoarthritis, joint replacement surgery is highly effective, resulting in large improvements in pain and quality of life [131]. While outcomes following knee

replacement continue to improve, for around 10% of patients surgery does not meet their expectations [81]. It is difficult to predict which patients will fall into this group, but many in this situation experience chronic pain [196]. Some do not seek help due to the belief that nothing further can be done [197]. Those seeking help must navigate a complex path through the healthcare system to access care [67].

Around two-thirds of patients with chronic pain after knee replacement report improvement in symptoms in the first five years following surgery [194]. Most are managed non-operatively. This may include different therapeutic modalities, such as physiotherapy, psychological treatment and pain management. For patients who remain in chronic pain, a small proportion return to discuss whether revision surgery may help their symptoms. However, the evidence to support surgical intervention for unexplained pain is limited. It is estimated that around half of patients who undergo revision knee replacement for unexplained pain experience a clinically meaningful improvement in pain and quality of life at six months, while half do not [198]. There is no evidence to indicate longer-term clinical outcomes following rKA for unexplained pain.

A previous study from our group explored patients' experiences with problematic knee replacements and the impact of undergoing elective revision knee replacement [68]. The aim of the present study was to understand the experiences of consultant knee surgeons treating patients with unexplained pain after knee replacement and the role they considered revision surgery to have in the management of this condition.

6.2 Methods

6.2.0.1 Patient and Public Involvement

This study was designed with the input of the 'SORE Knee' patient and public involvement (PPI) group at the University of Oxford.

6.2.0.2 Ethical approval

Ethical approval was obtained from the Health Research Authority (22/WA/0090).

6.2.0.3 Study design

Seven consultant knee surgeons with a revision knee replacement practice were purposively sampled. The sample was chosen to include different levels of consultant experience and operative caseloads. All surgeons had an NHS practice, while some also had a private practice. I directly approached all surgeons via email and conducted semi-structured face-to-face interviews with participants. A topic guide was used to facilitate discussion around surgeons' experiences treating patients with unexplained pain after knee replacement (Table 6.1). Each interview lasted around one hour and began with a *"get-to-know-you"* question where the surgeon was invited to describe their current practice. This was followed by a broad invitation to describe their experience treating patients with unexplained pain after knee replacement: *"Tell me your experience of treating patients with unexplained pain after knee replacement... You can share as much or as little as you wish."* After gaining consent, interviews were audio-recorded and transcribed verbatim in-house. Each transcript was checked for accuracy against the original recording. Transcripts were de-identified by removing names, places and other identifying data. Participants were given the opportunity to read their interview transcript and expand or redact sections as they felt appropriate ('member-checking').

Reflexive thematic analysis as described by Braun and Clarke was used to develop themes across participants. The six stages of analysis were: (i) familiarisation; (ii) coding; (iii) generation of initial themes; (iv) development and review of themes; (v) refining and naming of themes; and (vi) manuscript preparation. Interview transcripts were analysed using NVivo (Release 1.7.1, QSR International Pty Ltd., Doncaster, Victoria, Australia).

Each transcript was coded by the lead author (SAS), where a short phrase was assigned to a unit of meaning. Each code was then discussed with an experienced qualitative researcher (FT) to ensure that it encapsulated the meaning accurately and completely. Codes were then organised into initial themes around a central idea among the wider research team, which included orthopaedic surgeons, clinical

Table 6.1: Surgeon interview schedule

Tell me your experience of treating patients with unexplained pain after knee replacement
Prompts: - How do you make this diagnosis? - Is there anything that you find challenging about these cases? - Do you feel well supported to treat these patients? - How do you feel when treating patients with unexplained pain? - Can you describe some of the potential causes of unexplained pain?
Tell me your thoughts on offering further surgery to some patients with unexplained pain.
Prompts: - Can you describe a patient that you would consider to be unsuitable? And one who you think might really benefit? - What do you think are some of the risk factors for a poor outcome from further surgery? - Can you talk to me about any factors that may influence your decision beyond the clinical presentation? - What advice do you give to patients considering further surgery? - What would you consider to be a good outcome from further surgery? And, a bad outcome? - If you were to operate, what would be the important technical aspects of surgery? - Without identifying individuals, please can you share some examples of cases you have learnt from? - What advice would you give to other surgeons with less experience?

academic physiotherapists and qualitative researchers. The themes were developed by the research team through constant comparison and discussion.

6.3 Results

Seven consultant knee surgeons were recruited following direct invitation. Five worked at a Major Revision Centre and two at a District General Hospital within the NHS in England. Three surgeons had fewer than five years' consultant experience, one 5-10 years and three greater than 10 years. One surgeon performed fewer than five rTKR per year; two 10-20 rTKR per year; and four performed more than 20 rTKR per year.

Six themes drawn around surgeons' experiences treating patients with unexplained pain after knee replacement were identified: *(1) I need to understand a patient's journey and their expectations; (2) A difficult consultation; (3) I'm the 'fixer'; (4) It's complicated asking for help; (5) I'm uncomfortable operating for truly unexplained pain; and (6) It's a wound I carry with me.*

I need to understand a patient's journey and their expectations

This theme included the importance of understanding the *"journey"* patients had taken through the healthcare system, recognizing it may have been difficult:

> *"They've been pushed and pulled around... They're at various stages of having lost trust or looking for new avenues in terms of how their symptoms and everything else can be dealt with." (Surgeon E)*

> *"They won't have had an easy ride ... They will have come back to follow up appointments being seen by juniors who, quite reasonably, haven't got all the answers and may not have had a consistent message." (Surgeon E)*

Some surgeons felt they had been *"on the journey"* with the patient, especially if they had performed the original joint replacement.

> *"If you've been treating them all along, it's emotional... you're disappointed for them... they're disappointed with you. You wonder how much they trust you." (Surgeon D)*

Surgeons described the importance of honesty and trust in the doctor-patient relationship and, like any relationship, were mindful it may break down.

> *"The patient may lose faith in you... and the ability to look at things positively." (Surgeon A)*

> *"If a relationship has broken down, it's important to get someone else in. There is a lot to gain by going outside a unit, because it's very difficult to separate out a patient's experience from the individual surgeon and everything else." (Surgeon F)*

A difficult consultation

Surgeons described the challenges associated with consultations for unexplained pain. They referenced the importance of the consultation for the patient.

"It's the most important appointment of their life. They've got this terrible thing going on in their knee, they've waited and waited and waited... and finally met the person who can fix it." (Surgeon C)

There was the *"juggle" of* managing complex surgical decisions, fulfilling pastoral duties and trying to meet patient expectations, while needing a *"clinic to run on time"*.

"It can be a bit of a heart sink. You know that you are going to have a difficult conversation, and that you may not have an easy solution to offer... When I've got to the point of examining the patient, I'm already thinking about what I'm going to say and how I'm going to phrase it." (Surgeon E)

"It would be useful to do a clinic where time was not pressured where you could spend time with these patients. You know that if someone comes in and says: 'I have this problem, doctor' and you say: 'I've got an operation that will sort you out...' That's a three-minute consultation." (Surgeon F)

For some surgeons, consultations for unexplained pain were "*out of their comfort zone*", while others enjoyed their pastoral role.

"You have to remember the narrative of joint replacement... it's transformational. Without trying to talk it up too much, people say to me: 'You've given me my life back', and you get used to that, so this world is quite challenging for some surgeons, who are used to people being super happy." (Surgeon C)

"Even for people like orthopaedic surgeons who use hammers and chisels, it is quite a social thing that we're doing, isn't it?" (Surgeon E)

Some surgeons referenced the difficulties around breaking bad news.

"They will have had many moments where someone says: 'You need to see a doctor about your knee because your symptoms are so severe you can't do X, Y, and Z'. And they come to see you, deliver all of that, and I have to turn around and say: 'I'm very sorry but there is nothing much we can do for you'. That is a

difficult conversation to have. It takes an extended period of time... There's an emotional investment on both sides." (Surgeon A)

For some surgeons, the combination of these difficulties was a disincentive to arranging further consultations.

"These are not friendly consultations... If you ask: 'How are you doing?' They are going to say: 'Bloody awful!' You say:"What do you want to do about it?" And they say: 'I want to see you again.' And you can go round and round, so it's often easier to discharge the patient." (Surgeon B)

I'm the 'fixer'

Surgeons appeared to be most comfortable working within a biomedical model of health and illness: find a problem, and fix it. This included the need to identify a *"mechanical mandate"* to justify an operation.

"Part of you thinks, I really hope that I find something wrong here that I can fix... but, at the same time, you don't wish badly on the patient." (Surgeon A)

Some described the weight of expectations from patients to *"do something"*, despite the evidence suggesting it may be best to observe the natural history of the condition.

"We know that there is evidence that if you stick with it for a few years then a moderate number of patients are going to improve. However, a significant number do not improve – and only time will tell for these patients. Patients often find that slightly difficult to accept. And, as surgeons, we also deal with this badly. We are very used to someone coming in where you say: 'I can help you with that.' We are proactive... and it's a very personal interaction: 'I can help you with that'. It's not that: 'I am going to give you this medicine...'" (Surgeon F)

"As surgeons, we would like to be able to do something to make people better. And, when you can't operate on them, you can feel a bit helpless." (Surgeon G)

Surgeons described the *"dilemma... as to how hard you investigate"* chronic pain and the problems of imperfect diagnostic tests.

> *"The difficult balance is trying to avoid investigating unnecessarily, but you don't want to discard patients who have a problem you could help with." (Surgeon F)*

> *"You need to counsel the patient quite carefully before requesting tests... We may find things that are abnormal and not know how to interpret them... Even if something comes up, I wouldn't necessarily recommend revision surgery." (Surgeon B)*

> *"People cling very tightly to a diagnosis: 'a doctor told me that there was something wrong with my knee replacement'. It's very easy to get people bogged down into this thinking". (Surgeon F)*

Several surgeons described the idea that greater experience provided them with the confidence to organise fewer diagnostic tests.

> *"Perhaps, earlier in your career, the more you will investigate things and, as you get older, you will be more blunt with people and say: 'I could send you for a load of tests, but – in reality – if I send you for a hundred tests, two are going to come back positive and is this going to change what I would think is the right choice for you?'" (Surgeon E)*

It's complicated asking colleagues for help

Surgeons reported the benefits and pitfalls of asking for help from colleagues. On the one hand, there was the usefulness of the multidisciplinary team (MDT) meeting.

> *"Complex cases are much better shared... and their psychological baggage." (Surgeon D)*

> *"If I've run out of ideas and can't help, maybe there is someone else who can?" (Surgeon B)*

A caveat was that MDT meetings could over-simplify the problem and did not always include a patient voice.

"It is very easy to sit there and say: 'Do this', when the patient is not sat in front of you." (Surgeon F)

Second opinions meant *"a fresh pair of eyes"* to identify problems that may have been missed, a new start where a doctor-patient relationship had broken down and could provide a patient with confidence in the diagnosis. However, surgeons offering second opinions were concerned about consultations where patients had been set unrealistic expectations by their original surgeon.

"Patients often come to my service having been told: 'You are going to see Mr./Miss. X in the specialist centre and they are going to sort your knee out'. When patients then come and are told that there isn't anything surgically correctable within the knee, we aren't planning to offer an operation, and there isn't a magic bullet to take your pain away, they are clearly disappointed." (Surgeon D)

Some surgeons were worried about scrutiny from colleagues when requesting second opinions and recognized this influenced their referral practice.

"If I am seeing a patient as a second opinion, I will frequently use the phrase: 'I've been asked to see you because Mr./Miss. So-and-so recognises that we are in a difficult situation and, in those situations, two heads are better than one'. I think that's a great way of trying to be non-derogatory about your colleagues and that starting afresh, having a fresh pair of eyes, is a good thing. But, it comes with complexities for whoever is providing that second opinion, because I know that I balk at sending patients to other hospitals where I may feel they are looking down on my practice." (Surgeon E)

I'm uncomfortable operating for truly unexplained pain

Surgeons described the uncertainty when operating for unexplained pain.

"If I have a knee in front of me that moves well, is not infected, and has no other mechanical problem, I cannot see why a revision operation would work... I wouldn't know what to do... which bits to take out, and what to put back in". (Surgeon G)

Surgeons described a system set-up to discourage revision surgery for unexplained pain.

"In years gone by, surgeons would sometimes operate for unexplained pain, often with the best of intentions, but the evidence showed that a lot of patients didn't get better. And so, the guidelines have developed to reflect this. It would be a big thing now to go back and change this... You grow up, and go through training, being told never to operate on a painful knee without a diagnosis and so this would really be quite different." (Surgeon A)

Several surgeons questioned whether colleagues would support them if they chose to operate for unexplained pain and worried about complications resulting from revision surgery.

"I think it comes down to: 'Do no harm'. You are there in theatre with a knife in your hand, and for some of these patients you may make them much, much worse. It seems that, in surgery (compared to non-operative management), you can lose a lot more." (Surgeon B)

On the other side of the coin, surgeons worried that not offering revision surgery was *"depriving some patients of the opportunity to get better"*.

"It's very difficult if someone says to you: 'My knee's not right. Will you do something?' And you go: 'No.' And they say: 'Well, if you do, is there any chance it could get better?' And you would have to say: 'Yes. We might find something, or we might not. And it might get better or not. And we might not know why.' And then they go: 'Well, if I don't have it revised, is it going to get better?' 'Probably not'. There'd be a lot of patients who would say: 'Well, I'm at a stage where I want you to take that on.'" (Surgeon D)

The thing you have to come to terms with is persuading someone to continue with a course of action where the likelihood is that they're not going to improve. Your treatment options at 4-5 years down the line are: no change, or a punt with a 50-50 chance of an improvement in outcome. If you framed the question to patients, how many would choose surgery? I suspect a very high number. . . " (Surgeon C)

"The patient is looking at it from a different perspective. For them, it's all about: 'My knee is miserable, can you do anything to make it better? And I don't really care what the risks are.' And yours are: 'Ok, this is quite complex. I don't want to end up doing a big, long, complicated operation and having the patient come back to my clinic for the next 10 years where I haven't helped them, or I've made them worse.' " (Surgeon D)

It's a wound I carry with me

This theme describes the surgeon as a second victim. Surgeons described patients with unexplained pain as reminders of the limitations of their practice.

"If a patient is in pain after knee replacement, I'm going to question: Was it my fault? Was it a technical error? How can I avoid this in the future?" (Surgeon A)

This burden weighed heavily on some surgeons.

"I think it's really interesting to look at people who are doing craft specialties within medicine, those who are doing interventions to patients, how they manage their complications. I think most people take those complications with them. There are some people who take it with them so overtly that they cannot be surgeons, and they shouldn't be surgeons, because it will destroy their lives. . . When you get older and start going to peoples' retirements, how they talk about when they stopped doing clinical medicine. . . how much release they got from that psychological burden of complications and problems they were constantly aware of." (Surgeon D)

Some surgeons reflected on the limitations of a somewhat warped heuristic to evaluate the outcome of joint replacement:

"We discharge a lot of patients... those that do get better, of course, never come back to tell us they have". (Surgeon G)

6.4 Discussion

This study aimed to encapsulate the experience of surgeons treating patients with unexplained pain after knee replacement. Our findings indicate the importance of *understanding a patient's journey* through the healthcare system. Surgeons found consultations for unexplained pain challenging due to the complexity of the clinical assessment, while needing to adopt a pastoral role and communicate information sensitively to patients. Surgeons benefited from sharing complex decisions with colleagues, but worried about scrutiny of their practice. Surgeons reflected on their craft and patients returning with unexplained pain were reminders of the limitations of the interventions they offered. Surgeons were uncomfortable recommending surgery for unexplained pain: concerned about whether they would have the support of colleagues and worried about complications from surgical interventions that may have limited benefit.

The themes developed in this study resonate with those identified in an earlier qualitative evidence synthesis of healthcare professionals' experiences treating people with chronic pain [199]. A prominent shared theme was the *pull* of the biomedical model of health: find a diagnosis and treat it. For some surgeons, this was an *acid* test for what was perceived as a binary offer: an operation, or not. Other surgeons embodied a biopsychosocial model, recognising ideas from modern pain theory, where chronic pain is not solely the result of tissue damage, but influenced by individual perceptions, coping mechanisms and social contexts [200]. Both this study and the earlier evidence synthesis [199] described the challenges of consultations for chronic pain (*"A difficult consultation"*) and their emotional toll (*"It's a wound I carry with me"*). Surgeons wishing to reflect on their experience treating patients with chronic pain may benefit from review of the conceptual model developed by Toye and colleagues [199]. Their model highlights the complexity of

navigating therapeutic relationships. The current study identifies potential areas of dissonance in the doctor-patient relationship that may need to be *tuned* to better support patients with chronic pain. *"It's complicated asking for help"* described clinicians' experiences requesting second opinions and putting forward cases to MDT meetings. Most experiences were positive, including the opportunity to *reset* the doctor-patient relationship and to get new ideas on management. However, the theme also identified the stigma around asking colleagues for help [201] and the potential for MDT meetings not to fully encapsulate the patient voice. A previous study investigated patient experiences undergoing elective, aseptic revision knee replacement [68]. There was likely to be considerable overlap with the present study, and so I did not explore patients' experiences here. A recent qualitative evidence synthesis also highlighted the similarities across a range of conditions in the experience of chronic pain [202].

Our study has some limitations. These include the recruitment of a purposive sample of surgeons from a small geographical spread and within an NHS context. I may have found practices and attitudes to be different in other regions and healthcare systems. Our study sample is similar in size to other studies investigating healthcare professional experiences using thematic analysis [199]. The sample can be considered to have high "information power" [203]. This concept refers to the information held by the sample relevant to the aims of the study and is useful to guide adequate sample size for qualitative studies. Using the model proposed by Malterud and colleagues [203], the items supportive of including fewer individuals include: a narrow aim, recruitment of participants with specific experiences relevant to the aim, use of existing theory, strong dialogue and case-specific analysis, all of which apply in the present study.

This study has important implications for practice. It has highlighted the need for evidence-based interventions for patients with chronic pain after knee replacement. These need to be coupled with efficient referral pathways. Baroness Cumberlege [204] recently described the current healthcare system in the UK as "disjointed, siloed, unresponsive and defensive". Recent evidence suggests that personalized

referral pathways based on assessment of individuals' needs may be more clinically-effective and cost-effective than the current standard of care [193]. An example of this might be simultaneous referrals to an orthopaedic surgeon, a physiotherapist, and a pain specialist, each communicating effectively with one another.

In conclusion, this study has provided a deeper understanding of the important considerations for surgeons when managing patients with unexplained pain after knee replacement. Our study calls for a holistic approach to care that considers patients' experiences, embraces modern pain theory, and fosters collaboration among healthcare providers.

7 Conclusions

Each of the earlier chapters concluded with discussion on the main findings from each study, their strengths and limitations and relevance to clinical practice. This final chapter will summarise and discuss these findings in the context of the thesis as a whole and provide directions for future research.

7.1 Summary of main findings

The purpose of this thesis was to explore and investigate the delivery of elective, aseptic rKA, including any patient-relevant outcomes. This thesis has achieved its aims:

1. To investigate the epidemiology of elective, aseptic rKA in the United Kingdom (UK) to understand its incidence, trends over time and reasons for surgery;
2. To investigate the validity of existing patient reported outcome measures (PROMs) to measure joint function from the perspective of the patient; and
3. To investigate patient-relevant outcomes following elective, aseptic rKA by diagnosis to support better shared decision making with patients.

For some chapters the quality of the literature did not allow precise identification of elective, aseptic rKA. In other chapters, it was felt to be of interest to readers to provide information on 'urgent' and re-revision rKA. To support the generalisability of these chapters, Table 7.1 summarises the different rKA populations recruited.

Table 7.1: Summary of revision knee arthroplasty populations

Chapter	Title	Indication for rKA	Type of rKA
Chapter 2.1	National trends in revision knee arthroplasty over the past 15 years	Elective, aseptic and urgent rKA indications.	First- and re-revision rKA.
Chapter 2.2	Revision knee arthroplasty case-mix at the Nuffield Orthopaedic Centre, Oxford	Elective, aseptic and urgent rKA indications.	First- and re-revision rKA.
Chapter 3.1	Usage and measurement properties of Patient-Reported Outcome Measures in elective, aseptic revision knee arthroplasty	Elective, aseptic rKA (and a minority of rKA for urgent indications)	First- and re-revision rKA.
Chapter 3.2	Validation of the OKS for elective, aseptic revision knee arthroplasty	Elective, aseptic rKA (and a minority of rKA for urgent indications)	First- and re-revision rKA.
Chapter 4	Patient-relevant outcomes following elective, aseptic revision knee arthroplasty compared to non-operative management	Elective, aseptic rKA (and a minority of rKA for urgent indications)	First- and re-revision rKA.
Chapter 5	Patient-relevant outcomes by diagnosis for revision knee arthroplasty	Elective, aseptic and urgent rKA, stratified by diagnosis.	First rKA
Chapter 6	The experience of surgeons treating unexplained pain after knee arthroplasty: a reflexive thematic analysis	Surgeons treating patients with an unexplained, painful knee arthroplasty	N/A

Chapter 2.1 investigated trends in the rate and characteristics of rKA performed in the United Kingdom over the past fifteen years using data from the NJR. Reports of rKA to the NJR increased by 149% over the period of observation. The largest increases were observed at the start of the study period, with little change observed over the five years preceding the Covid-19 pandemic. This suggests that the incidence of rKA procedures may be 'leveling off' rather than increasing exponentially, as has previously been predicted [17; 74]. The trend in the incidence of rKA for patients aged 70-79 years or younger paralleled the overall trend. However, for patients aged 80 years and older the trend was of linear increase. The study highlighted the effects of the Covid-19 pandemic on rKA practice in the UK, demonstrating a 43.6% reduction in rKA procedures in 2020 compared to 2019. The study also characterised changes over time in the incidence and proportional

share of each indication for rKA. The incidence of rKA for infection increased year-on-year, and was the most common indication for rKA in 2019. Infection was highly prevalent in re-revision procedures, accounting for 36.7% of *second linked rKA* and 50.7% of *third or more linked rKA*. Aseptic loosening was the most common indication for rKA over the study period, accounting for 20.5% of rKA. However, the proportional share of rKA for aseptic loosening decreased nearly every year from the start of the study period and the incidence of these procedures declined from 2012.

Chapter 2.2 investigated the surgical practice, patterns of referral and resource utilisation of rKA at a major revision centre (MRC). The surgical complexity of rKA procedures performed at the MRC obeyed a 'rule of thirds': one-third of cases 'less complex', one-third 'complex' and one-third the 'most complex/salvage'. Among external referrals, nearly half of patients had a previous rKA prior to referral. Higher case complexity was associated to longer length of hospital stay (LOS). The 'most complex' cases had a median LOS of 11 days, compared to 5 days for 'less complex' cases. The methods used in this study are suitable for implementation by other surgical units to gain a more detailed understanding of their own operative practices, which may be used for planning delivery of services.

Chapter 3.1 scoped the literature to identify PROMs used to evaluate pain and function in the context of rKA and performed a systematic review to evaluate the validity of these instruments. This study identified eight different joint-specific PROMs in current use for rKA. However, only three instruments had a supporting validation study in rKA: KOOS, LEAS and WOMAC. According to COSMIN guidance, each of the validated instruments was found to require further evidence before recommendation for use. As such, a PROM was not put forward for recommendation in a core outcome set.

Chapter 3.2 addressed the lack of a validation study to support use of the OKS in rKA, despite widespread use of the instrument in this context. This chapter analysed data from 10,727 patients in the NHS PROMs dataset. The OKS was found to have a high level of internal consistency, good construct validity, was

responsive to change and did not demonstrate significant floor or ceiling effects. The anchor-based minimal important change (MIC) for an individual patient was found to be 7.5 points, the minimal important difference (MID) 5.2 points, and the minimal detectable change (MDC-90) 3.9 points.

Chapter 4 systematically reviewed the literature to summarise patient-relevant outcomes following aseptic, elective rKA. The included studies were all low-quality, uncontrolled, observational series. No studies were identified to compare aseptic, elective rKA to non-operative management or no treatment at all. As such, this chapter instead addressed the question: *"How long is an elective, aseptic rKA expected to last?"*. The survivorship of rKA was found to be ~96% at 1 year, ~91% at 5 years, ~87% at 10 years and ~83% at 15 years. All studies reporting on joint function and quality-of-life showed large improvements at early timepoints following rKA. This review also produced estimates for mortality, serious medical complications, and the length of hospital stay following aseptic, elective rKA. These estimates may be useful to guide conversations around informed consent prior to aseptic, elective rKA. However, the evidence was insufficient to support more precise estimates for subgroups within aseptic, elective rKA - including, the main exposure of interest in this thesis, the indication for rKA.

Chapter 5 investigated patient-relevant outcomes for different indications for rKA using routinely collected data from the NJR, HES APC, ONS and NHS PROMs datasets. A Shiny application was developed to allow readers to interact with the results of the study. The greatest contrast in the rate of serious medical complications and mortality was evident for rKA performed for urgent compared to aseptic, elective indications. Within aseptic, elective indications for rKA the rate of serious medical complications and mortality was relatively similar. However, there were large differences in joint function, patient satisfaction and perceived success. For example, rKA for progressive arthritis had excellent PROM outcomes (74% responders, 72% satisfied, 79% perceived success) while rKA for unexplained pain had less predictable outcomes (54% responders, 53% satisfied, 61% perceived success).

Chapter 6 was a qualitative study to understand consultant knee surgeons' experiences treating unexplained pain after rKA given the unpredictable outcomes described above. This study followed on from previous work to investigate patients' experiences undergoing elective, aseptic rKA [68]. This chapter identified six themes. *I need to understand a patient's journey and their expectations* described the difficulties of navigating through the healthcare system with chronic pain. *A difficult consultation* described the challenge of balancing complex clinical decisions while adopting a pastoral role and communicating information sensitively to patients. *I'm the 'fixer'* described the reliance of some surgeons on a biomedical model of health and the weight of expectations from patients to *"do something"*. *It's complicated asking for help* described the usefulness of getting *"a fresh pair of eyes"*, but cautioned against patients being set unreliastic expectations. *I'm uncomfortable operating for truly unexplained pain* encapsulated surgeons' concerns around complications from surgery and being supported by colleagues. *It's a wound I carry with me* described the impact of chronic pain and surgical complications on the psychology of the surgeon.

7.2 Recommendations for future research

The thesis achieved its aims to explore and investigate delivery of elective, aseptic rKA, including any patient-relevant outcomes. It has characterised the epidemiology of rKA in the UK over the past fifteen years finding large increases in the incidence of rKA followed by 'leveling off' in more recent years and a profound decrease in activity during the Covid-19 pandemic. In the future, re-analysis of this data using similar methodology would be useful to measure recovery of services following the pandemic. This analysis would also help to understand changes in the delivery of rKA following the introduction of *"Revision Networks"*. The rate estimates produced in this work have been directly standardised. This allows for practice in the UK to be compared with other populations, including those with different age- or gender-distributions. The thesis also investigated surgical practice at a major revision centre. There is an unmet need to apply similar methodology

at other types of units performing rKA to fully understand the *"Revision Network"* model. This research would support JLA Priority #3 *"What are the most effective ways to organize healthcare and avoid delay to improve the results and patients' experience of revision knee surgery?"* [3].

The thesis has improved understanding of PROMs used to evaluate pain and joint function after elective, aseptic rKA. However, the quality of the evidence was insufficient to put forward a PROM for use in a core outcome set. Higher quality validation studies are needed to better evaluate existing PROMs for their suitability in the context of elective, aseptic rKA. This should include investigation of the best mode and timing of PROM administration, and trajectories of recovery following surgery. For some indications for rKA (particularly urgent indications, such as infection and fracture), current PROMs may not capture the factors of greatest importance to patients (i.e. may lack content validity). For example, a patient with prosthetic joint infection may priorise infection eradication over improvements in joint function. For these patient groups, new PROMs may need to be developed. Outside the scope of this thesis, I have contributed to work to develop estimates for minimal important changes and differences for primary and revision hip and knee arthroplasties [131] and evaluated the OKS using an item response theory framework [132; 133]. The development of newer PROMs should consider modern psychometric techniques, such as computerised adaptive testing [205]. This research would further develop JLA Priority #7 *"How should we measure the outcomes following revision knee surgery in a way that is meaningful to patients, and is surgery cost-effective?"* [3].

This thesis highlighted the evidence gap concerning the non-operative management of patients with failed knee arthroplasties. Indeed, no studies were identified for inclusion in the systematic review in Chapter 4. This finding parallels that of a recent umbrella review of common elective orthopaedic procedures, which investigated their clinical effectiveness compared with no treatment, placebo, or non-operative care. That study found many procedures lacked high quality evidence to support their superiority over non-operative alternatives [206]. This corresponds

with the JLA Priority #8 *"Is there a way to manage some types of problematic knee arthroplasty to avoid revision knee surgery (through physiotherapy, lifestyle change, and/or self-management)?* [3].

In Chapter 5, our improved understanding of PROMs from earlier chapters was used to evaluate patient-relevant outcomes following different indications for rKA. This information has been presented in a Shiny application, and made available to surgeons and other healthcare professionals to assist communication of risks and benefits of rKA to patients. However, the application does not predict outcomes for *individual* patients. The thesis has shown that, after stratifying by indication for rKA, sample sizes dwindle. A challenge for future studies is to recruit patient cohorts of sufficient size to better individualise estimations of risk. This is likely to depend on mature registry data. This research would support JLA Priority #4 *"What factors determine (predict) whether revision knee surgery is likely to work?"* [3]. A predictor of current interest is: *Does surgeon or surgical unit caseload influence patient-relevant outcomes following rKA?* This question underpins a critical assumption that has been made for the introduction of revision networks: higher volume surgeons and surgical units achieve better clinical outcomes at lower cost. This relationship has previously been identified in primary hip, knee and shoulder replacement surgery [207; 208; 209]. Evidence for rKA is more limited. A number of studies have focused on the incidence of early re-revision surgery, with most [210; 211; 212] (but not all [213]) supportive of a lower incidence with higher caseload.

After observing unpredictable outcomes for patients revised for unexplained pain, the thesis explored surgeons' experiences treating unexplained pain after rKA. This has added to the literature encapsulating patients' experiences living with chronic pain [202] and undergoing aseptic, elective rKA [68]. This relates to the JLA Priority #6 *"What is the psychological impact of a problematic knee arthroplasty and what support do people need before, during and after revision knee surgery?"* [3].

Patients with stiffness are a similar group to those with unexplained pain, in that their outcome following rKA is unpredictable and often poor. The causes of stiffness, and the best management strategies to treat it, are incompletely understood. This is recognised in JLA Priority #9 *"What causes knee stiffness following knee arthroplasty? How can it be avoided and how is it best treated?"* [3].

7.3 Conclusions

In conclusion, the key findings of this thesis are:

- There have been large increases in the incidence of rKA in the United Kingdom over the past 15 years (149%). These increases appear to be 'leveling off' in more recent years.
- Infection is now the most common indication for rKA, and has overtaken aseptic loosening. Infection is highly prevalent in re-revision procedures (50.7% of *third or more linked rKA*).
- Two-thirds of rKA at a Major Revision Centre were 'complex' or 'the most complex cases', associated to considerable resource utilisation.
- Evidence to support the validity of PROMs to measure joint function in aseptic, elective rKA is limited and insufficient to support an instrument to be put forward for a core outcome set.
- Evidence for patient-relevant outcomes following elective, aseptic rKA is limited to uncontrolled, case series.
- Implant survivorship following elective, aseptic rKA is ~96% at 1 year, ~91% at 5 years and ~87% at 10 years, with most studies identifying large improvements in pain and joint function.
- Patients undergoing rKA for infection were at high risk of re-revision surgery (one in six at 2 years; one in four at 5 years). For other diagnoses, the rate

of re-revision surgery was much lower (ranging from one in 12 [instability] to one in 34 [progressive arthritis] at 2 years).

- The risk of death within 90 days was high for patients undergoing rKA for fracture (one in 31) and infection (one in 56), but less than one in 250 for all other diagnoses.

- There were large differences in joint function, patient satisfaction and perceived success within aseptic, elective indications for rKA. rKA for progressive arthritis had excellent PROMs (74% responders, 72% satisfied, 79% perceived success) while rKA for unexplained pain had less predictable outcomes (54% responders, 53% satisfied, 61% perceived success).

- Six themes were drawn around surgeons' experiences treating patients with unexplained pain after knee replacement: *(1) I need to understand a patient's journey and their expectations; (2) A difficult consultation; (3) I'm the 'fixer'; (4) It's complicated asking for help; (5) I'm uncomfortable operating for truly unexplained pain; and (6) It's a wound I carry with me.*

Appendices

A

Procedure codes for Revision Knee Replacement used in Hospital Episode Statistics

Procedure codes for revision knee replacement are provided in Table A.1:

A. Procedure codes for Revision Knee Replacement used in Hospital Episode Statistics

OPCS Code*	**Note(s)**	**Code Description**
O180		Conversion from previous hybrid prosthetic replacement of knee joint using cement
O182		Conversion to hybrid prosthetic replacement of knee joint using cement
O183		Revision of hybrid prosthetic replacement of knee joint using cement
O184		Attention to hybrid prosthetic replacement of knee joint using cement
W400		Conversion from previous cemented total prosthetic replacement of knee joint
W402		Conversion to total prosthetic replacement of knee joint using cement
W403		Revision of total prosthetic replacement of knee joint using cement
W404		Revision of one component of total prosthetic replacement of knee joint using cement
W410		Conversion from previous uncemented total prosthetic replacement of knee joint
W412		Conversion to total prosthetic replacement of knee joint not using cement
W413		Revision of total prosthetic replacement of knee joint not using cement
W414		Revision of one component of total prosthetic replacement of knee joint not using cement
W420		Conversion from previous total prosthetic replacement of knee joint NEC
W422		Conversion to total prosthetic replacement of knee joint NEC
W423		Revision of total prosthetic replacement of knee joint NEC
W424	A	Attention to total prosthetic replacement of knee joint NEC
W425		Revision of one component of total prosthetic replacement of knee joint NEC
W426		Arthrolysis of total prosthetic replacement of knee joint
W520	K	Conversion from previous cemented prosthetic replacement of articulation of bone NEC
W522	K	Conversion to prosthetic replacement of articulation of bone using cement NEC
W523	K	Revision of prosthetic replacement of articulation of bone using cement NEC
W530	K	Conversion from previous uncemented prosthetic replacement of articulation of bone NEC
W532	K	Conversion to prosthetic replacement of articulation of bone not using cement NEC
W533	K	Revision of prosthetic replacement of articulation of bone not using cement NEC
W540	K	Conversion from previous prosthetic replacement of articulation of bone NEC
W542	K	Conversion to prosthetic replacement of articulation of bone NEC
W543	K	Revision of prosthetic replacement of articulation of bone NEC
W544	K, A	Attention to prosthetic replacement of articulation of bone NEC
W582	K	Revision of resurfacing arthroplasty of joint

* OPCS - Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS-4) codes used in Hospital Episode Statistics Admitted Patient Care

K Must be combined with knee body part codes (Z846 Or Z765 Or Z845 or Z844 Or Z774 Or Z787)

A Must be combined with action codes (Y032 Or Y037)

Table A.1: OPCS Codes for Revision Knee Replacement

B

Search strategy for systematic review of PROM instrument utilisation and measurement properties using the COSMIN checklist

This search strategy incorporates the PROM filter from the Oxford PROM group [100].

Databases: MEDLINE, Embase, AMED, PsycInfo

Search strategy for Ovid MEDLINE:

Arthroplasty, Replacement, Knee/

((arthroplast* or replacement* or resurface*) adj3 knee*).ti,ab.

Knee Prosthesis/

((prosthes* or implant*) adj3 knee*).ti,ab.

(tka or tkr or ukr or uka).ti,ab.

1 or 2 or 3 or 4 or 5

revision*.ti,ab.

modular exchange*.ti,ab.

Reoperation/

(reoperation or re-operation or "repeat surg*").ti,ab.

7 or 8 or 9 or 10

6 and 11

(HR-PRO or HRPRO or HRQL or HRQoL or QL or QoL).ti,ab. or quality of life.mp. or (health index* or health indices or health profile*).ti,ab. or health status.mp. or ((patient or self or child or parent or carer or proxy) adj (appraisal* or appraised or report or reported or reporting or rated or rating* or based or assessed or assessment*)).ti,ab. or ((disability or function or functional or functions or subjective or utility or utilities or wellbeing or well being) adj2 (index or indices or instrument or instruments or measure or measures or questionnaire* or profile or profiles or scale or scales or score or scores or status or survey or surveys)).ti,ab.

12 and 13

C

Search strategy for systematic review of patient-relevant outcomes following elective, aseptic revision knee arthroplasty

(a) **Ovid Medline**

Arthroplasty, Replacement, Knee/

((arthroplast* or replacement* or resurface*) adj3 knee*).ti,ab.

Knee Prosthesis/

((prosthes* or implant*) adj3 knee*).ti,ab.

(tka or tkr or ukr or uka).ti,ab.

1 or 2 or 3 or 4 or 5

revision*.ti,ab.

modular exchange*.ti,ab.

Reoperation/

(reoperation or re-operation or "repeat surg*").ti,ab.

7 or 8 or 9 or 10

6 and 11

Treatment Outcome/

C. Search strategy for systematic review of patient-relevant outcomes following elective, aseptic revision knee arthroplasty

outcome*.ti,ab.

Patient Reported Outcome Measures/

patient reported outcome measure*.ti,ab.

PROMs.ti,ab.

Comorbidity/

comorbid*.ti,ab.

13 or 14 or 15 or 16 or 17 or 18 or 19

12 and 20

randomized controlled trial.pt.

controlled clinical trial.pt.

randomized.ab.

randomly.ab.

trial.ab.

group*.ab.

22 or 23 or 24 or 25 or 26 or 27

exp Cohort Studies/

(cohort adj (study or studies)).tw.

(Follow up adj (study or studies)).tw.

(observational adj (study or studies)).tw.

Longitudinal.tw.

Retrospective.tw.

Prospective.tw.

29 or 30 or 31 or 32 or 33 or 34 or 35

28 or 36

21 and 37

(b) **Embase**

C. Search strategy for systematic review of patient-relevant outcomes following elective, aseptic revision knee arthroplasty

knee arthroplasty/ or total knee arthroplasty/

((arthroplast* or replacement* or resurface*) adj3 knee*).ti,ab.

Knee Prosthesis/

((prosthe* or implant*) adj3 knee*).ti,ab.

(tka or tkr or ukr or uka).ti,ab.

1 or 2 or 3 or 4 or 5

revision*.ti,ab.

modular exchange*.ti,ab.

revision arthroplasty/

(reoperation or re-operation or "repeat surg*").ti,ab.

7 or 8 or 9 or 10

6 and 11

Treatment Outcome/

outcome*.ti,ab.

patient-reported outcome/

patient reported outcome measure*.ti,ab.

PROMs.ti,ab.

Comorbidity/

comorbid*.ti,ab.

13 or 14 or 15 or 16 or 17 or 18 or 19

12 and 20

randomized controlled trial/

single blind procedure/ or double blind procedure/

crossover procedure/

random*.ab.

trial.ab.

C. Search strategy for systematic review of patient-relevant outcomes following elective, aseptic revision knee arthroplasty

(random or ((singl* or doubl*) adj (blind* or mask*)) or crossover or cross over or factorial* or latin square or assign* or allocat* or volunteer*).ti,ab.

22 or 23 or 24 or 25 or 26 or 27

Cohort analysis/

(cohort adj (study or studies)).tw.

(Follow up adj (study or studies)).tw.

(observational adj (study or studies)).tw.

Longitudinal.tw.

Retrospective.tw.

Prospective.tw.

29 or 30 or 31 or 32 or 33 or 34 or 35

28 or 36

21 and 37

D

Research ethics, data access and permission to link datasets without patient consent

Health Research Authority
2 Redman Place
Stratford
London
E20 1JQ

Tel: 020 7104 8100
Email: cag@hra.nhs.uk

05 March 2021

Professor Andrew Price
Price Knee Group - Botnar Research Building
Nuffield Orthopaedic Centre
Oxford
OX3 7LD

Dear Professor Price

Application title:	**Revision Hip and Knee Replacement: Evaluation of Clinical, Psychological and Surgical Outcomes**
CAG reference:	**20/CAG/0044**
IRAS project ID:	**278592**
REC reference:	**20/LO/0428**

Thank you for your amendment request to the above research application, submitted for support under Regulation 5 of the Health Service (Control of Patient Information) Regulations 2002 to process confidential patient information without consent. Supported applications enable the data controller to provide specified information to the applicant for the purposes of the relevant activity, without being in breach of the common law duty of confidentiality, although other relevant legislative provisions will still be applicable.

The role of the Confidentiality Advisory Group (CAG) is to review applications submitted under these Regulations and to provide advice to the Health Research Authority on whether an application should be supported, and if so, any relevant conditions.

Health Research Authority decision

The Health Research Authority, having considered the advice from the Confidentiality Advisory Group as set out below, has determined the following:

1. The amendment, to revise the data flows so that Northgate Public Services disclose confidential patient information from the NJR to NHS Digital for linkage to HES, PROMS and ONS datasets, and the disclosure of a pseudonymised dataset to the University of Oxford, is supported, subject to compliance with the standard conditions of support.

Amendment request

The applicants have existing support to allow the disclosure of confidential patient information from the National Joint Registry (NJR) to NHS Digital for linkage to PROMs, HES and ONS datasets.

In this amendment, the applicants are seeking to revise the data flows, as NHS Digital have updated their internal patient linkage methodology to the Master Patient Service (MPS). Under the current support, the disclosure of confidential patient information from Northgate Public Services (NPS) to the NJR to NHS Digital for linkage to HES, PROMS and ONS datasets will form Stage 1.

However, instead of the pseudonymised dataset, including the NJR ID, being sent to the NPS, the NPS will disclose confidential patient information from the NJR to NHS Digital. NHS Digital will use these identifiers to link to the HES, PROMS and ONS datasets, and generate a cohort of patients who are not already in the NJR, and the send the complete, pseudonymised dataset directly to the University of Oxford (rather than to the NJR, who then send the dataset to the University). The NJR will also send pseudonymised joint replacement records with the Study ID directly to the University of Oxford. NHS Digital will retain the NJR identifiers until MPS is available, when the identifiers will be used to undertake a second linkage to the PROMS dataset.

Once the MPS is available for the PROMS dataset, a second stage will be added. NHS Digital will repeat the linkage to the NJR cohort, using the same identifiers used in Stage 1. NHS Digital will send two fields, the PROMS_SERIAL_NO and Study_ID to the University of Oxford as a look up table.

Confidentiality Advisory Group advice

The amendment requested was considered by the Confidentiality Advisory Group. The Group agreed that the NJR will be enhanced by data from HES that is missing from the NJR at resent because patient data from Trusts has not submitted to the NJR through error. The new service from NHS Digital will enable much more accurate matching of the NJR data to PROMS allowing much greater accuracy in the audit.

Confidentiality Advisory Group Team conclusion

In line with the considerations above, the CAG agreed that the minimum criteria under the Regulations appeared to have been met for this amendment, and therefore advised recommending support to the Health Research Authority.

Specific conditions of support

1. Confirmation provided from the IG Delivery Team at NHS Digital to the CAG that the relevant Data Security and Protection Toolkit (DSPT) submission(s) has achieved the 'Standards Met' threshold:

   (Confirmed: Northgate Public Services (by NHS Digital email dated 08 January 2021) and NHS Digital (by check of the NHS Digital DSPT Tracker) have confirmed 'Standards Met' grade on DSPT 2019/20).

2. Confirmation of a favourable opinion from a Research Ethics Committee. **Confirmed 05 February 2021.**

Reviewed documents

Document	*Version*	*Date*
Amendment request form		18 January 2021
Revision Hip and Knee Data Flow Diagram		
278592_Favourable_opinion_of_a_substantial_amendment-05Feb2021		05 February 2021

Please do not hesitate to contact me if you have any queries following this letter. I would be grateful if you could quote the above reference number in all future correspondence.

Yours sincerely

Kathleen Cassidy
Confidentiality Advisor

On behalf of the Health Research Authority

Email: cag@hra.nhs.uk

Enclosures: Standard conditions of Support

cc. bromley.rec@hra.nhs.uk
approvals@hra.nhs.uk

Standard conditions of support

Support to process confidential patient information without consent, given by the Health Research Authority, is subject to the following standard conditions of support.

The applicant and those processing the information will ensure that:

1. The specified confidential patient information is only used for the purpose(s) set out in the application.
2. Confidentiality is preserved and there are no disclosures of information in aggregate or patient level form that may inferentially identify a person, nor will any attempt be made to identify individuals, households or organisations in the data.
3. Requirements of the Statistics and Registration Services Act 2007 are adhered to regarding publication when relevant, in addition to other national guidance.
4. All staff with access to confidential patient information have contractual obligations of confidentiality, enforceable through disciplinary procedures.
5. All staff with access to confidential patient information have received appropriate ongoing training to ensure they are aware of their responsibilities.
6. Activities remain consistent with the General Data Protection Regulation and Data Protection Act 2018.
7. Audit of data processing by a designated agent is facilitated and supported.
8. The wishes of patients who have withheld or withdrawn their consent are respected.
9. Any significant changes (for example, people, purpose, data flows, data items, security arrangements) must be supported via formal amendment prior to changes coming into effect.
10. An annual review report is submitted to the CAG every 12 months from the date of the final support letter, for the duration of the support.
11. Any breaches of confidentiality around the supported flows of information should be reported to CAG within 10 working days of the incident, along with remedial actions taken / to be taken. This does not remove the need to follow national/legal requirements for reporting relevant security breaches.

Health Research Authority

London - Bromley Research Ethics Committee
Temple Quay House
2 The Square
Temple Quay
Bristol
BS1 6PN

Tel: 0207 104 8372

Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implemented at NHS sites in England until the outcome of the HRA assessment has been confirmed.

05 February 2021

Mr Shiraz Sabah
Price Knee Group - Botnar Research Building
Nuffield Orthopaedic Centre
Oxford
OX3 7LD

Dear Mr Sabah

Study title:	**Revision Hip and Knee Replacement: Evaluation of Clinical, Psychological and Surgical Outcomes**
REC reference:	**20/LO/0428**
Protocol number:	**000000**
Amendment number:	**Substantial Amendment 1**
Amendment date:	**20 January 2021**
IRAS project ID:	**278592**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Completed Amendment Tool [Amendment Tool]	1	20 January 2021

NHS
Health Research Authority

Research protocol or project proposal [Revision Ethics Protocol v7 - Tracked]	7	20 January 2021
Research protocol or project proposal [Revision Ethics Protocol v7]	7	20 January 2021

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Amendments related to COVID-19

We will update your research summary for the above study on the research summaries section of our website. During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you have not already done so, please register your study on a public registry as soon as possible and provide the HRA with the registration detail, which will be posted alongside other information relating to your project.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS Project ID - 278592:	**Please quote this number on all correspondence**

Yours sincerely

pp. Philip Evans

Dr Koula Asimakopoulou
Chair

E-mail: bromley.rec@hra.nhs.uk

Enclosures:	*List of names and professions of members who took part in the review*
Copy to:	*Mr Shiraz SabahConfidentiality Advise Team*

Health Research Authority

London - Bromley Research Ethics Committee

Attendance at Sub-Committee of the REC meeting described as 09 February 2021

Committee Members:

Name	*Profession*	*Present*	*Notes*
Mrs Frances Riggs	Retired Deputy Head Teacher	Yes	
Dr Jacqueline Tavabie (Vice-Chair)	General Practitioner	Yes	Chair of the meeting

Also in attendance:

Name	*Position (or reason for attending)*
Nina Bakhshayesh	Approvals Administrator
Philip Evans	Approvals Administrator

D. Research ethics, data access and permission to link datasets without patient consent

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To: Andrew Price, Principal Investigator
By email via: andrew.price@ndorms.ox.ac.uk

26 March 2019

Dear Andrew,

Study title; 'Determining the outcome of revision hip and knee arthroplasty using linked national data'; University of Oxford; NJR REF: RSC2017/26; External

Thank you for resubmitting the above named research application to the NJR Research Committee (RC). The chair has reviewed this application. I write to confirm **'approval'** of this work subject to the following conditions.

1. The applicants should provide evidence of CAG support to flow identifiers to NHS Digfital for linkage
2. The applicants should provide evidence of an in progress application to NHS Digital before HQIP DARG can consider the application.

A condition of this approval is that you agree to provide 6 monthly progress reports to the NJR. Please submit these to me electronically within 30 days of the review date. These progress reports will be circulated to the NJR RSC and the final report summary will be published on the NJR website.

I enclose the contract paperwork ('Data Sharing Agreement'). Please return a signed copy of the document to me. Subject to RC approval, the application will then be referred to HQIP DARG for final approval of data release.

Wishing you all the best with this research study.

Yours sincerely,

Chris Boulton
Associate Director-Research & Governance (NJR)
On behalf of the NJR Research Committee

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Company Limited by guarantee
Registered in England No. 6498947
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D. Research ethics, data access and permission to link datasets without patient consent

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