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Knee Replacement Revision: An international Comparison

Peter Lewis is an Orthopaedic Surgeon, living and practicing in Australia. After medical school and specialist training in Adelaide, and then a fellowship in Canada, the main focus of his working life has been hip and knee replacement surgery. He is also a Deputy Director of the AOANJRR.

This thesis' main aim was to gain an international perspective of knee replacement revision using data resources of the arthroplasty registries of Sweden, Australia and the Kaiser Permanente organization in the USA. It is hoped that these findings can be used to inform surgeons of best practice, and thereby help to improve outcomes for patients requiring knee replacement surgery.

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Knee Replacement Revision:
An International Comparison

PETER LEWIS
DEPARTMENT OF ORTHOPEDICS | FACULTY OF MEDICINE | LUND UNIVERSITY

Knee Replacement Revision: An International Comparison

Knee Replacement Revision:

An International Comparison

Peter Lewis

LUND UNIVERSITY

DOCTORAL DISSERTATION

Doctoral dissertation for the degree of Doctor of Philosophy (PhD) at the Faculty of Medicine at Lund University to be publicly defended on 8th of September 2022 at 09.00 in Belfrage, BMC, Lund.

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Title and subtitle: Knee Replacement Revision: An International Comparison

Abstract

Background and purpose: The need for knee replacement revision arises from a combination of patient, prosthesis and surgeon factors. Registry data can help study these relationships. Pooling data from multiple registries may increase both reliability and generalizability. The study aim was to gain a multi-national overview of knee replacement revision, to inform best-practice and improve outcomes.

Patients and methods: Data was obtained from the Swedish Knee Arthroplasty Register (SKAR), the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR), and the Kaiser Permanente Joint Replacement Registry (KPJRR) from the US. Procedure numbers, demographic characteristics, prosthesis factors, revision diagnoses and revision procedure information were used. Equivalent diagnosis groups were created to allow analysis. Similarities and differences between registries were determined, as were time-related trends, and meta-analytic techniques were used to estimate the influence of patient or prosthesis factors on revision. More detailed study of revision for instability was carried out.

Results: Primary knee replacement incidence had increased and revision procedures too, but by a smaller amount. Most common reasons for revision were infection, loosening and instability. Revision for infection had increased. Practice variations were seen between registries, particularly with prosthesis constraint and patella component usage, and also over time, with bearing mobility and polyethylene type. All-cause revision rates were higher with posterior stabilized, cementless and mobile-bearing components. Posterior stabilized prostheses had increased revision for infection, fracture and loosening, mobile-bearing components had increased revision for arthrofibrosis, instability and patella reasons, cementless fixation revisions for wear and procedures where patella components were not used had increased revision for patella reasons. Further prosthesis factors related to revision for instability were non-cruciate retaining components and inserts made of non-cross-linked polyethylene and those >14mm thick. Insert exchange was the most common revision procedure, but fewer 2nd revisions were seen with a major revision using more constrained implants.

Interpretation: Practice variation can partially explain between-registry differences in incidence, and variability in reasons for revision. Understanding interactions between prosthesis factors and revision can help inform prosthesis choices. Use of lower risk prostheses can improve all-cause revision, revision for specific reasons, and additionally, revision and 2nd revision for instability.

Key words: knee replacement, knee arthroplasty, TKR, registry, multi-registry, revision, revision reason, patient factors, prosthesis factors, post-TKR instability

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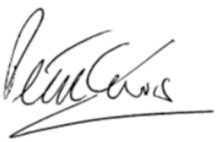
Signature  Date 2022-08-01

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Table of Contents

Abstract

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Interpretation: Practice variation can partially explain between-registry differences in incidence, and variability in reasons for revision. Understanding interactions between prosthesis factors and revision can help inform prosthesis choices. Use of lower risk prostheses can improve all-cause revision, revision for specific reasons, and additionally, revision and 2nd revision for instability.

Sammanfattning på svenska

Bakgrund och syfte: Anledningen till att behöva operera om tidigare insatta knäproteser är en kombination av patient-, protes- och kirurgfaktorer. Registerdata kan hjälpa till att studera dessa samband. Att använda data från flera register och flera länder kan öka både tillförlitligheten och generaliserbarheten. Syftet med avhandlingen var att på detta sett få en bred bild över knäprotesrevisioner, för att kunna informera om bästa praxis och förbättra resultaten.

Patienter och metoder: Data inhämtades från Svenska knäprotesregistret (SKAR), det australiensiska ledprotesregistret (AOANJRR) och Kaiser Permanentes ledprotesregister (KPJRR) från USA. Antal operationer, demografi, protesfaktorer, revisionsorsaker och information om revisioner användes. Likvärdiga diagnosgrupper skapades för att möjliggöra analyser. Likheter och skillnader mellan registren fastställdes, liksom tidsrelaterade trender. Metaanalytiska tekniker användes för att uppskatta patient- eller protesfaktorers påverkan på revision. En mer detaljerad studie av revision för instabilitet genomfördes.

Resultat: Incidensen av primär knäprotesoperation ökade över tid och så även antalet revisionsprocedurer, men de senare i mindre utsträckning. De vanligaste orsakerna till revision var infektion, lossning och instabilitet, där revision för infektion ökade över tid. Variationer i användning sågs mellan register, särskilt avseende protesens inbyggda stabilitet och användning av patellakomponent, och även över tid, tibiaplastens rörlighet och typ.

Revisionsfrekvensen oberoende av orsak var högre med bakre stabiliserade, cementfria och rörliga komponenter. Bakre stabiliserade proteser hade ökad risk för revision på grund av infektion, fraktur och lossning. Rörliga plastkomponenter hade ökad risk för revision på grund av ledstelhet, instabilitet och patellaproblem. Cementfri fixation hade ökad risk för revision på grund av slitage och att inte använda en patellakomponent hade ökad risk för revision på grund av patellaproblem.

Ytterligare protesrelaterade faktorer som utgjorde risk för revision för instabilitet var när det inte hade använts bakre korsbanssparande teknik och plastinlägg >14 mm tjocka med UHMWPE-plast. Byte av plast var den vanligaste revisionen i denna grupp, men det var färre andragångs revisioner om det vid revisionen användes mer stabiliserande implantat.

Tolkning: Variation i användning av olika protesmodeller kan delvis förklara skillnader i incidens mellan register liksom variationen i anledningar till revision. Att förstå interaktioner mellan protesfaktorer och revision kan bidraga till att informera om val av protes. Att välja protesmodeller som uppvisar en generellt lägre risk för revision

kan förbättra de övergripande resultaten, men även påverka specifika skäl såsom stelhet, lossning, fraktur och revision och 2:a revision för instabilitet.

List of papers

The thesis is based on the following papers, referred to in the text by their Roman numerals.

I. **Increases in the rates of primary and revision knee replacement are reducing: a 15-year study across 3 continents.**
Peter L Lewis, Stephen E Graves, Otto Robertsson, Martin Sundberg, Elizabeth W Paxton, Heather A Prentice & Annette W-Dahl
Acta Orthopaedica 2020 91:4, 414-419 DOI:10.1080/17453674.2020.1749380

II. **Variation and trends in reasons for knee replacement revision. A multi-registry study of revision burden.**
Peter L Lewis, Otto Robertsson, Stephen E Graves, Elizabeth W Paxton, Heather A Prentice & Annette W-Dahl
Acta Orthopaedica 2021 92(2) 182-188 DOI:10.1080/17453674.2020.1853340

III. **The effect of patient and prosthesis factors on revision rates after total knee replacement using a multi-registry meta-analytic approach.**
Peter L Lewis, Annette W-Dahl, Otto Robertsson, Michelle Lorimer, Heather A Prentice, Stephen E Graves, Elizabeth W Paxton
Acta Orthopaedica 2022 93: 284–293 DOI:10.2340/17453674.2022.1997

IV. **Impact of patient and prosthesis characteristics on common reasons for total knee replacement revision: A registry study of 36,626 revision cases from Australia, Sweden and USA.**
Peter L Lewis, Annette W-Dahl, Otto Robertsson, Heather A Prentice, Stephen E Graves
Acta Orthopaedica 2022; 93: 623–633 DOI:10.2340/17453674.2022.3512

V. **Primary total knee arthroplasty revised for instability: A detailed registry analysis.**

Peter L Lewis, David G Campbell, Michelle Lorimer, Francisco Requicha,
Annette W-Dahl, Otto Robertsson
J Arthroplasty 2022 Feb;37 (2):286-297
DOI:10.1016/j.arth.2021.11.002.

Abbreviations

Registries and institutions

AOANJRR: Australian Orthopaedic Association National Joint Replacement Registry

ISAR: International Society of Arthroplasty Registries

KPJRR: Kaiser Permanente Joint Replacement Registry

NARA: Nordic Arthroplasty Register Association

SAHMRI: South Australian Health and Medical Research Institute

SAR: Swedish Arthroplasty Register

SKAR: Swedish Knee Arthroplasty Register

Prosthesis terms (to be read in conjunction with definitions below)

Anti-Ox: Antioxidant

AS: Anterior stabilized

CR: Cruciate retaining

DAIR: Debridement, antibiotics and implant retention

DD: Deep-dished

FS: Fully stabilized

FB: Fixed bearing

KR: Knee Replacement

MB: Mobile bearing

MPD: Medial pivot design

MS: Minimally stabilized

Non-XLPE: Non-cross-linked polyethylene

PFR: Patellofemoral Replacement

PROM: Patient Recorded Outcome Measure

PS: Posterior stabilized

TKA: Total Knee Arthroplasty

TKR: Total Knee Replacement

XLPE: Cross-linked polyethylene

UHMWPE: Ultra-high molecular weight polyethylene

UKA: Uni-compartmental Knee Arthroplasty

Definitions

Anterior Stabilized: A subset of the MS group, that has an insert with increased anterior conformity intended to provide some additional anterior stability

Antioxidant: An additive to polyethylene to minimise oxidation, (often vitamin E) and perhaps wear-related deterioration

ASA score: American Society of Anesthesiology physical status classification score

Body Mass Index (BMI): Calculated by weight (in kgs) divided by the square of height (in m) expressed as kg/m^2, classified into World Health Organization categories

Cemented (fixation): Fixation of both major components has required bone cement

Cementless (fixation): Neither of the major components has been used with bone cement, instead using an ingrowth surface to achieve fixation

Cement Spacer: Use of a cement "block" (usually containing antibiotic) to fill the void created by component removal, as the first stage of revision for infection

Confidence Interval (CI): A range either side of the mean, (with a degree of certainty, usually 95%) that a parameter will fall between.

Constraint: A characteristic of a knee prosthesis determined by the level of inherent stability conferred by the prosthetic design.

Conformity: Degree of congruency between the femoral and tibial articular surfaces (classes are Cruciate Retaining, Anterior Stabilised or Deep Dished)

Cruciate Retaining: A subset of the MS group (where the posterior cruciate ligament is retained) that does not have an anterior stabilised or deep dished configuration

Cumulative Percent Revision (CPR): Cumulative percent revision determined as the inverse of the Kaplan Meier estimate of survivorship

Deep Dished: A subset of the MS group, that has ultra-congruent inserts that are intended to give additional sagittal stability without the need for a peg-and-box design, also called ultra-congruent

Equivalent Diagnosis Groups (EDG): The creation of harmonised diagnosis categories from the original surgeon-nominated reason for revision, based on the diagnostic categories of the SKAR.

Electronic Health Record (EHR): Computer-based patient records.

Fixation: Method used to secure the prosthesis to bone (can be Cemented, Hybrid or Cementless).

Fixed Bearing: A design of prosthesis where the tibial insert is not intended to move with respect to the tibial baseplate

Fully Stabilized: Prostheses with a large peg-and-box design designed to give some collateral as well as posterior stability (sometimes also called varus-valgus constrained or condylar constrained components)

Hazard Ratio (HR): A measure of how often an event occurs in one group compared to how often it occurs in another group, over time

Hinged: Prostheses that have a hinge mechanism to link the femoral and tibial components

Hybrid (fixation): Only one of the major components has been fixed with cement (usually the tibial component), while the other is inserted without cement

Interquartile Range (IQR): The limits of the middle 50% of values when ordered from lowest to highest.

Instability (for revision): The symptom of feeling the knee is unsafe or unreliable and may give-way, slip, buckle or collapse. In the EDG it combines the revision diagnoses of instability, bearing dislocation or arthroplasty dislocation

Major Revision: A revision procedure where either the femoral or tibial component, or both are removed or exchanged

Medial Pivot Design: Prostheses that have a ball-and-socket medial portion of the articulation

Minimally Stabilized: Prostheses that have a flat or dished tibial articulation, regardless of congruency

Minor Revision: A revision procedure where neither the femoral or tibial components are exchanged, usually involving the exchange of the polyethylene insert or the patella component, or addition of a patella component where no patella component was used in the primary procedure

Non-cross-linked Polyethylene: Ultra-high molecular weight polyethylene (UHMWPE) that has not been irradiated

Mobile bearing: A design of prosthesis with a tibial insert designed to move relative to the tibial baseplate

Non-obese: Those with a BMI $<30 kg/m^2$

Obese: Those with a BMI ≥ 30 kg/m^2

Osteoarthritis (OA): A painful destructive degenerative disorder of joints characterised by the loss of chondral tissue, sometimes bone as well and often associated with inflammation

Patella Reasons (for revision): Combined revisions for patella pain, patella erosion and patella mal-tracking

Patello-femoral Replacement: A partial knee replacement that resurfaces the patella and femoral trochlea surfaces

Posterior Stabilized: Prostheses that provide posterior stability, most commonly using a peg-and-box design (sometimes also called cruciate sacrificing)

"Prostalac": Prosthesis made with Antibiotic Loaded Acrylic Cement (an alternative to a Cement Spacer), used in first stage revision for infection

Revision: A further operation after a primary procedure where one or more components are removed, added or exchanged

Second Revision: The revision of a 1st revision procedure

Standard Deviation (SD): A summary measure of the differences of each measure from the mean

Total Knee Replacement: A surgical procedure to replace both of the femoral and tibial surfaces of the knee, sometimes combined with a patella resurfacing component as well

UHMWPE: Ultrahigh molecular weight polyethylene

Uni-compartmental Knee Arthroplasty: A partial knee replacement which resurfaces a single compartment of the knee, usually the medial, but sometimes the lateral compartment

XLPE: Ultrahigh molecular weight polyethylene that has been irradiated by high dose (>50kGy) gamma or electron beam radiation. May have an added antioxidant.

Thesis at a glance

PAPER	I	II	III	IV	V
Study Type	Descriptive, Observational, Multi-Registry	Descriptive, Observational, Multi-Registry	Analytical, Observational, Multi-Registry	Analytical, Observational, Multi-Registry	Analytical, Observational, Single Registry
Question	How have primary and revision knee replacement volumes changed over 15 years?	How have reasons for revision changed and are there inter-registry differences?	What effect do patient and prosthesis factors have on revision rates?	What impact do the patient and prosthesis factors have on the common reasons for revision?	What factors affect revision for instability? How is instability treated, and what is the treatment outcome?
Data Inclusion	All knee replacement.	All revision knee replacement.	Primary TKR for OA and their revisions.	Primary TKR for OA and their revisions.	Primary TKR for OA revised for instability.
Data Period	2003 until end 2017	2003 until end 2017	2003 until end 2019	2003 until end 2019	1999 until end 2019
Study Populations	1,133,079 knee replacements.	78,151 revision knee replacements.	1,072,924 primary TKR and 36,626 revisions.	1,072,924 primary TKR and 36,626 revisions.	2605 TKR revised for instability and 385 2nd revisions.
Results	Procedure numbers and incidence have increased, but the rate of increase is slowing. The amount of increase varies between regions.	Between-registry differences in revision reasons are common. Infection, loosening and instability were frequent reasons for revision.	Marked variation in patella component use, prosthesis constraint, fixation and polyethylene type found. Despite practice variations use of MS, fixed bearing and cemented components led to fewer revisions.	PS components had increased revision for infection, fracture and loosening, MB prostheses revision for arthrofibrosis, instability and for patella reasons, cementless fixation revision for wear and not using a patella component revision for patella reasons.	Age <65, females, non-CR TKR with thick, mobile bearings & UHMWPE inserts at higher risk. Insert exchange most common treatment. 24% had 2nd revision by 14 years, often for recurrent instability. Major revision and increased constraint lowered 2nd revision rates.
Clinical Perspective	Predictions for future knee procedures numbers may need to be revised down.	Practice differences may account for variability in revision diagnoses. Of concern is the universal increase in revision for infection.	Choice of lower risk prosthesis characteristics can improve all-cause revision rates.	TKR factors can influence revision rates for specific reasons.	Prosthesis choices effect revision for instability, and also alter the outcome of the revision procedure.

Description of contributions

Paper I

Study design: Peter Lewis

Provision of Summary Data: from SKAR-Otto Robertsson, from AOAJRR-Michelle Lorimer, from KPJRR- Heather Prentice and Brian Fasig

Statistical analysis: Peter Lewis

Interpretation of data: Peter Lewis, Annette W-Dahl, Otto Robertsson

Manuscript preparation: Peter Lewis

Manuscript editing/revision: Annette W-Dahl, Otto Robertsson, Heather Prentice, Stephen Graves, Elizabeth Paxton

Paper II

Study design: Peter Lewis

Provision of Summary Data: from SKAR-Otto Robertsson, from AOAJRR-Michelle Lorimer, from KPJRR- Heather Prentice and Brian Fasig

Statistical analysis: Peter Lewis

Interpretation of data: Peter Lewis, Annette W-Dahl, Otto Robertsson, Stephen Graves, Elizabeth Paxton

Methodology advice: Otto Robertsson

Manuscript preparation: Peter Lewis

Manuscript editing/revision: Annette W-Dahl, Otto Robertsson, Heather Prentice, Stephen Graves, Elizabeth Paxton

Paper III

Study design: Peter Lewis, Annette W-Dahl

Provision of Summary Data: from SKAR-Otto Robertsson, from AOAJRR-Michelle Lorimer and Carl Holder, from KPJRR- Heather Prentice

Statistical analysis: Peter Lewis, Michelle Lorimer, Otto Robertsson, Heather Prentice

Data synthesis: Peter Lewis

Interpretation of data: Peter Lewis, Annette W-Dahl, Otto Robertsson, Stephen Graves, Elizabeth Paxton

Methodology advice: Otto Robertsson, Michelle Lorimer

Manuscript preparation: Peter Lewis

Manuscript editing/revision: Annette W-Dahl, Otto Robertsson, Heather Prentice, Stephen Graves, Elizabeth Paxton

Paper IV

Study design: Peter Lewis

Provision of Summary Data: from SKAR-Otto Robertsson, from AOAJRR-Michelle Lorimer and Carl Holder, from KPJRR- Heather Prentice

Statistical analysis: Peter Lewis

Data synthesis: Peter Lewis

Methodology advice: Annette W-Dahl

Interpretation of data: Peter Lewis, Annette W-Dahl

Manuscript preparation: Peter Lewis

Manuscript editing/revision: Annette W-Dahl, Heather Prentice, Stephen Graves

Paper V

Study design: Peter Lewis

Provision of Summary Data: Michelle Lorimer

Statistical analysis: Peter Lewis, Michelle Lorimer

Data synthesis: Peter Lewis, Francisco Requicha

Interpretation of data: Peter Lewis, David Campbell, Annette W-Dahl, Otto Robertsson

Methodology advice: David Campbell, Michelle Lorimer

Manuscript preparation: Peter Lewis

Manuscript editing/revision: David Campbell, Francisco Requicha, Annette W-Dahl, Otto Robertsson

Introduction

General background

The yearly incidence of total knee replacement (TKR) during the last 20 years has more than doubled in Sweden and Australia (1). Patients currently receiving TKR are said to be relatively younger, more active, and heavier than before (2). With increased use of TKR, along with an aging population that has improving life expectancy, more people are living with a TKR (3). Although knee prosthetic components are becoming more durable, it is expected that a growing number will require revision (4). Why modern knee replacements are revised is a poorly studied area, but for the reason just stated, it is likely to be of increasing importance. Studying revision of knee replacements can be difficult, as it involves heterogeneous groups of patients who may have a variety of reasons for revision. The need for revision surgery arises from an interaction of patient, prosthesis and surgeon factors. Studies from large centers can be criticised for lacking complete follow-up, making clinical quality registries better positioned to undertake these investigations. (5). However, findings from a single national or regional registry are sometimes discounted, as there is the thought that somehow the "results are different where we are". Combining data from multiple registries should not only help to silence some of the disbelievers, but also add gravitas to registry-generated results when these are put together. To minimise factors specific to individual healthcare systems or those regarding particular prosthesis or technique choices, pooling of results from multiple registries increases the reliability and generalisability of the findings (6). Also, revision reasons and procedures change with time, as prostheses improve and techniques are modified (7). These interactions and time-related changes can be analysed using data from large arthroplasty registries and their impact on revision determined.

Specific background

The development of modern knee replacement

Knee replacement is a surgical procedure with a relatively short history. Early attempts at arthroplasty to relieve pain in joints severely damaged by bacterial infection or rheumatoid arthritis were by metallic interposition devices, such as the MacIntosh hemiarthroplasty described in the 1950s (8). An alternative approach was a metal hinged prosthesis, with one of the more popular devices having a Swedish origin, coming from Börje Walldius in the same decade (9). These initial designs met with limited success. Further development occurred, and the precursor to today's knee replacements using a metal-against-polyethylene approach with a bicondylar design was first described by Frank Gunston in 1971 (10).

Modifications followed through the 1980s by teams led by Michael Freeman (11), John Insall (12) and others (13), and subsequently through the following decades, with advancement of materials, designs and techniques, knee replacement grew in "maturity", sophistication and acceptance. Knee replacement is no longer just for treatment of end-stage diseases where the alternative is arthrodesis; now the majority of cases are performed to relieve the pain and dysfunction of osteoarthritis (14). Knee replacement has become a reliable and reproducible procedure with survivorship of over 95% at 10 years (14). Review of knee replacement outcomes can inform and enable further refinement. Registry data can aid this process.

Initiation of this project and selection of registries

This project was first proposed to study the similarities and differences between knee replacement patients in Australia and Sweden. The arthroplasty registries from these two countries have similar status for their scientific output and data quality. Both registries belong to the International Society of Arthroplasty Registries (ISAR), which has a goal of improving outcomes of individuals receiving joint replacements world-wide. This is achieved, in part, by fostering information sharing and by collaborative studies among registries, such as originally intended by this project.

That initial plan may have had very limited appeal to researchers from these two countries, but few others, so it was suggested to add another data source to make the comparisons have a more "international" flavour. Additional registry data was offered by Liz Paxton who is Director of the National Implant Registries of the Kaiser Permanente Integrated Managed Health Care Consortium in the USA. This was thought to be a good inclusion as the Kaiser Permanente Joint Replacement Registry also has an outstanding reputation, and by co-incidence provides health care cover to a similar number to the population of Sweden. Inclusion of a representative organisation from the US not only allowed comparison to a population from a third continent, but it was additionally considered that the level of health care system sophistication was similar to Sweden and Australia. It is also a convenient fact that Liz Paxton is the wife of Stephen Graves who is the Director of the AOANJRR.

A literature search of the 10 years prior to commencement of these studies, found there had been some published collaborative multi-registry papers regarding hip replacement, but very few concerning knee replacement outcomes. Formal attempts to combine data from registry groups had been via the Nordic Arthroplasty Register Association

(NARA) collective and the International Consortium of Orthopedic Registries (ICOR) group, which was an initiative of the US Food and Drug Administration (FDA). These collaborations had resulted in a small number of publications (15-18). Cooperative efforts between 2 registries had resulted in a few additional studies. (19-21). Other more global comparisons had assessed life-time risk of knee replacement (22) or simply compared incidence between countries, but not revision outcomes (23). Although I may have missed some others, the limited number of papers combining registry data to study revision rates and reasons was disappointing.

As registries individually have so much potential to influence knee replacement surgery, combination of multiple registries should have an even greater capacity to guide future advancement. I hoped to not only add to the small contribution from multi-registry studies but use this opportunity to provide a more informed "global" view of knee replacement and fill some of the knowledge deficit in this area.

Contributing registries

The Swedish Knee Arthroplasty Register (SKAR)

In 1975 the Swedish Knee Arthroplasty Register (SKAR) was set up by Professor Göran Bauer, head of the Orthopaedic Department in Lund, with encouragement from the Swedish Orthopaedic Association, to monitor knee arthroplasty surgery (24). It was the first arthroplasty register, and many other countries and orthopaedic groups have now followed Sweden's lead. In September 2021 the SKAR was merged with the Swedish Hip Arthroplasty Register to become the combined Swedish Arthroplasty Register (SAR) (25). Data used in this thesis originated from the SKAR, (with the most recent inclusions until 31st Dec 2019), so throughout I have kept this "old" nomenclature. The SKAR (now SAR) collects data on patients, techniques, revision and re-operation rates as well as patient reported outcomes (PROM). Procedure data is collected on a specific form that is filled out in the operating room and sent to the register, while PROM data is collected electronically. In 2019 almost 17,000 primary knee procedures were performed in Sweden (25).

Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR)

At the instigation of the Arthroplasty Society of Australia, the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) was established in 1999 and coverage of all states and territories was completed in 2002 (26). Funding is by grant from the Australian Government's Department of Health to the Australian Orthopaedic Association. Data provision is voluntary, but widespread participation by surgeons and hospitals has been achieved. Government legislation describes the AOANJRR as a Federal Quality Assurance Activity. The AOANJRR collects data on all types of joint replacement and has records of over 900,000 knee replacement procedures up until 2021 (27). The registry collects patient and prosthesis information recorded in the operating theatre using a paper-based system posted to the registry. PROM data collection commenced in 2017 and this is captured electronically via the custom RAPID (Real-time Automated Platform for Integrated Data capture) program, created for the Registry. The AOA contracts the South Australian Health and Medical Research Institute (SAHMRI) to provide data management and statistical analysis.

Kaiser Permanente Joint Replacement Registry (KPJRR)

The Kaiser Permanente Total Joint Replacement Registry (KPJRR) was created in 2001 by the Kaiser Permanente Integrated Health Care System as a part of its National Implant Registries (now termed Medical Device Surveillance and Assessment) (28). The KPJRR monitors arthroplasty procedures for over 12 million members of this US integrated healthcare system in 8 regions of the United States (Northern and Southern California, Georgia, Hawaii, Colorado, Mid-Atlantic states, Oregon and Washington). The population covered by Kaiser Permanente has been shown to be representative, both demographically and socioeconomically, of the regions covered (29,30). The KPJRR is not to be confused with the American Joint Replacement Registry, which is owned by the American Academy of Orthopaedic Surgeons and collects data from a selective sample of hospitals and ambulatory care centres that elect to contribute. The KPJRR was developed as a quality assurance mechanism to track total joint procedures, identify patients at risk of complications and revisions, assess implant performance and identify clinical best practices (31). The KP registry currently has records of over 400,000 total joint replacement procedures to date. Surgeon participation is voluntary, with an over 95% participation rate (32). This registry uses standardized but specific Electronic Health Record (EHR) documentation at the point of care to capture patient information, surgical techniques, implant characteristics and outcomes.

Data completeness, accuracy, and "missingness"

SKAR

Data validation of the SKAR has been carried out in several ways. A postal survey of patients was carried out in 1999 (33), comparison to the National Patient Register occurs yearly and ad hoc random assessments of hospital data were performed between

2010 and 2016 (25). Completeness of inclusion by the registry evaluated through linkage to the National Patient Register revealed the capture rate was assessed at 97.1% of all admissions in 2020 (25). From random hospital data checking only one of 957 procedures was missing (25).

With regard to data accuracy, when the 'essential" data (which includes date, hospital, laterality and diagnosis) was reviewed with the random hospital audits, only 15 errors in the 3832 data points were found. In addition to the usual data form, the operation record and discharge summary are sent to the register for revision procedures. All data are checked by the register staff on data entry (25).

The SKAR has little missing data, particularly for the fields studied in the scope of this manuscript. For instance, regarding the data set for Papers III and IV, there were only 28 of 5613 revisions where the diagnosis was unknown (0.5%). Within all attributes of the prostheses studied there was never more than 0.5% categorised as "missing". The proportion of missing data was higher for assessments of ASA and BMI, because the commencement of data collection occurred in 2009 which is midway into the study period. This should, more correctly, be considered as "incomplete" rather than missing data.

AOANJRR

Data collected by the AOANJRR are validated against State and Territory Government Health Department data. Validation is by a sequential multi-level matching process. Where data discrepancy exists, further information or clarity is obtained from the hospital co-ordinators by request. The initial capture rate of hip and knee replacement data in 2020 was reported as 97.3% but increased to almost full coverage (estimated 99.4%) after the verification and cross-checking process (27).

The AOANJRR collects data including patient information, implant details, surgical techniques, revision and reasons for revision. Where more than one reason for revision is recorded, a hierarchical system is used to determine the most important (see Table 1). Mortality information is added twice yearly by matching against the National Death Index. There is little net migration among the joint replacement population. The AOANJRR also has minimal loss to follow-up and minimal missing data (27).

I performed an internal (but unpublished) audit of AOANJRR revision data accuracy in 2019-2020, where 26 surgeons from the Arthroplasty Society of Australia were asked to correlate their own operation records with data held by the registry. Of the 4329 revision procedures matched, an incorrect revision diagnosis was recorded in 69

(1.6%). In 31 of these cases the registry had recorded a diagnosis of infection when the surgeon had an alternate diagnosis, or vice-versa. These latter differences were thought to arise due to the completion of the registry record sheet in the operating theatre, when later a true diagnosis relating to infection may be revealed on the basis of microbiological results. There were also another 5% of revision procedures where the surgeon had noted multiple diagnoses, and while all diagnoses are recorded, due to the diagnosis hierarchy system, the surgeon's main reason for revision was different from the registry records. The main diagnostic differences occurred with 2 groups, firstly loosening/lysis/wear/instability, and secondly pain/patella pain.

Missing data from the AOANJRR for the categories studied is minimal. Although there were some unknown prosthesis details, such as prosthesis constraint, these were always less than 0.05%, which reflects the vigour the data managers pursue illegible, illogical or incomplete forms by asking for clarity from the submitting hospitals theatre liaisons. Like the Swedish register, ASA and BMI data collection in Australia began during the data inclusion period, and so there were limited data available for analysis of these variables.

KPJRR

Data captured by the KPJRR specific joint replacement forms are validated against data from the EHR, as well as from the claims database using International Classification of Disease (ICD) codes (28). A further validation process involving patient record review is carried out for all complications and outcomes according to the Agency for Healthcare Research and Quality guidelines. Cessation of health plan membership from the Membership Information database and mortality data from State death records are used to censor data. Quarterly reports to participating hospitals can identify missing procedures, that are then added retrospectively. These made up 3% of procedures in 2010. Although participation rate of surgeons is 95%, patients, demographics and revision details of those initially not captured are included secondarily from the EHR database (31).

The registry has over 95% capture of the patients in the healthcare system, less than 8% loss to follow-up over 17 years, and minimal missing data (31).

For the prosthesis details studied in Papers III and IV the KPJRR had some categories with missing data. This was as high as 5.6% for polyethylene type, but other variables were less than 3% and down to 0.8% for fixation, with most of the unknown data arising from early years in the study period when registry methods and both surgeon and hospital acceptance were still developing.

Aim

To gain an international perspective of knee replacement revision, to inform of best-practice and improve TKR outcomes.

Specific aims

Paper I

To document the changing procedure volume and incidence of primary and revision knee replacement over a 15-year period (2003–2017)

Paper II

To determine variations and trends in reasons for knee replacement revision over the same 15-year period using equivalent diagnosis groups

Paper III

1) To document regional and temporal variation in primary TKR practice between 2003 and 2019
2) To determine the influence of 9 patient and prosthetic factors on the risk of revision at 5, 10 and 15 years using a meta-analytic technique

Paper IV

1) To analyse patient and prosthesis factors associated with 8 common reasons for TKR revision
2) (To describe the procedures used for those revisions)

Paper V

1) To document the frequency of TKR revised for instability, and the patient and prosthesis factors associated with this revision diagnosis
2) To describe the procedures used to treat TKR instability
3) To compare the outcome of these surgical strategies by calculating the cumulative rate of 2nd revision

Patients and methods

Data inclusions

Papers I and II

For these 2 papers data was obtained from the 3 registries for the time period Jan 1, 2003, until December 31, 2017. These papers were intended to study the clinical workload or volume of all knee replacement procedures for each year recorded by each registry. Therefore, all knee replacement procedures were included, so that this was inclusive of all primary procedures (total knee replacement, uni-compartmental replacement and patello-femoral replacement) and all revision knee replacement, regardless of whether the primary was a partial knee replacement or a total replacement or if it was the first or any subsequent procedure in chronology. Where knee replacements were bilateral both knees were included separately.

There were 1,133,079 KR included in the analysis for Paper I. The SKAR contributed 199,020 KR (186,473 primary and 12,547 revision procedures), there were 732,521 KR from the AOANJRR (674,045 primary and 58,476 revision procedures), and 201,350 KR from the KPJRR 188,538 primary and 12,812 revision procedures).

Paper II included 78,151 revision knee replacement procedures. As mentioned, the intention was to look at all knee replacement revisions done in each registry each year. The SKAR contributed 12,612 revision procedures, the AOANJRR 53,853 revisions, and the KPJRR 11,686 revisions. The numbers of revisions included here are marginally different from those included in Paper I, as all needed to have a clear reason for revision (no missing data regarding revision diagnosis), and some procedures (such as amputation, or removal of cement loose fragments) were excluded as these did not fit the strict criteria of a revision procedure used in this paper.

Papers III and IV

The study population for these 2 papers was slightly different from the first 2. The procedures included primary TKR this time (excluding partial and revision knee replacement), and only those for the specific diagnosis of osteoarthritis. The time span of data inclusion was from January 1, 2003, again, but this time until December 31, 2019. These criteria were used to keep the data more complete, to limit confounding by procedure type or initial indication, but also to study only those from this group that were revised, excluding revisions of primary procedures performed prior to this start date, and thereby keeping the findings contemporaneous.

During this inclusion period there were 1,072,924 primary TKR for OA that were studied (188,290 from the SKAR, 663,982 from the AOANJRR, and 220,652 from the KPJRR). Of these 5,613 from Sweden were revised, 24,931 from Australia and 6,082 from the KPJRR, (making a total of 36,626 revised), and these form the basis of the analysis comparing the patient and prosthesis attributes and the reason for the revision procedure. Only the first revisions were analysed, excluding second or subsequent procedures.

Paper V

Following on from the findings of Papers II and IV, it was noticed that revision for instability was increasing, and there was not an immediately obvious reason why this was occurring. This prompted more detailed study. The study population for Paper V was drawn from just the AOANJRR. The data period was from the beginning of registry recording of arthroplasty in Australia (September 1999) until December 31, 2019. Once again, the study was limited to TKR for OA. The data source was restricted to the single registry on this occasion as it was intended to perform, as already mentioned a detailed "in depth" analysis using more difficult to obtain data (such as changes of polyethylene insert thickness between the primary and revision procedure or differences in polyethylene conformity) and also to analyse the second revisions of those firstly revised for instability. Another advantage of using this single data source was there was greater practice variation in prosthesis use in Australia compared to Sweden or the KPJRR, (particularly regarding prosthesis constraint, method of fixation, bearing mobility, polyethylene type and patella component use) so that the influence of variability of these factors could be assessed more reliably.

During this time there were 699,283 primary TKAs for OA recorded and 27,580 of these had undergone a 1st revision. Instability was the reason for revision in 2605 (9.4%), and these form the main study population. Further analysis was carried out for the 385 that had undergone a 2nd revision.

Methods

Paper I

This was mostly a descriptive paper with little in the way of statistical analysis. Comparisons were made between registries for yearly procedure volumes and incidence per 100,000 adult population (defined as over 20 years of age). An age stratified sub-analysis was also carried out dividing patients into ages <65 years and 65 years and over. Sex and mean ages were also documented by registry for both primary and revision knee replacement. Annual percentage change in both primary and revision procedure volume for each 5-year period was calculated for each registry, and the mean for each period determined, using a previously described method (34), in order to summarize trends and allow comparisons.

Paper II

A revision knee replacement was defined as a further procedure of a previous replacement where 1 or more components were added, removed or exchanged, and this was irrespective of whether it was the first or subsequent revision procedure for that knee. To assess the "revision burden" we needed to capture *all* revisions, so revisions of any type of previous knee replacement were included, and this therefore included revisions of uni-compartmental knee replacements, total knee replacements and further revisions of previously revised knee replacements.

Equivalent diagnosis groups (EDGs) were created by harmonizing diagnosis categories used by each registry which recorded the original surgeon-nominated reason for revision. The EDGs were based on the diagnostic categories of the SKAR. The "harmonized" category was created by simple addition of the appropriate diagnostic groups from each registry. Only 1 revision diagnosis was permitted for each revision, and if more than 1 was listed a published diagnosis hierarchy was used to determine the most important of these. The diagnosis hierarchy used by the AOANJRR is shown below, and the EDG table follows. (Tables 1 and 2).

Table 1. Diagnosis Hierarchy used by the AOANJRR for determining most important knee replacement revision reason.

RANK	DIAGNOSIS	CATEGORY
1	Tumour	Dominant diagnosis independent of prosthesis/surgery
2	Infection	
3	Incorrect Side	Surgical procedure
4	Incorrect Sizing	
5	Malalignment	
6	Metal Related Pathology	Reaction to prosthesis
7	Loosening	
8	Lysis	
9	Wear Knee Insert	Wear and implant breakage
10	Wear Tibial Tray	
11	Wear Femoral	
12	Wear Patella	
13	Implant Breakage Femoral	
14	Implant Breakage Knee Insert	
15	Implant Breakage Tibial Tray	
16	Implant Breakage Patella	
17	Bearing Dislocation	Stability of prosthesis/knee
18	Patellar Dislocation	
19	Prosthesis Dislocation	
20	Instability	
21	Patellar Maltracking	
22	Fracture (Femur/Tibia/Patella/Periprosthetic)	Fracture of bone
23	Progression of Disease	Progression of disease on non-operated part of joint
24	Patellar Erosion	
25	Synovitis	New diseases occurring in association with joint replacement
26	Arthrofibrosis	
27	Osteonecrosis/AVN	
28	Heterotopic Bone	
29	Patellofemoral Pain	Pain
30	Pain	
31	Other	Remaining diagnoses

Table 2. The Equivalent Diagnosis Groups (EDGs) used to "harmonize" revision diagnoses to allow cross-registry comparison.

HARMONIZED DIAGNOSES	SWEDISH DIAGNOSES	AUSTRALIAN DIAGNOSES	KP DIAGNOSES
1) LOOSENING	Loosening	Loosening	Aseptic Loosening Ingrowth Failure
2) WEAR	Implant Wear	Wear Tibial Insert Lysis Metal Related Pathology Wear Tibia Wear Patella Wear Femur	Poly Liner Wear Osteolysis Implant Wear
3) INSTABILITY	Instability Dislocated Polyethylene	Instability Bearing Dislocation Prothesis Dislocation	Instability
4) INFECTION	Infection	Infection	Infection Wound Drainage
5) PATELLA CAUSES	Patella Causes	Patellofemoral Pain Patella Erosion Patella Mal-tracking	Patellofemoral Joint Malfunction Failed Extensor Mechanism Patella Causes
6) PAIN	Pain	Pain	Pain
7) PROGRESSION OF DISEASE	Progress of Disease	Progression of Disease	Osteoarthritis Inflammatory Arthritis Old Rheumatoid Post Traumatic Arthritis
8) FRACTURE	Bone Fracture	Fracture	Fracture
9) IMPLANT BREAKAGE	Implant Fracture	Implant Breakage Tibial Insert Implant Breakage Tibia Implant Breakage Patella Implant Breakage Femur	Component Fracture/Breakage
10) STIFFNESS	Stiffness	Arthrofibrosis	Arthrofibrosis/Stiffness
11) OTHER	Other Tumour Surgical Error Missing	Malalignment Incorrect Sizing Synovitis Osteonecrosis Tumour Heterotopic Bone Incorrect Side Other	Failed TKR Failed UKA Failed Unispacer AVN Synovial Impingement Hematoma Other
12) EXCLUDED (NON-REVISION PROCEDURES)	Gangrene Cement/Free Body		Wound Dehiscence Failed ORIF

The 10 most common reasons for revision were chosen for further analysis and discussion. These were loosening, wear, instability, infection, patella causes, pain, progression of disease, fracture, implant breakage, stiffness and the remainder classified as "other".

The annual proportions for each revision reason were calculated and trends over time were shown graphically. For revision for infection further comparisons were made after calculating the incidence per 100,000 adult population to determine if the rise in proportion of this revision reason was a "true" increase, and not simply due to a fall in other reasons for revision, such as loosening and wear.

Paper III

Characteristics of patients and their TKR prostheses formed the basis of study for this paper. Patient factors included age, sex, ASA score and BMI. Unfortunately, collection of ASA and BMI data from Sweden and Australia began at differing times during the period of data collection for this study, so that these factors only permitted limited analysis. Prosthesis factors included constraint, fixation method, bearing mobility, polyethylene type and patella component use. Variations between registries and trends over time were shown graphically for these characteristics.

Meta-analyses were carried out to give summary estimates for each factor's effect on revision rates. For age, ASA score, and BMI assessments these categories were dichotomised into age <65 years and ≥ 65 years, ASA 1 &2 and ASA 3 or more (to compare those with no or little systemic disease to those with severe disease), and BMI <30 and BMI 30 and above (to compare those without obesity to those with obesity). Analysis of constraint compared the 2 most common types, minimally stabilized and posterior stabilized, as the use of the more constrained prostheses (fully stabilized and hinged) made up less than 1% of primary TKR procedures. The 2 most common forms of fixation (cemented and cementless) were selected as hybrid fixation was rarely recorded in Sweden or the KPJRR. Analysis of polyethylene types compared UHMWPE (or "standard" polyethylene) to a combined group of XLPE and XLPE with antioxidant. Comparisons of the remaining factors (sex, bearing mobility and patella component use) were more straight-forward as there were only 2 alternatives for these.

Using time-to-event statistics for analysis of the effect of these factors on revision rates can be difficult as the hazard ratios can change with time. To ensure equality, hazard ratios calculated from Cox models were determined at fixed time point 5, 10 and 15 years.

Paper IV

As for the Paper III, the same selection of patient and prosthesis factors were used again to study TKR revisions, using the same defined categories within each factor. In this study not only were the characteristics of the revised TKR compared to primary TKR, but further analyses were carried out for the 8 most common revision diagnoses. These were arthrofibrosis, fracture, infection, instability, loosening, pain, patella reasons and wear. The EDGs from Paper II were used to allow cross-registry comparisons. Unfortunately, incomplete data for ASA score and BMI led to small numbers when broken down for the individual revision diagnoses and this prevented further analysis for these 2 factors.

Again, in a similar method to Paper III, categories were dichotomized, or the two most common alternatives chosen to allow the number revised for each specific reason for revision to be calculated from the number of primary TKR with that particular attribute. This was done for each registry independently. For each attribute the number revised was compared to the number not revised with that attribute (A for example) to calculate the odds of revision with attribute A. The compliment of, or alternative to, attribute A was then used for similar calculations (i.e., the number revised compared to the number not revised). The odds of revision for the two alternatives were then compared to give rise to odds ratios for each of the 7 patient and prosthesis factors for the 8 common revision diagnoses, which were then compared across the 3 registries.

Where agreement was found in direction of the factor/reason analyses from all 3 registries, and the confidence intervals of the odds ratios did not contain 1 (i.e., were statistically significant), these were chosen for further analysis to determine a "summary" effect by meta-analysis, again in a similar technique to paper III.

Additionally, the procedures used for the revisions were classified and compared, but due to word limits and content flow these further analyses were not included in the submitted manuscript. I will include it here as "Additional Data". Between registry comparisons were made for all revision procedures, and for revisions for each of the 8 common reasons for revision.

Paper V

"Instability" for the purpose of this study was defined as the combination of the recorded diagnoses of instability, bearing dislocation and prosthesis dislocation, as the latter two are considered to be more extreme versions of instability (35,36). Revision was the main outcome studied, so the overall CPR was calculated for revisions for instability according to this definition, and sub-analyses were performed for sex, age, ASA score and BMI. In addition, prosthesis characteristics of insert thickness and mobility, fixation, polyethylene type and prosthesis constraint were also analysed. Additional complexity involved considering the "contour" or conformity of the minimally stabilized insert designs. These were classified as cruciate retaining, anterior stabilized and deep dished (which are sometimes also referred to as ultra-conforming).

Revision procedures were studied, and these ranged from a simple tibial insert exchange to complex revisions of both the femoral and tibial components, sometimes with stems, sleeves and augments. Revision procedures were classified according to component(s) revised. Where the insert was changed, the increase in thickness was documented, as well as changes in insert contour for the MS group.

When the outcome of the revision procedure was studied, we assessed these further revisions and used the term "cumulative percent 2nd revision" (CP2R). For these analyses, we included comparison of minor and major revision types, as well as comparisons of prosthesis characteristics such as constraint, insert thickness and conformity, but on this occasion, related to the prosthesis used in the revision procedure rather than the primary.

Statistics

Paper I

Incidence: Incidence was calculated as the number of procedures per 100,000 population over age 20 years for each registry. The population statistics were obtained from Statistics Sweden, the Australian Bureau of Statistics, and from the yearly active membership numbers of the Kaiser Permanente integrated health care consortium.

Mean percentage change of procedure volume: Annual change in procedure volume averaged over each 5-year time period.

Paper II

Incidence: See definition for Paper I.

Paper III

Kaplan-Meier estimates of survivorship: This is the calculation of the proportion of subjects who have not yet experienced a defined event (for this study, revision of the prosthesis or death) versus time. The Kaplan-Meier method considers subjects whose ultimate survival time is unknown, by a phenomenon called 'censoring'. The survival estimate at each time is accompanied by a confidence interval based on the method of Greenwood.

Cumulative percent revision (CPR): The cumulative percent revision is the proportion revised by a certain time, rather than the proportion not being revised ('surviving'). This is defined as 100 x [1-S(t)] where S(t) is the survivorship probability estimated by the Kaplan-Meier method. The cumulative percent revision gives the percent of procedures revised up until time t and allows for right censoring due to death or closure of the database for analysis.

Cox hazard ratio. The Cox model produces hazard ratios that allow comparisons between groups of the rate of the event of interest. In this case the event is revision (accounting also for death). The main assumption of a Cox model is that the ratio of hazards between groups that are compared do not vary over time. This is referred to as the 'proportional hazards assumption'. However, if the hazard ratio is not proportional over the entire time of observation, then a time varying model is used, where a set algorithm is used that iteratively chooses time points until the assumption of proportional hazards is met for each time period. As changes in hazard with time can make it difficult to compare registries, for this study the time varying method was not appropriate, and a model using hazards calculated at fixed times of 5, 10 and 15 years was chosen.

Meta-analysis: A statistical method to quantitatively summarize effect estimates from independent studies of a mutual outcome into a single effect estimate.

Generic inverse-variance method: The inverse-variance method is a statistical method used for meta-analysis involving time-to-event data, to amalgamate effect estimates, where the weight given to each study is the inverse of the variance of the effect estimate for the study (i.e., 1 over the square of its standard error).

Paper IV

Mean time to revision: Mean times to revision, which is the average time from primary surgery until revision, with standard deviations, were calculated as this metric in commonly used when discussing revision reasons. (However, as more than half of revisions occur early (within 2 years) the time-occurrence of revision is skewed to the left. For this reason, median time to revision may in fact be a more meaningful statistic, but as this is not the convention, it was not used here.)

Odds ratios: The likelihood of an event happening compared to the likelihood of not happening with exposure A, as a ratio of the likelihood of the same event happening compared to not happening with an alternate exposure that is not A. In this study, the odds of revision for a specific reason (for instance loosening) were calculated compared to the odds of not being revised for that reason when categorical patient or prosthesis factors were present (for instance cementless fixation), and the ratio of this was determined and compared to the odds of revision in the presence of the competing factor (in this example cement fixation).

Meta-analysis: See definition for Paper III.

Mantel-Haenszel method: The Mantel-Haenszel method is another statistical method used in meta-analysis to provide a summary statistic where dichotomous outcomes are being analysed. Of the methods used for dichotomous outcomes, this method is thought more reliable when data are sparse, and event numbers low.

Paper V

Kaplan-Meier estimates of survivorship: See definition for Paper III.

Cumulative percent revision (CPR): See definition for Paper III.

Cox proportional hazards: See also definition for Paper III. In this instance the time varying model was used, where the time points are selected based on where the greatest change in hazard occurs between the two comparison groups, weighted by the number of events in that time period.

Cumulative percent 2nd revision (CP2R): Calculated as the cumulative rate of further revision of the 1st revision of a primary procedure. (In this instance, the cumulative rate of further revision of the 1st revision (performed for instability) of primary TKR for OA).

Ethical considerations

Analyses such as these involves research subjects, which in this instance are patients having knee replacement surgery. For this reason, the appropriateness of data collection and ethical considerations of how these data are collected and used needs reflection.

Data regarding patients, prostheses and procedures are enrolled by the various registries. In Sweden it is assumed that participants do not object to register data collection and register-based research. This is part of an informal contract between the individual and the government, with the awareness that health care is provided almost free of charge, and that registers are used to monitor health care quality (37). The KP registry has data collection as a condition of health care coverage, and also uses this data to monitor quality of health care. In Australia consent to be included in the registry is done on an individual opt out basis, after patients are informed of data collection at the time of consenting to their operative procedure. An opt-out approach is acceptable for registry data, as the collection of this poses little or no risk to the patient, it would be virtually impossible to collect consent from each person enrolled, and the public benefits of collecting the data are large. Additionally, collecting individual consent would not only be expensive but also reduce the validity of the data, and in certain cases, bias against those in whom obtaining consent would be difficult (due to literacy or language difficulties, for instance) (37). On receiving information regarding protections of individual privacy, and as arthroplasty data is unlikely to be seen as "sensitive" personal information, very few opt out. In the AOANJRR there have been 46 opt-out in a total of almost 2 million procedures.

While in Sweden collection of patient information by registers is commonplace, in Australia and the USA it is not. In Australia the activities of the AOANJRR are declared a Quality Assurance Activity under section 124X of the Health Insurance Act, 1973 by the Commonwealth of Australia, and as such, ethical approval for individual analyses is not required, if the studies are conducted in accordance with ethical principles of research (Helsinki Declaration II). Ethical approvals for registry analyses within the Kaiser Permanente database in the US are given on a yearly basis from the governing body, and similarly in Sweden for analyses within the SKAR. These approvals are for the Kaiser Permanente Joint Replacement Registry approval (#5488) granted Nov 15, 2018, with the latest approval dated 08/09/2021, and for Sweden ethics approval for use of data from the SKAR for Registry studies is granted by the Ethics Board of Lund University (LU20-02).

As a further safeguard to protect individual privacy, for the data used in these studies, no information that would identify patients, surgeons or hospitals was provided. Data was anonymized and aggregated to mitigate these identification issues. Data security was maintained by installing firewalls, password protection for transferred data files and for the computer on which it is stored. A data sharing agreement for the purpose of these studies initiated on 20th Nov 2018, and further refreshed on 10th Dec 2020 by the directors of the SKAR, AOANJRR and KPJRR.

Conflicts

There were no conflicts of interest.

Sponsorship/Payments

Almost all aspects of this PhD were self-funded with no external sponsorship, apart from the supplement from Lund University to aid with completion of the thesis.

Results

Paper I

Procedure numbers for primary knee replacement (KR) increased in all registries over the study period (from 8,832 in 2003 to 14,964 in 2017 in Sweden, from 26,008 to 59,002 in Australia and from 4,271 to 20,672 in the KPJRR). The increase was 69% in Sweden, over double in Australia (127%) and almost four times the starting number in the KPJRR (384%). The proportion of primary TKR was consistent at 96% in the KPJRR but rose from 83% in both Sweden and Australia to 92% and 93% respectively, while the proportion of UKA fell in these 2 registries. Patello-femoral replacement made up <1% in all registries. Revision knee replacement also increased (from 596 in Sweden to 945, from 2,314 in Australia to 4,791, and from 274 in the KPJRR to 1,309) giving proportionate increases of 59% in Sweden, 107% in Australia and 378% in the KPJRR.

As population differences can influence procedure numbers, perhaps a more meaningful measure is incidence. The incidence (per 100,000 population) of primary KR increased in Sweden from 93 to 149 and revision KR incidence increased from 6.6 to 9.4, while in Australia primary KR incidence rose from 132 to 240 and revision KR incidence increased from 11.7 to 19.5 and for the KPJRR cohort primary KR incidence (per 100,000 insured) increased from 52 to 187 and revision KR from 3.3 to 11.8 (Figures 1 & 2). This corresponded to an increased incidence of 60% in Sweden, 82% in Australia and 260% in the KPJRR for primary knee replacement and by 42% in Sweden, 67% in Australia and 258% in the KPJRR for revision surgery. In both Sweden and Australia, the increase in revision incidence was less than the increase in primary surgery.

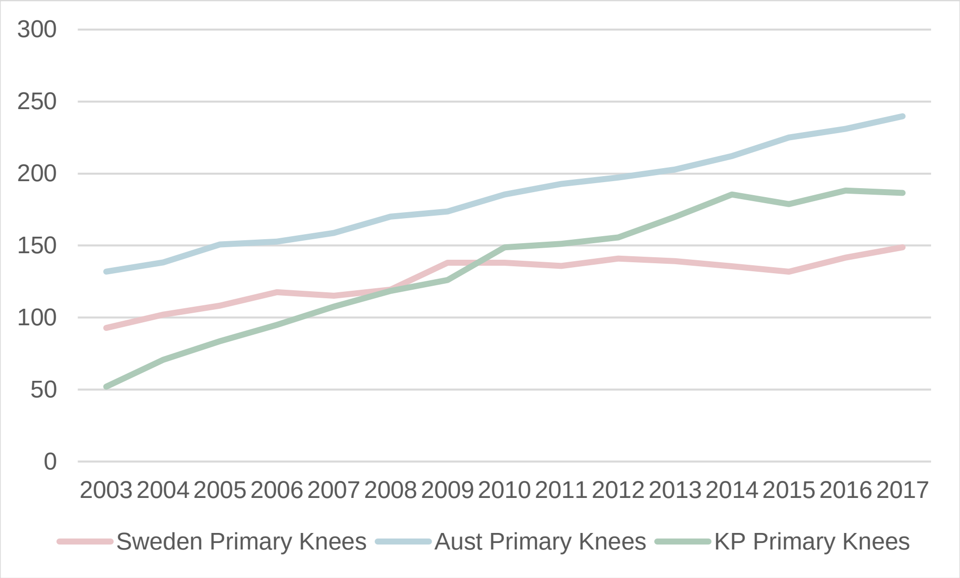


Figure 1. Yearly incidence of primary knee replacement per 100,000 population recorded by the SKAR, AOANJRR and the KPJRR from 2003 to 2017

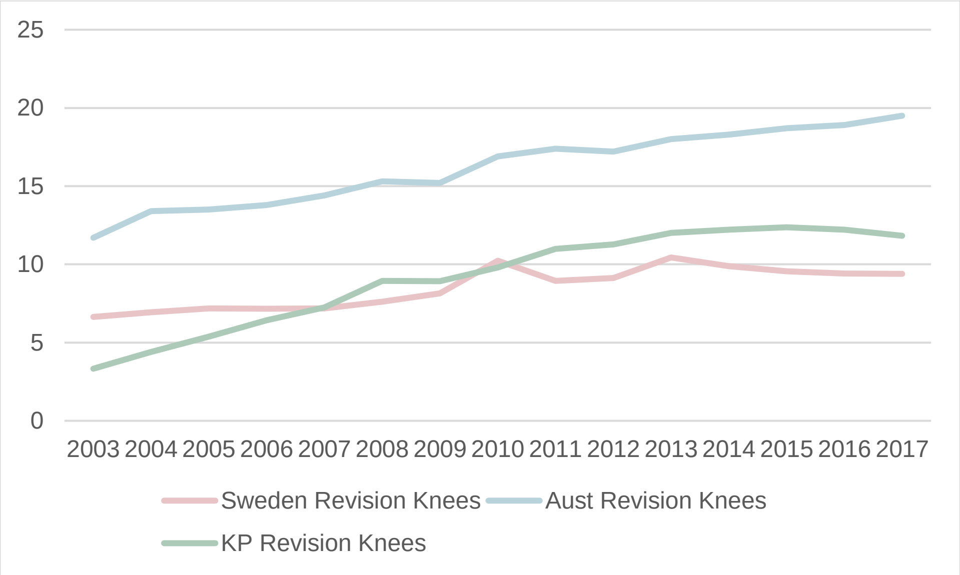


Figure 2. Yearly incidence of revision knee replacement per 100,000 population recorded by the SKAR, AOANJRR and the KPJRR from 2003 to 2017.

The population pyramid may also vary between countries, so an analysis by age group is also important. When stratified by age <65 and ≥65 years, the annual incidence per 100,000 population for the younger group remained less than 90 for primary KR and less than 8 for revision KR in all 3 registries. While the incidence/100,000 in the younger age group remained low, the proportional change over the 15 years in this group for primary KR for Sweden, Australia and the KPJRR was 76%, 141% and 276% respectively, while it was 35%, 58% and 177% for the age ≥65 years group. Revision KR incidence also increased (for the age <65 years group by 39%, 85% and 277%, and for the age ≥65 years group by 26%, 32% and 171% in Sweden, Australia and the KPJRR respectively).

When the annual percentage change in procedure volume was studied, there were the largest increases at the beginning of the study period and the amount of increase reduced over time. The mean change for both primary and revision KR for each of the 3 5-year periods all showed a deceleration of the increase. The only exception was an increase in revision in Sweden between the periods 2003-2007 to 2008-2012 (Figure 3).

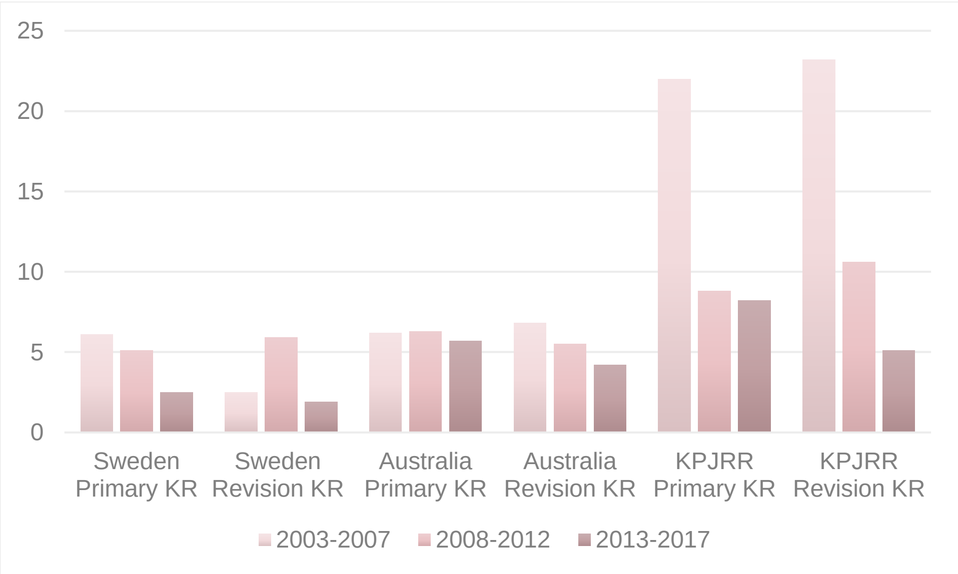


Figure 3. Mean 5-yearly percentage increases in procedure volume in SKAR, AOANJRR and the KPJRR

Throughout the study the demographic details didn't change greatly. The mean age of primary and revision KR patients remained stable in all countries. The proportion of females undergoing primary KR decreased (by 5%, 2% and 4% in Sweden, Australia and KPJRR), while the proportion of females undergoing revision KR was lower than that for primary surgery in all countries and showed less change with time.

Infection was the most frequent reason for TKR revision in the SKAR and the KPJRR, while loosening was most common in the AOANJRR. Instability, patella causes, progression of disease, wear and pain showed variable proportions across the registries (Figure 4).

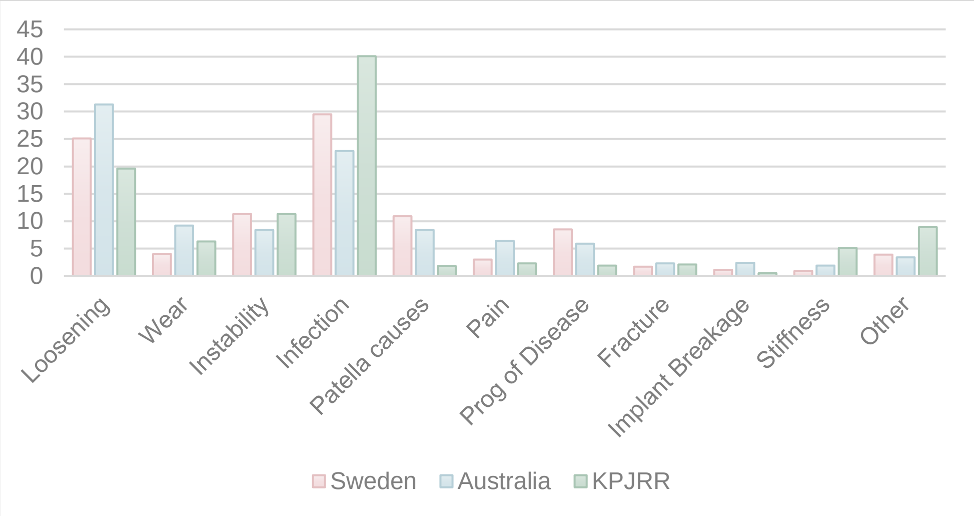


Figure 4. Overall revision diagnoses shown as a proportion for each registry.

There was an increase in the proportion of revisions for infection through the study period seen in all registries rising from 20%, 16% and 22% in the SKAR, AOANJRR and KPJRR in 2003 to 35%, 30% and 43% in 2017 respectively. To determine if this was a true rise, not just a proportionate increase, the yearly incidence of revision procedures for infection was calculated. This also increased in all registries (Figure 5).

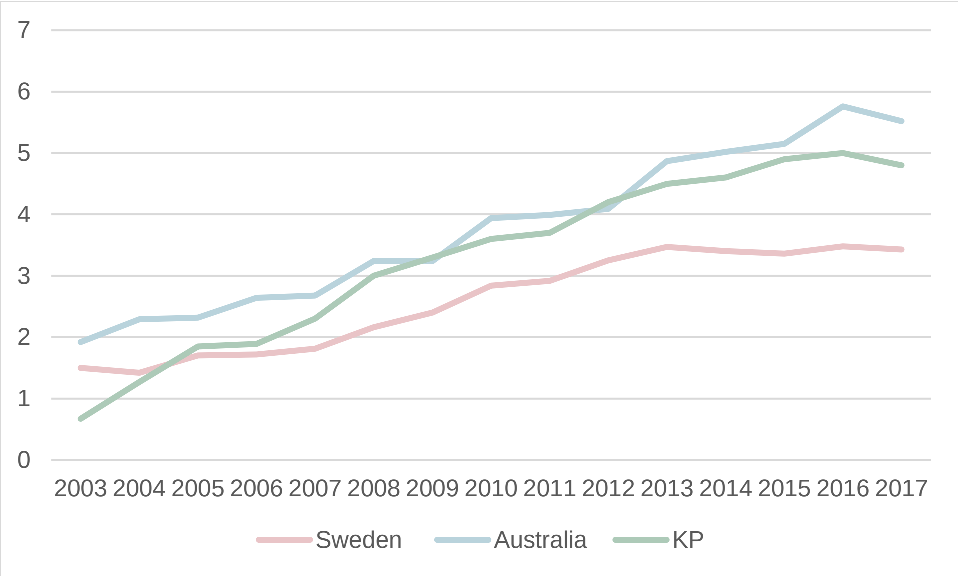
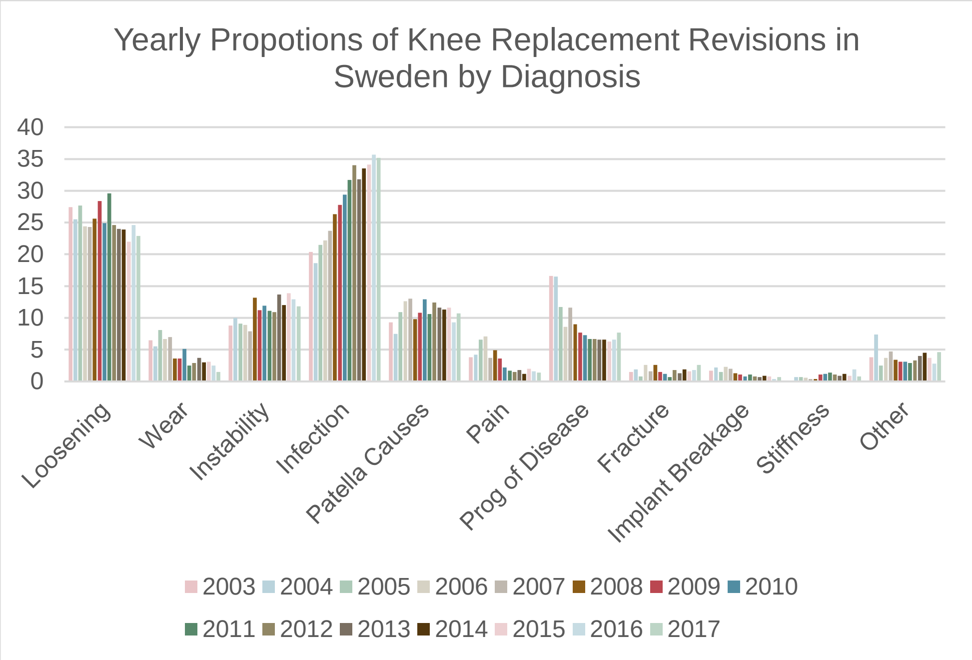
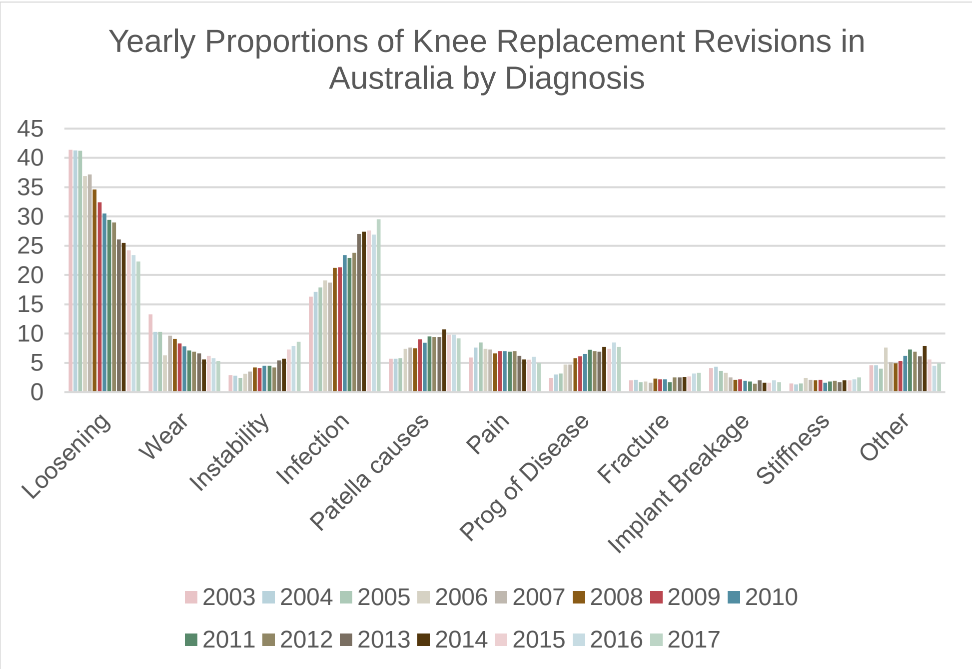


Figure 5. The yearly incidence of revision knee replacement for infection per 100,000 population for the SKAR, AOANJRR and KPJRR.

Revision for loosening fell from 41% from 2003 to 22% in 2017 in the AOANJRR but a smaller decline was seen in the SKAR (27% to 23%), while the proportion in the KPJRR fell from 27% in 2003 to 14% 2008 but then rose and remained around 20% from 2011 to 2017. There was a universal decrease in revisions for wear with the proportions declining from 6.5% to 1.5% in Sweden, 13% to 5.3% in Australia and 21% to 4.5% in the KPJRR. The revision diagnosis of instability showed a trend for increase in Sweden and Australia but fluctuated in the KPJRR. Revisions for patella reasons made up a higher proportion of revisions in Sweden than Australia, showing a modest increase in these 2 countries but this diagnosis was infrequent in the KPJRR. Stiffness contributed proportionally more as a revision diagnosis in the KPJRR where this reason showed a small increase with time. There was a general tendency for fewer revisions for pain throughout all registries toward the end of the time period. Progression of disease as a reason for revision decreased over time in both Sweden and the KPJRR while it increased in Australia. Fracture and implant breakage were uncommon causes of revision in all registries (Figure 6).


Yearly Propotions of Knee Replacement Revisions in Sweden by Diagnosis
40
35
30
25
20
15
10
5
0
Loosening
Wear
Instability
Infection
Patella Causes
Pain
Prog of Disease
Fracture
Implant Breakage
Stiffness
Other
2003 2004 2005 2006 2007 2008 2009 2010
2011 2012 2013 2014 2015 2016 2017


Yearly Proportions of Knee Replacement Revisions in Australia by Diagnosis
45
40
35
30
25
20
15
10
5
0
Loosening
Wear
Instability
Infection
Patella causes
Pain
Prog of Disease
Fracture
Implant Breakage
Stiffness
Other
2003 2004 2005 2006 2007 2008 2009 2010
2011 2012 2013 2014 2015 2016 2017

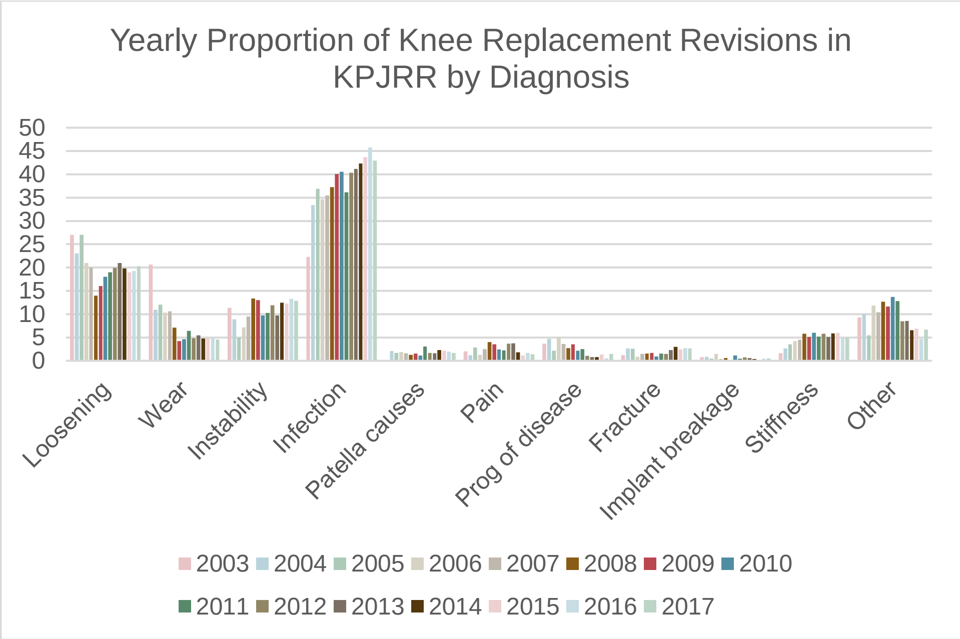


Figure 6. The yearly proportions of knee replacement revision recorded in the SKAR, the AOANJRR and the KPJRR, respectively.

Paper III

The discussion section of Paper II suggested there may be some practice variation across the registries and determining if this was true was the main aim of this study. While age and sex of TKR patients were similar, there were higher proportions of TKR patients in Sweden with no or mild systemic disease and without obesity. Prosthesis factors showed greater variation. Minimally stabilized prostheses were used in 93% of TKR in Sweden, 73% in Australia, and in only 30% in the KPJRR. Surgeons in the KPJRR preferred PS prostheses in 67% of TKR. Cement fixation of both components was favored in 96% and 94% of procedures in the SKAR and KPJRR, but in only 59% in the AOANJRR. The remaining cases in Australia were hybrid (tibial component cemented) (22%) or cementless (18%). All registries had over 80% fixed bearing use. Patella resurfacing showed greatest variation; 4% in the SKAR, 98% in the KPJRR, with 57% in the AOANJRR. UHMWPE was used in the majority of procedures in all registries.

Time-related trends

As seen with Paper I, in all registries the mean age of TKR recipients showed little change, while there was a small reduction in the percentage of females with time.

The major difference between Sweden and the KPJRR for the use of MS TKR persisted without change, while the proportion in Australia varied from 67% to 83%. The use of PS TKR varied between 57% and 70% in the KPJRR, varied from 17% to 32% in Australia, while in Sweden PS use remained below 9%. Cement fixation was consistently used in >93% and >88% of TKR in the SKAR and the KPJRR respectively, while increasing in the AOANJRR from 44% to 68%.

Mobile bearing prostheses were not common in Sweden (used in a maximum of 2% of procedures), while a decline in use with time was observed in both Australia and the KPJRR. Patella resurfacing tendency remained low in Sweden (11% falling to 2%), while in the KPJRR patella component use was consistently high (over 97%). In Australia, patella resurfacing rose from 44% to 73%. There was a trend for increased use of XLPE in all registries.

Meta-analysis of patient and prosthesis factors

Meta-analyses showed a higher revision risk associated with age <65 years, with increasing summary hazard ratios over time (HR=1.6 at 5 years, HR=2.0 at 10 years and HR=2.2 at 15 years). At 5 years males showed a higher risk of revision compared to females (HR=1.2), as did patients with severe systemic disease compared to patients with no or mild systemic disease (HR=1.3), and obese patients when compared to non-obese (HR=1.2).

Prosthesis factor meta-analyses showed a higher risk of revision for PS TKR compared to MS (Figures 7 to 9). Cementless fixation gave a higher risk of revision compared to cemented fixation but no risk difference at 10 years (Figures 10 to 12). Mobile bearing TKR had a higher risk of revision compared to fixed bearing at 5 years but at 10 and 15 years there was no observed difference (Figures 13 to 15). Analyses of patella component use and polyethylene type showed no observed difference in risk of revision (Figures 16 to 20). There were insufficient data to permit a 15-year comparison by polyethylene type.

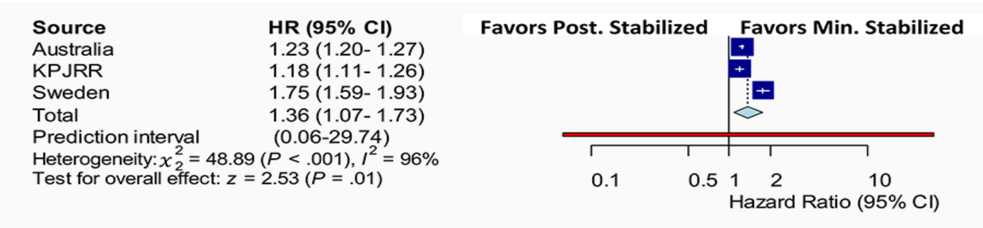


Figure 7. Meta-analysis of prosthesis constraint and revision at 5 years.

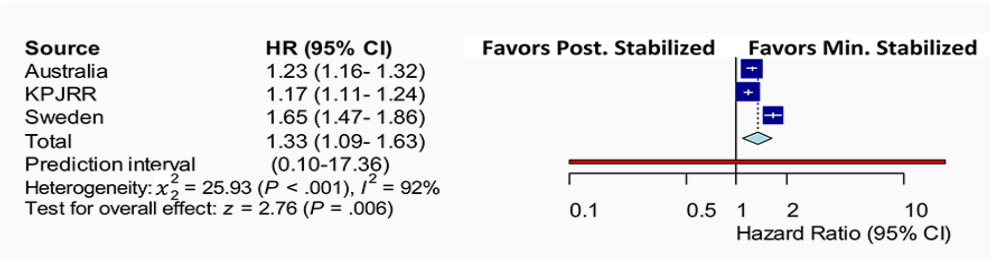


Figure 8. Meta-analysis of prosthesis constraint and revision at 10 years.

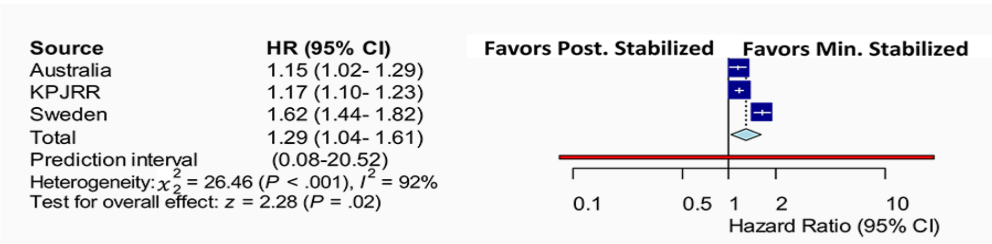


Figure 9. Meta-analysis of prosthesis constraint and revision at 15 years.

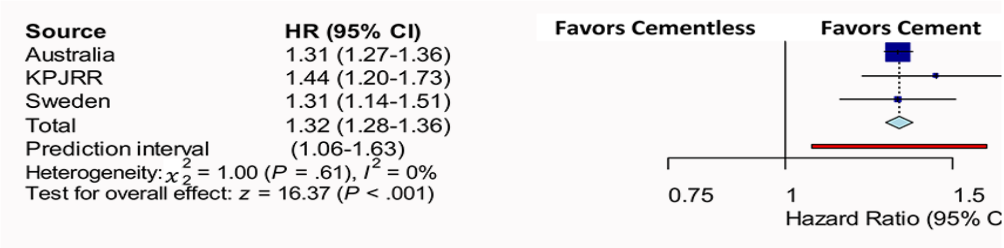


Figure 10. Meta-analysis of fixation and revision at 5 years.

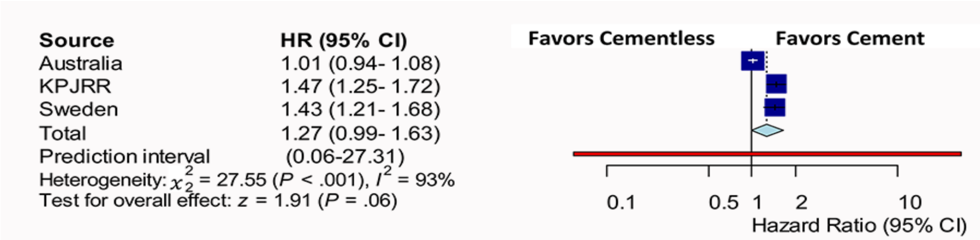


Figure 11. Meta-analysis of fixation and revision at 10 years.

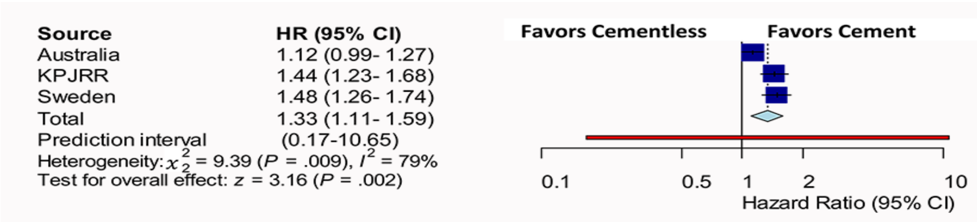


Figure 12. Meta-analysis of fixation and revision at 15 years.

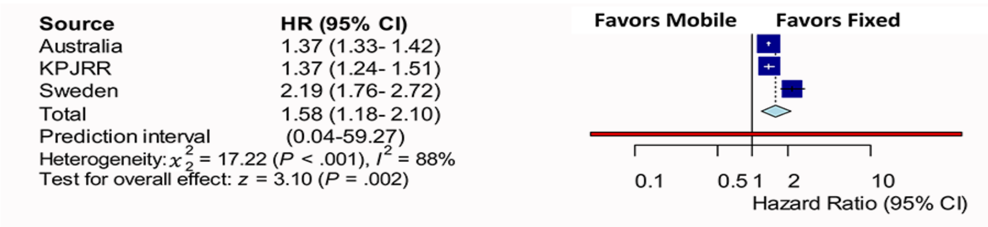


Figure 13. Meta-analysis of bearing mobility and revision at 5 years.

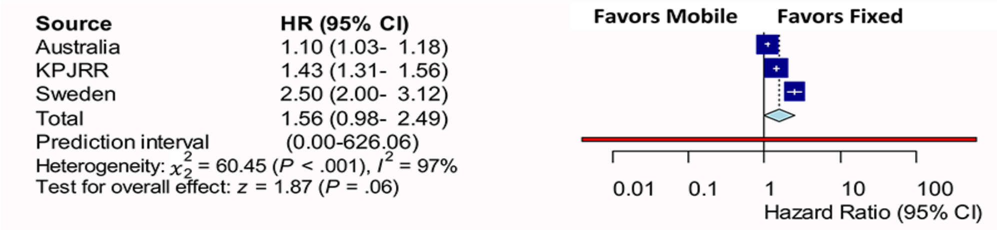


Figure 14. Meta-analysis of bearing mobility and revision at 10 years.

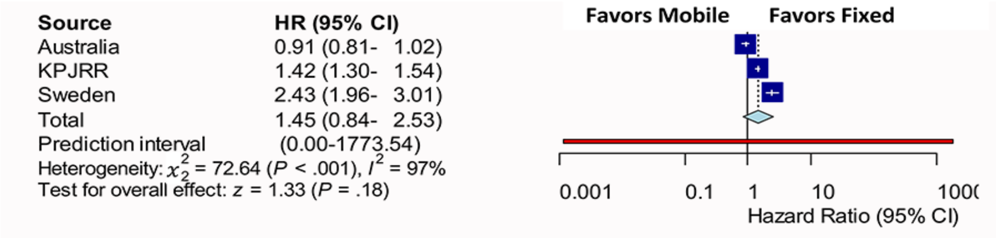


Figure 15. Meta-analysis of bearing mobility and revision at 15 years.

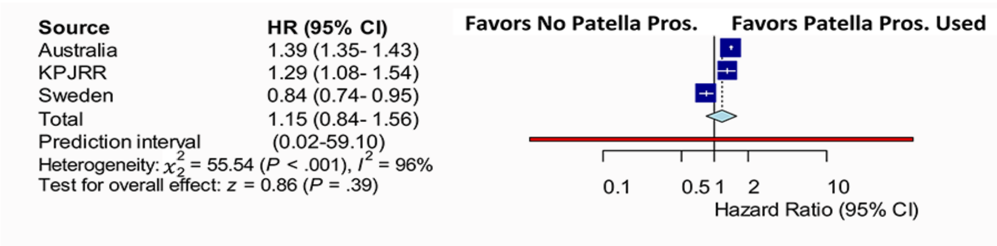


Figure 16. Meta-analysis of patella component use and revision at 5 years.

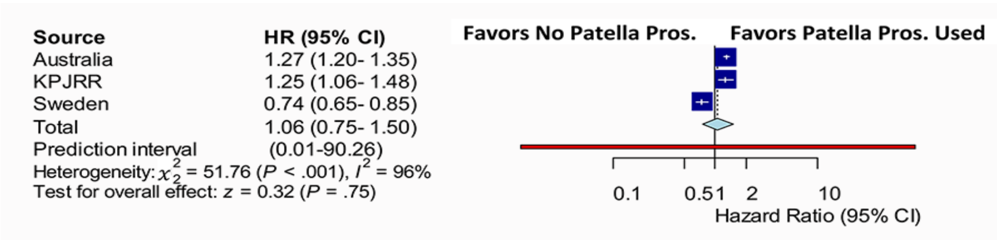


Figure 17. Meta-analysis of patella component use and revision at 10 years.

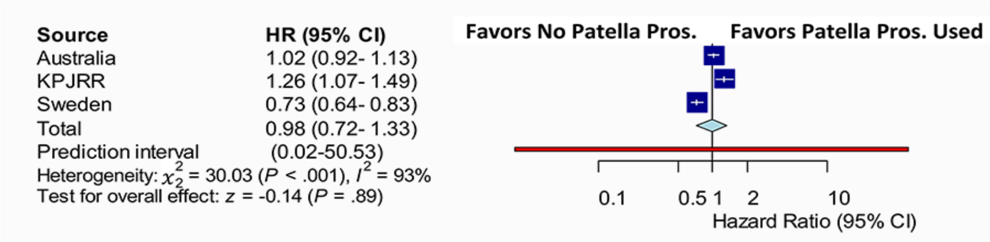


Figure 18. Meta-analysis of patella component use and revision at 15 years.

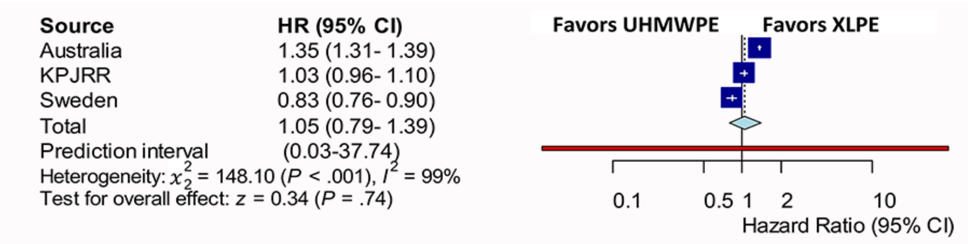


Figure 19. Meta-analysis of polyethylene type and revision at 5 years.

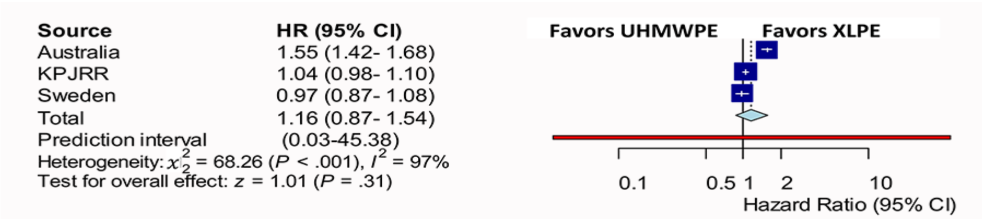


Figure 20. Meta-analysis of polyethylene type and revision at 10 years.

Paper IV

Consistent with the findings of Paper I, the mean patient ages for primary TKR were similar to those revised, while there were marginally greater proportions of males undergoing revision compared to primary TKR. Study of ASA status and BMI both showed a small shift in proportion to higher categories for revised patients compared to primary, but there were limited data for these analyses. Prosthetic factor comparisons between primary TKR and those revised showed small increases in proportions of PS components revised, mobile bearing (MB) prostheses and those using UHMWPE, but no consistent differences regarding fixation type or patella component use.

Reasons for revision

Like Paper II, infection, loosening, instability, and patella reasons were the most common diagnoses for revision of TKR for OA in all 3 registries, with the only difference seen in the KPJRR where 98% of TKR had a primary patella resurfacing and patella causes for revision were rare. The mean times to revision were shortest for infection and arthrofibrosis and longest for wear, loosening and fracture (Figure 21).

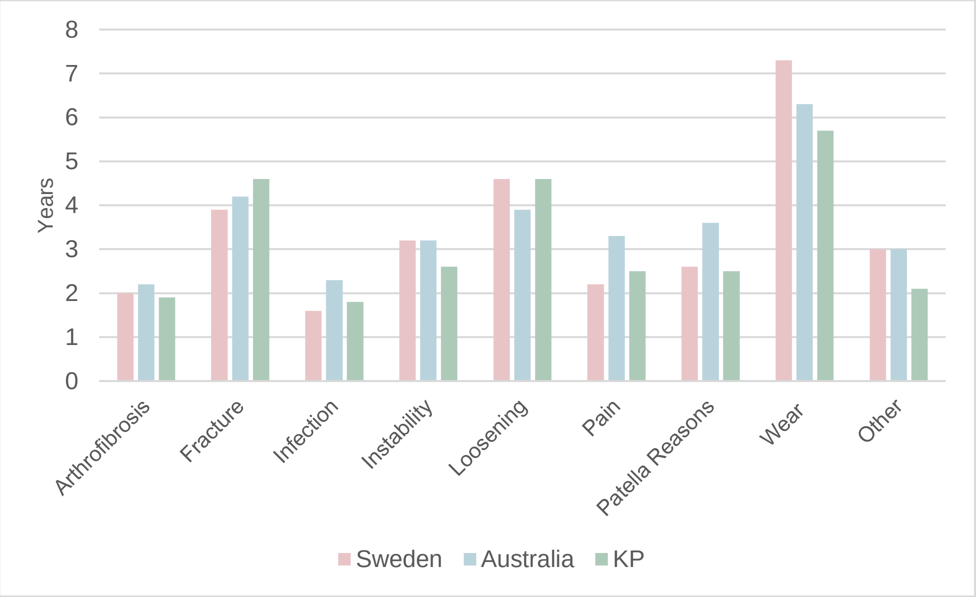


Figure 21. Mean time to revision (years) by revision reason.

Patient factors analyses for each of the more common reasons for revision showed the mean age at time of revision ranged from 64 to 77 years, being lowest for revisions for arthrofibrosis and highest for revisions for fracture. The proportion of females revised ranged from 39% to 88%, being lowest for revisions for infection and highest for revisions for fracture.

Influence of prosthesis factors on reasons for revision

Odds ratio determinations for individual reasons for revision showed that there was inconsistency between registries for many of the factors studied, and in other comparisons no differences were shown between the factor alternatives. Fifteen factors (out of 56 possible) with consistent findings, went to further analysis by the meta-analytic approach.

Analyses of arthrofibrosis showed that young age and MB designs were risk factors for revision (Figures 22 & 23). Higher odds for revision for fracture was seen for females, age 65 and over, and with PS prostheses (Figures 24 to 26). Factors affecting revision for infection were male gender and PS components (Figures 27 & 28). Younger age and MB designs had higher odds for revision for instability, (Figures 29 & 30) while PS, as well as MB designs and UHMWPE inserts had higher odds for revision for loosening (Figures 31 to 33). There was no consistency found when factors were assessed regarding revision for pain. MB components and not using a patella component increased odds for revision for patella reasons (Figures 34 & 35). Cementless fixation increased the odds for revision for wear (Figure 36).

	<65		65+		
Source	Events	Total	Events	Total	OR (95% CI)
Australia	389	220574	537	443408	1.46 (1.28- 1.66)
KPJRR	274	81608	221	139044	2.12 (1.77- 2.53)
Sweden	47	58275	39	130015	2.69 (1.76- 4.11)
Total		360457		712467	1.95 (1.39- 2.72)
Prediction interval					(0.03-112.25)

Heterogeneity: $\chi^2_2 = 15.69$ ($P < .001$), $I^2 = 87\%$
Test for overall effect: $z = 3.87$ ($P < .001$)

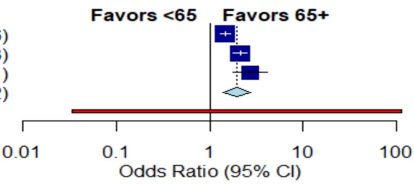


Figure 22. Meta-analysis of age and revision for arthrofibrosis.

	Mobile		Fixed		
Source	Events	Total	Events	Total	OR (95% CI)
Australia	214	129788	712	539194	1.25 (1.07- 1.46)
KPJRR	61	18226	434	202426	1.56 (1.19- 2.04)
Sweden	4	1610	82	186680	5.67 (2.08- 15.48)
Total		149624		928300	1.66 (1.09- 2.52)
Prediction interval					(0.01-184.31)

Heterogeneity: $\chi^2_2 = 9.97$ ($P = .007$), $I^2 = 80\%$
Test for overall effect: $z = 2.38$ ($P = .02$)

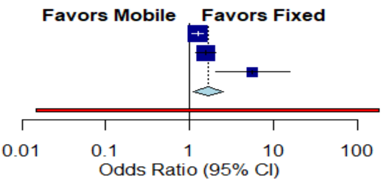


Figure 23. Meta-analysis of bearing mobility and revision for arthrofibrosis.

Source	Female Events	Female Total	Male Events	Male Total	OR (95% CI)
Australia	594	372774	187	291208	2.48 (2.11- 2.93)
KPJRR	138	135715	26	84937	3.32 (2.19- 5.05)
Sweden	92	109060	13	79240	5.15 (2.88- 9.20)
Total		617549		455385	3.23 (2.18- 4.79)
Prediction interval					(0.04-276.15)

Heterogeneity: $\chi^2_2 = 6.67$ (P = .04), I^2 = 70%
Test for overall effect: z = 5.85 (P < .001)

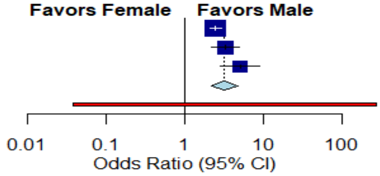


Figure 24. Meta-analysis of gender and revision for fracture.

Source	<65 Events	<65 Total	65+ Events	65+ Total	OR (95% CI)
Australia	146	220574	635	443408	2.17 (1.81- 2.59)
KPJRR	22	81608	142	139044	3.79 (2.42- 5.94)
Sweden	14	58275	91	130015	2.91 (1.66- 5.12)
Total		360457		712467	2.75 (1.89- 3.99)
Prediction interval					(0.04-174.54)

Heterogeneity: $\chi^2_2 = 5.69$ (P = .06), I^2 = 65%
Test for overall effect: z = 5.29 (P < .001)

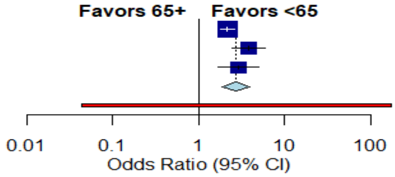


Figure 25. Meta-analysis of age and revision for fracture.

Source	MS Events	MS Total	PS Events	PS Total	OR (95% CI)
Australia	256	172530	503	487626	1.44 (1.24- 1.67)
KPJRR	132	146780	22	66489	2.72 (1.73- 4.27)
Sweden	15	11340	86	175667	2.70 (1.56- 4.68)
Total		330650		729782	2.10 (1.27- 3.47)
Prediction interval					(0.01-839.03)

Heterogeneity: $\chi^2_2 = 10.71$ (P = .005), I^2 = 81%
Test for overall effect: z = 2.89 (P = .004)

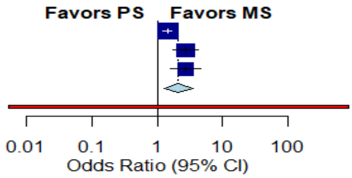


Figure 26. Meta-analysis of constraint and revision for fracture.

Source	Female Events	Female Total	Male Events	Male Total	OR (95% CI)
Australia	2401	372774	3727	291208	2.00 (1.90-2.11)
KPJRR	1180	135715	1289	84937	1.76 (1.62-1.90)
Sweden	771	109060	1041	79230	1.87 (1.70-2.05)
Total		617549		455375	1.88 (1.73-2.04)
Prediction interval					(0.73-4.87)

Heterogeneity: $\chi^2_2 = 7.49$ (P = .02), I^2 = 73%
Test for overall effect: z = 15.04 (P < .001)

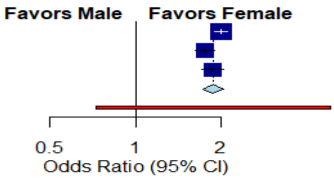


Figure 27. Meta-analysis of gender and revision for infection.

Source	PS Events	PS Total	MS Events	MS Total	OR (95% CI)
Australia	2062	172530	3948	487626	1.48 (1.40- 1.56)
KPJRR	1727	146780	639	66489	1.23 (1.12- 1.34)
Sweden	194	11340	1576	175667	1.92 (1.65- 2.23)
Total		330650		729782	1.50 (1.24- 1.83)
Prediction interval					(0.13-17.05)

Heterogeneity: $\chi^2_2 = 27.05$ (P < .001), I^2 = 93%
Test for overall effect: z = 4.11 (P < .001)

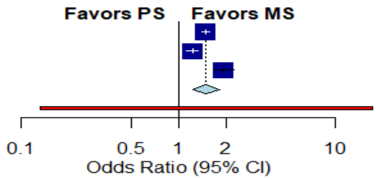


Figure 28. Meta-analysis of constraint and revision for infection.

Source	<65 Events	Total	65+ Events	Total	OR (95% CI)
Australia	974	220574	1463	443408	1.34 (1.24- 1.45)
KPJRR	489	81608	490	139044	1.70 (1.50- 1.93)
Sweden	362	58275	495	130015	1.64 (1.43- 1.87)
Total		360457		712467	1.54 (1.31- 1.82)
Prediction interval					(0.21-11.34)

Heterogeneity: χ^2_2 = 12.70 (P = .002), I^2 = 84%
Test for overall effect: z = 5.16 (P < .001)

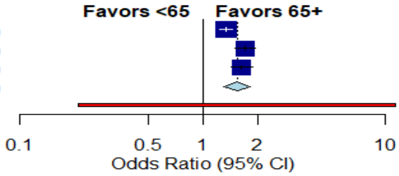


Figure 29. Meta-analysis of age and revision for instability.

Source	Mobile Events	Total	Fixed Events	Total	OR (95% CI)
Australia	533	129788	1904	539194	1.16 (1.06- 1.28)
KPJRR	134	18226	845	202426	1.77 (1.47- 2.12)
Sweden	14	1610	843	186680	1.93 (1.14- 3.29)
Total		149624		928300	1.52 (1.06- 2.17)
Prediction interval					(0.02-107.68)

Heterogeneity: χ^2_2 = 18.01 (P < .001), I^2 = 89%
Test for overall effect: z = 2.30 (P = .02)

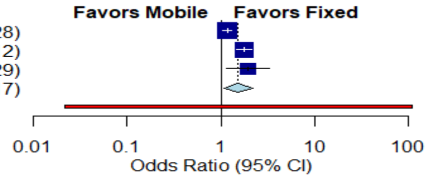


Figure 30. Meta-analysis of bearing mobility and revision for instability.

Source	PS Events	Total	MS Events	Total	OR (95% CI)
Australia	2025	172530	3839	487626	1.50 (1.42-1.58)
KPJRR	936	146780	296	66489	1.44 (1.26-1.64)
Sweden	123	11340	1110	175667	1.72 (1.43-2.08)
Total		330650		729782	1.51 (1.41-1.61)
Prediction interval					(0.83-2.74)

Heterogeneity: χ^2_2 = 2.57 (P = .28), I^2 = 22%
Test for overall effect: z = 11.93 (P < .001)

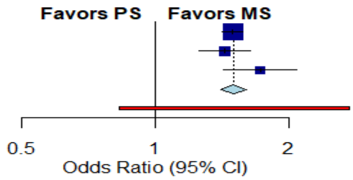


Figure 31. Meta-analysis of constraint and revision for loosening.

Source	Mobile Events	Total	Fixed Events	Total	OR (95% CI)
Australia	1771	129788	4117	539194	1.80 (1.70- 1.90)
KPJRR	164	18226	1092	202426	1.67 (1.42- 1.97)
Sweden	40	1610	1206	186680	3.92 (2.85- 5.39)
Total		149624		928300	2.17 (1.59- 2.97)
Prediction interval					(0.05-103.30)

Heterogeneity: χ^2_2 = 23.38 (P < .001), I^2 = 91%
Test for overall effect: z = 4.85 (P < .001)

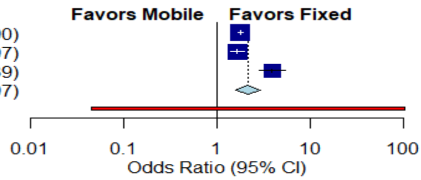


Figure 32. Meta-analysis of bearing mobility and revision for loosening.

Source	UHMWPE Events	Total	XLPE Events	Total	OR (95% CI)
Australia	4725	395665	1159	268036	2.78 (2.61- 2.97)
KPJRR	1022	147384	189	60906	2.24 (1.92- 2.62)
Sweden	1143	162648	99	24968	1.78 (1.45- 2.18)
Total		705697		353910	2.26 (1.75- 2.92)
Prediction interval					(0.10-53.62)

Heterogeneity: χ^2_2 = 20.83 (P < .001), I^2 = 90%
Test for overall effect: z = 6.27 (P < .001)

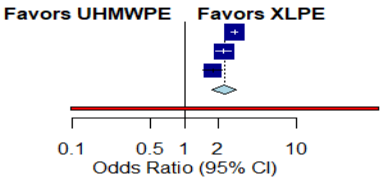


Figure 33. Meta-analysis of polyethylene type and revision for loosening.

Source	Mobile Events	Total	Fixed Events	Total	OR (95% CI)
Australia	1033	129788	2970	539194	1.45 (1.35- 1.56)
KPJRR	19	18226	107	202426	1.97 (1.21- 3.21)
Sweden	30	1610	1175	186680	3.00 (2.08- 4.32)
Total		149624		928300	2.00 (1.22- 3.29)
Prediction interval					(0.00-838.36)

Heterogeneity: $\chi^2_2 = 15.90$ ($P < .001$), $I^2 = 87\%$
Test for overall effect: $z = 2.75$ ($P = .006$)

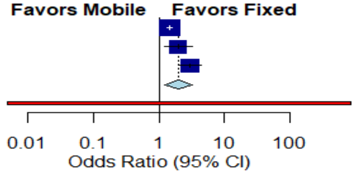


Figure 34. Meta-analysis of bearing mobility and revision for patella reasons.

Source	Not Used Events	Total	Used Events	Total	OR (95% CI)
Australia	3912	258573	91	375409	63.36 (51.46- 78.00)
KPJRR	24	4728	102	215924	10.80 (6.91- 16.86)
Sweden	1190	180315	15	7975	3.53 (2.12- 5.87)
Total		443616		599308	13.56 (2.25- 81.82)
Prediction interval					(0.00-154150857348.74)

Heterogeneity: $\chi^2_2 = 135.83$ ($P < .001$), $I^2 = 99\%$
Test for overall effect: $z = 2.84$ ($P = .004$)

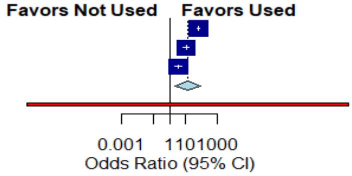


Figure 35. Meta-analysis of patella component usage and revision for patella reasons.

Source	Cementless Events	Total	Cemented Events	Total	OR (95% CI)
Australia	574	120616	386	389650	4.82 (4.24- 5.49)
KPJRR	17	3746	174	208391	5.46 (3.31- 8.99)
Sweden	6	7424	26	180220	5.61 (2.31-13.62)
Total		131786		778261	4.87 (4.31- 5.52)
Prediction interval					(2.18-10.88)

Heterogeneity: $\chi^2_2 = 0.32$ ($P = .85$), $I^2 = 0\%$
Test for overall effect: $z = 25.07$ ($P < .001$)

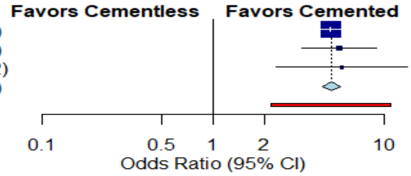


Figure 36. Meta-analysis of fixation and revision for wear.

The meta-analytic findings of papers III and IV have been combined for the patient and prosthesis factors found to be associated with a lower risk of revision (Table 3).

Table 3. Summary of patient and prosthesis factors with lower revision risk (combined findings from Papers III and IV).

	ALL-CAUSE REVISION			STIFFNESS	FRACTURE	INFECTION	INSTABILITY	LOOSENING	PAIN	PATELLA CAUSES	WEAR
REASON	5yrs	10yrs	15yrs								
Patient Factor											
Age (years)	65+	65+	65+	65+	<65		65+				
Sex	Female				Male	Female	Male				
ASA class	1+2										
BMI (kg/m²)	<30										
Prosthesis Factor											
Constraint	MS	MS	MS		MS	MS		MS			
Fixation	C'ted		C'ted								C'ted
Bearing Mobility	Fixed			Fixed			Fixed	Fixed		Fixed	
Patella Component										Used	
Poly. Type								XLPE			

(Legend: Poly type=polyethylene type, C'ted=cemented, if cell blank=no difference found, if cell grey=unable to calculate due to insufficient data)

Revision procedures (Additional data)

Revision of both femoral and tibial components (TKR revision) was the most common revision procedure in the SKAR and AOANJRR, followed by insert only exchange, but the KPJRR reversed the order of these two most frequent procedures. Patella only revision was third most common, except again for the KPJRR, where 98% have a patella component inserted in the primary procedure. Isolated revision of a single major component was uncommon (less than 9%) (Figure 37).

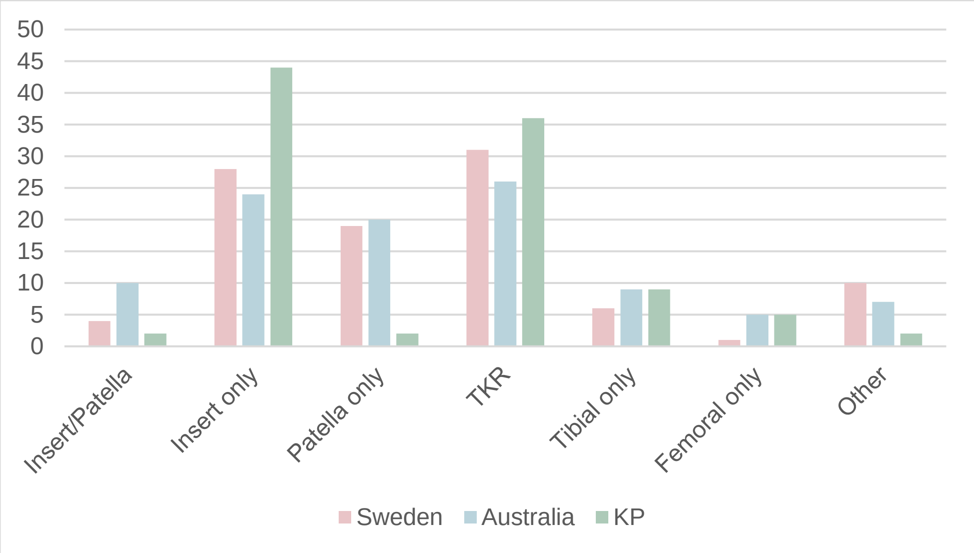


Figure 37. Proportions of revision procedures by registry (primary TKR for OA).

Assessment of revision procedures by individual reasons for revision was undertaken (Table 4). Revision procedures for arthrofibrosis most commonly involved insert exchange, often combined with patella revision in Australia, with TKR revision second most common. When revision for fracture was carried out, most often this required TKR revision, but less commonly one of either the tibial or femoral components. An insert exchange was the most frequent procedure for infection, followed by removal of components and cement spacer in the SKAR and AOANJRR, but TKR revision was second most popular in the KPJRR. Treatment of instability most often involved insert exchange in the AOANJRR and the KPJRR, followed by TKR revision, but SKAR results reversed the order of these procedure types. Procedures for loosening most commonly involved TKR revision, followed by tibial only revision. Most patella reason revisions were isolated patella component procedures or with additional exchange of the insert. Procedures used when revising for pain in Sweden and Australia were similar to patella reason revisions but insert exchange and TKR revisions were favored in the KPJRR. TKR revision was most common for wear, followed by insert exchange in the AOANJRR and KPJRR, but the order was reversed in the SKAR where revisions for this reason were rare (Table 4).

Table 4. Revision procedures by registry for each reason for revision.

REASON FOR REVISION BY REGISTRY	TOTAL N	INSERT/ PATELLA N (%)	INSERT ONLY N (%)	PATELLA ONLY N (%)	TKR N (%)	TIBIAL ONLY N (%)	FEMORAL ONLY N (%)	REMOVAL/ PROSTALAC N (%)	OTHER N (%)
Arthrofibrosis									
SKAR	**86**	6 (7)	35 (41)	8 (9)	28 (33)	6 (7)	3 (3)	0 (0)	0 (0)
AOANJRR	**926**	134 (14)	259 (28)	79 (9)	290 (31)	64 (7)	95 (10)	5 (1)	0 (0)
KPJRR	**495**	24 (5)	235 (47)	1 (0)	113 (23)	48 (10)	74 (15)	0 (0)	0 (0)
Fracture									
SKAR	**105**	0 (0)	2 (2)	5 (5)	70 (67)	14 (13)	6 (6)	0 (0)	8 (8)
AOANJRR	**781**	21 (3)	30 (4)	82 (10)	393 (50)	135 (17)	87 (11)	9 (1)	24 (3)
KPJRR	**164**	1 (1)	4 (2)	9 (5)	126 (77)	9 (5)	14 (9)	1 (1)	0 (0)
Infection									
SKAR	**1812**	6 (0)	1148 (63)	1 (0)	89 (5)	7 (0)	1 (0)	519 (29)	41 (2)
AOANJRR	**6128**	94 (2)	3449 (56)	33 (1)	855 (14)	100 (2)	231 (4)	1366 (22)	0 (0)
KPJRR	**2469**	6 (0)	1602 (65)	0 (0)	708 (29)	19 (1)	14 (1)	120 (5)	0 (0)
Instability									
SKAR	**857**	49 (6)	313 (37)	2 (0)	422 (49)	32 (4)	35 (4)	1 (0)	3 (0)
AOANJRR	**2437**	341 (14)	1001 (41)	42 (2)	801 (33)	51 (2)	189 (8)	6 (0)	6 (0)
KPJRR	**979**	25 (3)	499 (51)	7 (1)	313 (32)	53 (5)	81 (8)	1 (0)	0 (0)
Loosening									
SKAR	**1246**	5 (0)	2 (0)	31 (2)	936 (75)	254 (20)	11 (1)	5 (0)	2 (0)
AOANJRR	**5888**	381 (6)	523 (9)	385 (7)	2585 (44)	1468 (25)	448 (8)	34 (1)	64 (1)
KPJRR	**1256**	18 (1)	39 (3)	29 (2)	714 (57)	370 (29)	86 (7)	0 (0)	0 (0)
Patella Reasons									
SKAR	**1205**	137 (11)	16 (1)	970 (80)	57 (5)	17 (1)	7 (1)	0 (0)	1 (0)
AOANJRR	**4003**	773 (19)	10 (0)	3192 (80)	13 (0)	4 (0)	9 (0)	1 (0)	1 (0)
KPJRR	**126**	27 (21)	37 (29)	40 (32)	12 (10)	3 (2)	6 (5)	1 (1)	0 (0)
Pain									
SKAR	**72**	4 (6)	5 (7)	33 (46)	24 (33)	5 (7)	1 (1)	0 (0)	0 (0)
AOANJRR	**2040**	442 (22)	182 (9)	922 (45)	332 (16)	83 (4)	56 (3)	12 (1)	11 (1)
KPJRR	**146**	5 (3)	52 (36)	12 (8)	47 (32)	19 (13)	11 (8)	0 (0)	0 (0)
Wear									
SKAR	**32**	1 (3)	15 (47)	1 (3)	14 (44)	1 (3)	0 (0)	0 (0)	0 (0)
AOANJRR	**1159**	208 (18)	233 (20)	42 (4)	586 (51)	43 (4)	40 (3)	3 (0)	4 (0)
KPJRR	**197**	11 (6)	59 (30)	1 (1)	105 (53)	14 (7)	7 (4)	0 (0)	0 (0)
Total									
SKAR	**5613**	213 (4)	1560 (28)	1060 (19)	1755 (31)	355 (6)	73 (1)	526 (9)	71 (1)
AOANJRR	**24931**	2536 (10)	6106 (24)	4918 (20)	6368 (26)	2121 (9)	1300 (5)	1458 (6)	124 (0)
KPJRR	**6092**	120 (2)	2647 (43)	120 (2)	2212 (36)	560 (9)	307 (5)	126 (2)	0 (0)

Footnote: Total includes 170, 1564 and 250 from SKAR, AOANJRR and KPJRR respectively revised for "Other" reasons.

When major components were exchanged for any reason 99% of all femoral and tibial components used cement fixation for the revision, a finding consistent across registries. Further analysis of revision for instability revealed a larger proportion of FS devices and hinge components (45% in the SKAR, 30% in the AOANJRR and 34% in the KPJRR) were used for revision compared to the prosthesis constraint of the primary TKR. When stem extensions were used in revisions for loosening, the most common procedure was to use stems on both femoral and tibial components, followed by a stem only on the tibial side (Figure 38).

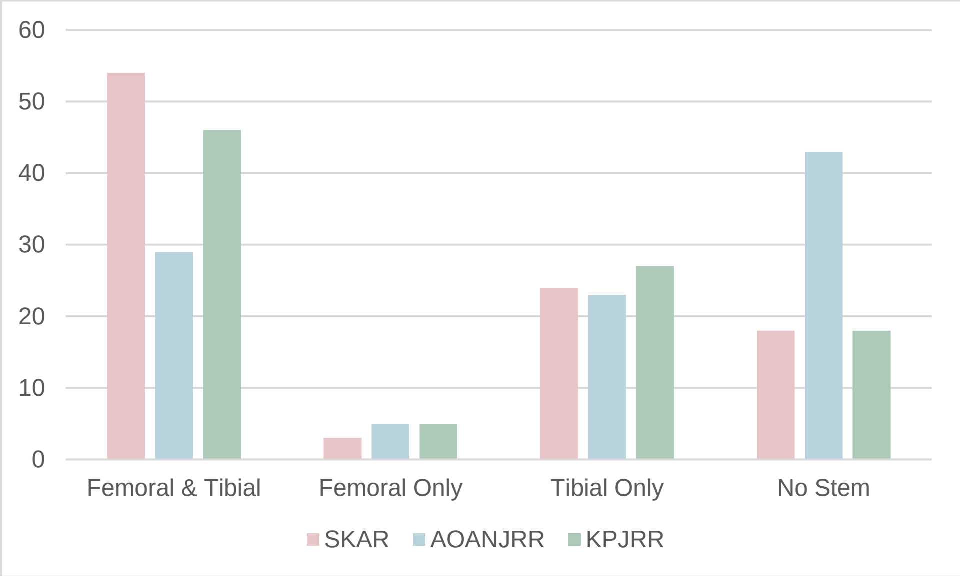


Figure 38. Proportion of stem extension use in revision TKR for loosening by registry (primary TKR for OA).

Paper V

Patient and prosthesis characteristics of primary TKR revised for instability

To assess the magnitude of the problem of revision for instability, the population from which these revisions were derived was described. There were 699,283 primary TKR for OA recorded from 1999 to 2019, and 27,580 of these had undergone a 1st revision. Instability was the reason for revision in 9.4% (2,605/27,580) and was the 3rd most common reason after loosening and infection. The surgeon description was "instability" in 90%, "bearing dislocation" in 7.1%, and "prosthesis dislocation" in 2.9%.

There was an increase in the annual numbers of revisions for instability (Figure 39).

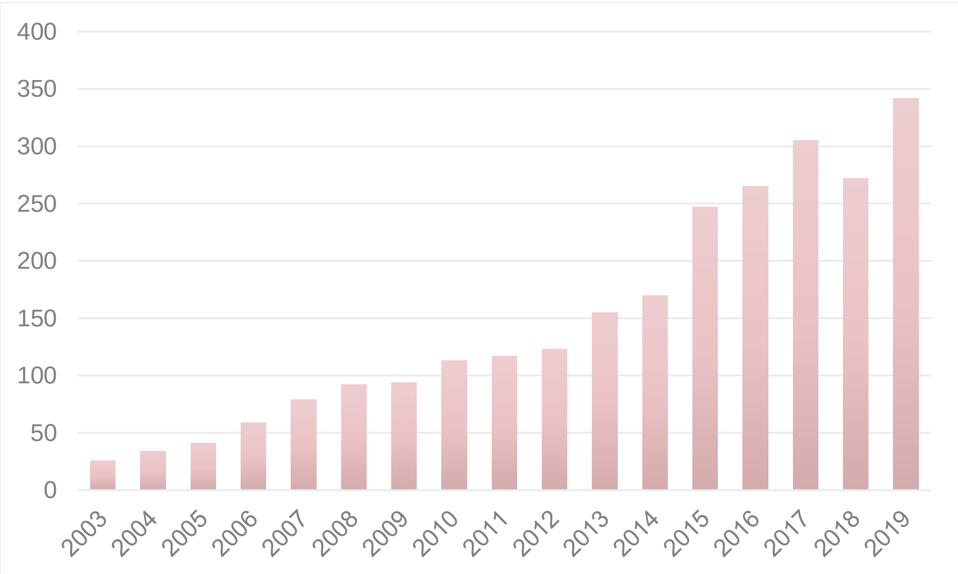


Figure 39. Annual procedure numbers for revision for instability by year of revision procedure.

Females had a higher revision risk for instability compared to males., and after 3 months patients aged <65 years had a higher risk of revision when compared to patients aged ≥65 years. A counter-intuitive finding was that both PS and MPD designs had a higher rate of revision compared to MS prostheses. When comparing the sub-groups of primary MS implants, there was no difference between CR, AS and DD inserts. Insert thickness >14mm (for both MS and PS implants) had a higher risk of revision compared to thinner inserts. Those with mobile bearings had a higher risk of revision for instability compared to fixed bearing prostheses for the first 3 months, after which there was no difference. Procedures using non-XLPE also had a higher rate of revision for the first 6 months when compared to XLPE, after that time there was no difference.

Types of revision TKR procedures for instability

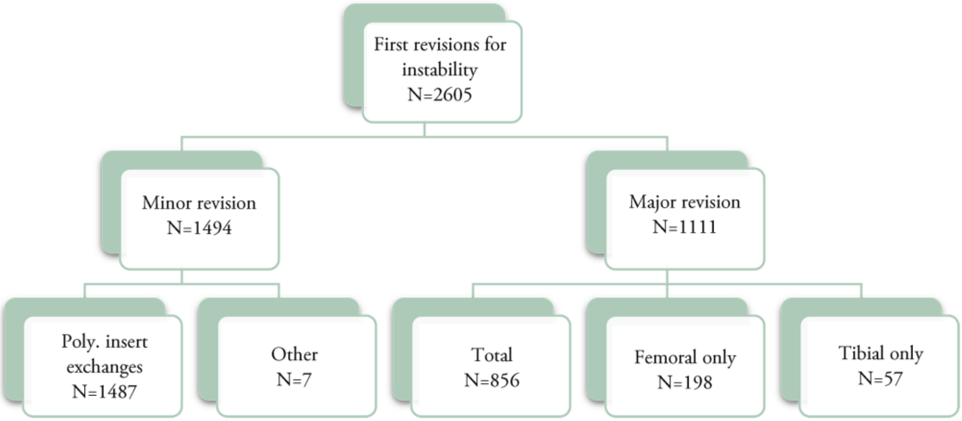


Figure 40. Flow diagram of revision of primary TKA for instability.

Minor revisions accounted for 57.4% (1494/2605) of all revision procedures for instability. The polyethylene insert was exchanged in 99.5% (1487/1494), with addition of adjunct components (staples, screws and suture anchors) making up the remainder (Figure 40). For the 887 MS knees that had a minor revision for instability, the 93% had an increase in insert thickness and 27% increased insert conformity, noting that some knee designs do not have options for conformity change. The insert thickness increases in the 490 minor revisions of PS knees was seen in 88%, and in 11% an FS insert was used in the few designs where this is possible without femoral component exchange (Table 5).

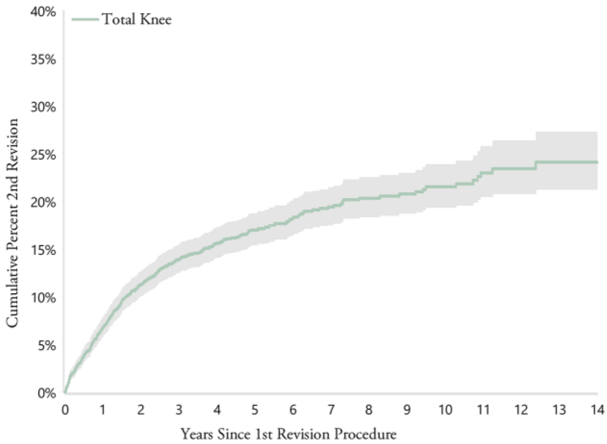
Table 5. Minor revisions for instability showing amount of change in polyethylene insert thickness by constraint of primary TKA.

THICKNESS CHANGE	MINIMALLY STABILIZED		POSTERIOR STABILIZED	
	N	%	N	%
Nil	52	6	43	9
1-3mm	333	38	168	34
3-5mm	359	40	187	38
>5mm	136	15	79	16
Thinner	7	1	3	1
Unknown	0	0	10	2
Total	**887**		**490**	

With the major revisions there was a tendency to increase prosthetic constraint with the revision procedure. Constraint increased in 87% (954/1099) of major revisions, while in 12% it remained the same and in 2% decreased.

Results of revision TKR for instability

Of the 2605 revisions for instability, 385 had required a 2nd revision. There was a cumulative percent 2nd revision of 24% at 14 years (Figure 41). The most common reason for 2nd revision was further instability (Table 6).



Number at Risk	0 Yr	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs	8 Yrs	9 Yrs
Total Knee	2605	2082	1712	1383	1106	872	701	552	447	349

Number at Risk	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs	16 Yrs	17 Yrs	18 Yrs	19 Yrs
Total Knee	261	187	125	83	55	35	24	13	3	1

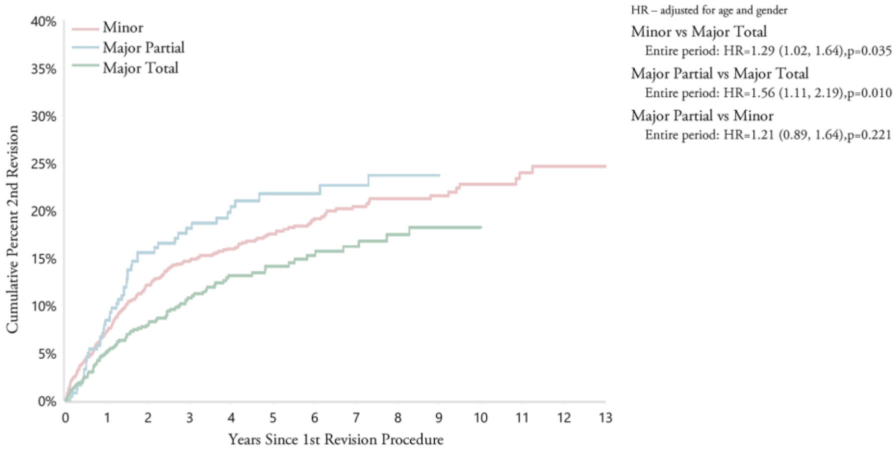
Figure 41. Cumulative percent 2nd revision of TKR for OA where 1st revision was for instability.

Table 6. Reasons for 2nd revision following 1st revision for instability.

2nd REVISION DIAGNOSIS	N	%
Instability	122	32
Loosening	103	27
Infection	78	20
Patella causes	22	6
Pain	17	4
Other	43	11
Total	**385**	**100**

There was a lower rate of 2nd revision when a major total revision was used compared to minor revision (insert exchange) or major partial revisions. (Figure 42).

When primary MS knees were revised for instability using a major revision there was no statistical difference with prosthesis constraint used for the revision, but there was a trend for a lower rate of 2nd revision with FS and hinged devices. When PS knees were revised with a major revision there was a higher rate of 2nd revision using another PS design when compared to a FS design.



Number at Risk	0 Yr	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs	8 Yrs	9 Yrs
Minor	1487	1201	1001	800	648	519	411	328	270	216
Major Partial	255	211	178	154	133	102	87	76	64	45
Major Total	856	668	532	428	324	250	203	148	113	88

Number at Risk	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs	16 Yrs	17 Yrs	18 Yrs	19 Yrs
Minor	164	123	85	54	37	22	15	8	3	1
Major Partial	39	25	16	11	6	5	4	1	0	0
Major Total	58	39	24	18	12	8	5	4	0	0

Figure 42. Cumulative percent 2nd revision of TKR for OA where 1st revision was for instability, by type of revision.

General discussion

Knee replacement has increased. This was shown in all 3 registries studied, and this result was the same from all perspectives, whether it was measured by procedure numbers or incidence, for primaries or revisions, and for all knee replacement or just total knee replacement for osteoarthritis (Papers I, II and IV). There were some differences in the rate of increase between registries, which were proposed to reflect local factors, such as government health policies, community obesity levels, surgeon and hospital accessibility and practice variations like thresholds for surgery and the availability and acceptance of pre-surgery measures for osteoarthritis treatment (2,38,39).

An important finding was the rate of increase in revision was less than that of primary knee replacement. This may be due to improvements in prosthesis performance related to design and materials, expansion of size choices or improvements in the precision of insertion due to the addition of assistive technologies such as computer navigation, image derived instrumentation or robotic assistance (40-42).

Symptom levels and extent of disease present can vary among patients having knee replacement surgery. However, the operation to insert a knee replacement is defined, and easily documented and logged. The event of revision is a little less clear-cut. Disease severity leading to revision can vary, just like the initial process leading to the primary knee replacement. For the same clinical setting, patients and surgeons may have different thresholds for undertaking revision, some patients may be too unwell to undergo a further procedure, and some may decide that they would prefer to live with their level of symptoms rather than have more surgery. In addition, a small proportion of further procedures can be missed in registry records as some do not require replacement or addition of a component. This is particularly true for repeat operations for infection, or fracture (43,44). These underestimates are noted limitations.

However, revision is the major endpoint that is captured by registries, and is certainly also a distinct, readily recorded and sentinel event. Undertaking a revision procedure is a major incident, particularly for patients, but also for surgeons and health care systems. Revision data is objective and relatively easy to collect on a population basis, without needing a response from individual patients. It is preferred over alternate measures of knee replacement outcome, such as patient satisfaction, as it is less subjective, or the attainment of a particular level of PROM which is difficult to interpret. Noting the limits stated above, revision is what was used for assessing the outcome for the studies included in this thesis, and in fact, for most registry analyses.

Observational data about revision procedures from quality registries are a valuable information source. Data is collected on a population level, not just from a specific cohort from specialist centers. It captures almost all revision procedures, with very little loss to follow-up. It is valuable for studying rare events, can document changing trends and detect emerging problem techniques or prostheses. For ease-of-use it is necessary for observational data to be grouped, and that process may create its' own challenges.

Each reason for revision (a main component for analysis for papers II and IV) has been used as a distinct category. This may be a less-than-perfect categorization. In many instances the revision diagnosis is quite obvious. However, for the identical patient some surgeons may classify the reason for revision differently. For instance, for a patient with extensive polyethylene wear, loosening, osteolysis and even component breakage, it can be difficult to determine the primary reason for revision. In others, one surgeon may nominate "patella erosion", while another claims "pain" as the reason for revision. Each reason has been considered separately and there has been no allowance for interactions between the reasons for revision (for instance wear and instability). These weaknesses are acknowledged, but the information we have to work with has been accepted as correct. The revision diagnosis audit performed on the AOANJRR cohort is reassuring in this regard and gives this approach some credence.

While reasons for revision have been classified into distinct groups there may be some differences within each of these groups. For instance, the revision diagnosis of "instability" includes different forms such as flexion, extension, hyperextension and mid-flexion instability, and these may each be distinct entities and require different approaches for treatment. Revision for loosening may be due to loosening of either femoral or tibial components or both. Revision for infection would include both acute post-operative wound-related disease and also chronic blood-borne infections, which have the same diagnosis, but are likely to be different clinical conditions. Restriction to diagnostic groups is necessary, as firstly, this is the level of granularity of registry data, and additionally, to avoid making analyses too complex and difficult to interpret.

The grouping of EDGs, which is a technique used for Papers II and IV, is often self-evident, but may also have some limitations. Categorization may be subject to an element of subjectivity. As an example, the revision reason of inflammatory arthritis in the KPJRR has been included in "progression of disease" but may be the equivalent of "synovitis" in the AOANJRR which is included in the "other" group. Use of a diagnosis hierarchy to rank reasons for revision may alter the relative importance of reasons for revision where more than one has been recorded. The impact of these minor imperfections should not greatly influence the findings.

While acknowledging all of these considerations, it was found that infection, loosening and instability were among the top 5 most common reasons for revision, while the ranking between registries varied and changed with time (Paper II). There were common increases in revisions for infection, and decreases in revisions for wear, but differences occurred in 8 of the other 10 common revision reasons. Increasing revisions for instability and loosening were seen over time in the SKAR and the AOANJRR, but not the KPJRR, where they remained steady. Revision for patella causes was more frequent in the SKAR and AOANJR, but uncommon in the KPJRR.

Many of the differences in reasons for revision found in Paper II were proposed to be related to differences in surgical practice. Variation was, in fact, shown to exist between surgeons of Sweden, Australia and the US (as measured by the KPJRR), and many of these practices have changed over time (Paper III). The use of posterior stabilized prostheses and patella components for primary TKR showed greatest diversity, with surgeons from the KPJRR using mostly PS prostheses and almost all had a patella component inserted, while the surgeons from the SKAR used MS prostheses and very few patella components. These differences between the SKAR and KPJRR remained constant, while the surgeons from Australia varied in both aspects, with fluctuating use of PS components and increasing patella prosthesis use with time. There were common trends in all registries for the declining use of mobile bearing components and use of UHMWPE. Cement fixation was used for most of the knee replacements in the SKAR and KPJRR, but Australian surgeons chose cementless and hybrid fixation for roughly 20% each for their knees.

Meta-analysis was used to combine registry data to create combined effects for patient and prosthesis characteristics, as only summary data (rather than individual patient data) was available from each registry. This was primarily due to concerns about data ownership, data security, and regulations concerning which data can be shared without identifying patients or their surgeons. A meta-analytic approach has been previously shown effective for this use (6).

Meta-analysis can be a powerful tool to cumulate and summate results from multiple sources. As a technique it is not without some controversy. A drawback for these studies is the inclusion of data from only 3 registries; it would have been nice to have even more information to work with. While all the registries involved have large numbers to study, and similar methodologies for data collection, classification and analysis (statistical homogeneity), there is clinical heterogeneity due to practice variations. For many of the analyses the statistic to measure heterogeneity (I^2) was of the level considered to indicate “substantial” or “considerable” heterogeneity (45). However, there is uncertainty of the accuracy of the I^2 measure when there are few studies included. While the Cochrane methodology considers heterogeneity to diminish the certainty of the findings, I feel that if consistent results are found in the presence of clinical diversity, then this should actually strengthen the validity of the results (45).

Where time-to-event data was collated, the appropriate meta-analytic technique is the inverse-variance method, and this was chosen (Paper III). Estimates of the log hazard ratio and standard errors were obtained by Cox regression models. Random effects models were used to take into account the levels of heterogeneity.

When patient factors were studied regarding all-cause revision, lower revision rates were found at 5, 10 and 15 years for patients aged ≥65 years. Female sex, low ASA score and absence of obesity were associated with lower rates of revision at 5 years. While age and gender generally can't be altered, younger patients could be advised to delay their surgery, if symptoms permit, until they have a lower risk of revision. It would also seem reasonable to recommend optimization of comorbidities and weight loss prior to TKR to decrease the revision risk.

Prosthesis factor analyses for constraint showed lower revision rates with MS prostheses at 5, 10 and 15 years. In Sweden where this design was used in over 90% of procedures, MS revision rates were lower, but this was also seen in the KPJRR data where PS components were far more popular. The consistency of the findings for all registries, and for each time analysis, adds strength to these findings. It could be argued that PS components are selectively used for the more difficult cases which have a higher likelihood of revision, however these results favor the use of MS components overall. While many previous studies have shown similar findings, others show no difference regarding constraint (46-48).

Cement fixation gave a lower risk of revision at 5 and 15 years, suggesting cement may aid initial fixation and protect against early migration, as well as later loosening that may be a response to polyethylene wear. Cement fixation was used for >90% of TKR in both the SKAR and KPJRR, but only 60% in the AOANJRR where cementless and hybrid fixation account for roughly 20% each. Other studies claim similar superior results for the use of cement, however newer ingrowth surfaces have re-ignited interest in cementless components (49-51).

There was a generalized declining trend in the use of mobile bearing components, which showed a higher revision risk at 5 years, but no difference after this time. The revision risk difference may relate to bearing dislocation and "spin out" which can occur early in the mobile group (36).

There were conflicting results regarding the primary use of patella components. In the KPJRR where patella resurfacing was used in >98% of cases there was a lower risk of revision if a patella component was used, but in Sweden the usual practice of not using a patella component was shown to have a lower risk of all-cause revision. This may also reflect the selective use of patella components in specific, and perhaps difficult, clinical settings. Alternatively, this may relate to the use of different prostheses, as CR components are thought more "patella friendly" than PS (52). In Australia where patella component use was 60% of procedures and increasing, there was a higher revision risk seen at 5 and 10 years if a patella component was not used but no difference at 15 years. Perhaps an all-cause revision analysis is not sensitive enough to show differences between these alternatives. Proponents for patella component use suggest that using a patella prosthesis may protect against early revision for anterior knee pain and patella erosion, while the alternate argument for not using a patella component is out of concern for problems seen with patella component use, namely extensor mechanism rupture, mal-tracking, patella polyethylene wear, patella fracture and fragmentation (53-55).

Analyses of polyethylene type showed no revision risk difference if XLPE was used compared to UHMWPE. At 5 years there was a lower revision risk in the AOANJRR with XLPE, but in the SKAR a lower risk was seen with UHMWPE. These disparate findings may be due to performance differences between the limited prostheses that are offered with XLPE, or perhaps differences in durability of the different types of XLPE. Findings of no difference have been reported by others (56,57). The common global shift to XLPE use seems to be a marketing approach, rather than based on result-driven clinical demand.

Based on these meta-analyses, the use of MS prostheses using cement fixation and fixed bearings was encouraged to decrease the all-cause risk of revision. Of course, these suggestions should also consider individual circumstances, and be altered if necessary.

Building on the work of Papers II and III, we then continued to study the impact that the same patient and prosthesis factors had on each of the 8 common reasons for revision (Paper IV). For instance, we wished to determine the influence of fixation on revision for loosening, of prosthesis constraint on revision for instability and other associations. As some reasons for revision were infrequent, the numbers for sub-categories were even lower (for instance there were no PS prostheses revised for wear in Sweden). This study did not have survivorship data available, only total numbers revised for each of the reasons within the 17-year study period. The patient and prosthesis factors of primaries within the time period were also known, so that the number revised could be determined as well as the number not revised. A limitation of this approach is that TKR included later in the time period may not have time to be revised.

As there were limited data for ASA and BMI, further analysis by these factors was not possible, leaving 7 patient and prosthesis characteristics for the 8 reasons for revision that were calculated for each registry. Concordance between the 3 registries in significant odds ratios were found for 15 of the possible 56 permutations. These then were subject to meta-analysis to give a summary effect for each factor/reason combination.

In this instance, using dichotomous categorical data, the Mantel-Haenszel meta-analytic method was selected (Paper IV). This is thought to be the more reliable method when the event rates are low, such as for revision for different diagnoses (45). Odds ratios, rather than risk ratios, were calculated as this seemed the more commonly used statistic. There is said to be difficulty interpreting the odds ratio differences in terms of a difference in risk, but these two approximate each other when the result is close to 1 (as was the case for most of these analyses) (58). Once again random effects models were used.

Revision risk for stiffness (or arthrofibrosis) was higher in patients <65 years of age and for those with a mobile bearing prosthesis. Revision for this reason is uncommon as most are treated non-surgically by manipulation rather than further operation. There may be cultural differences in the acceptance of a stiff knee, and varying thresholds for surgeons offering revision (59). Why bearing mobility is associated is unclear, but in one recent study arthrofibrosis was the most common reason for revision in a mobile bearing cohort (60). Further study of this is required. There was uniformity in surgical treatment, when performed. Polyethylene insert exchange was the most common procedure, possibly to decrease the insert thickness, or alternatively to allow access to divide adhesions. While it is often hoped that division of adhesions will help, unfortunately this commonly results in further stiffness (61). The second most common method was to perform a major revision. Limited success with this rare revision approach has been reported in a recent systematic review and a small series (62,63).

Likelihood of revision for fracture was higher with older patients (age ≥65 years), female sex and use of PS components. It is the older female population that have higher rates of osteoporosis, an association of these fragility fractures (64). The "box" cut for the PS femoral component may predispose to distal femoral fracture (65). Revision for fracture most likely under-reports the true incidence of periprosthetic fracture, as some may be treated by conservatively or by internal fixation and not require revision. The most common treatment choice was to revise both major components of the knee replacement, increasingly using a distal femoral replacement (66).

Revision for infection was shown to be increasing in all registries. The problem may be larger than recorded, since registries are said to under-report infection as some procedures do not have components revised (washouts or debridement alone) and in others the diagnosis is not truly confirmed until after the procedure and may be misreported as revision for loosening or pain. Males and PS components had a higher risk of revision. Males have been shown to have a higher risk of knee infection, but the reason remains unclear (67). PS components are proposed to cause increased polyethylene debris which alters the intra-articular environment and permits infection (68). Treatment of infection was most frequently by insert exchange (as part of the DAIR approach), a technique becoming more popular, and secondly most commonly by removal of the knee components, seen as the "gold standard" for infection eradication (69,70).

Loosening as a cause for revision was found to be decreasing in the SKAR and AOANJRR. The risk for revision for this reason was lower with MS components, with fixed bearings and XLPE inserts. There was no clear association with fixation type, but perhaps this was due to the overwhelming predominance of cement usage in both the SKAR and KPJRR. The relationship with XLPE may be due to fewer reactive polyethylene wear particles created by this bearing compared to UHMWPE (71). This concept may also explain the benefit of MS over PS prostheses, as the latter create more wear debris, with greater forces on an insert needed to "drive" tibio-femoral motion and with wear of the tibial "peg" portion (72). An alternative explanation is that greater stresses transmitted through to the tibial baseplate by the PS peg-box linkage may lead to loosening. Surgical management of loosening was most commonly by revision of both major components with stems often used on both femoral and tibial components. This approach is frequently used, with debate about extent of cement use (baseplate and/or stem as well) and, more recently, the addition of metaphyseal sleeves to aid fixation (73-75).

Revisions for pain are difficult to understand as a group. There were no factors shown to be related to this revision reason. Post-surgical pain is thought to be multi-factorial, and often related to systemic conditions such as depression and catastrophizing (76). Procedures used in revision for pain also disparate, as these were similar in the SKAR and the AOANJRR to those used to treat patella causes (i.e., a patella component addition), but in the KPJRR procedures were mostly insert exchanges and TKR revisions.

A strong association was seen in the risk of revision for patella reasons when analyzed by patella component use. Previously, in Paper III, we were unable to show a difference in all-cause revision with patella component use, but here the use of a patella component showed much lower odds for revision for this group of diagnoses compared to where a patella component was not used. Patella resurfacing protects against the need for further surgery for patella pain, patella erosion and mal-tracking. MB prostheses also had an increased risk of revision compared to FB. This may relate to the commonly used "gap balancing' technique used for many MB designs, where femoral component rotation is determined after ligament releases (77). It almost goes without needing statement, that the most common procedure when revising for patella reasons is for addition of a patella component, sometimes with an exchange of insert as well.

Polyethylene type was not shown to alter risk of revision for wear, but the risk of revision for this infrequent reason was found to be increased if cementless fixation was used. It is possible that cementless fixation is chosen for the more active patients, or possibly, when these components are revised surgeons have difficulty differentiating between wear and loosening as the primary mechanism leading to revision. In addition, in Sweden revision for wear is rare and the use of XLPE is relatively low and recent, so it is possible that the few prostheses with this polyethylene have not had time be revised for wear. The most common procedure when revising for wear was to revise both major components, with the second most common being an insert exchange, except in Sweden where this order was reversed. There has recently been a wave of interest in insert exchange, particularly for a well-fixed and aligned knee replacement (78,79).

The multi-registry analysis of revision for instability showed a lower risk of revision for older patients (aged ≥65 years) and with FB components, but analyses of prosthesis constraint gave inconsistent results between the registries and was not chosen for meta-analysis. Previous studies have highlighted the risk of instability in the younger group, who may place more physical demands on their knees and/or be less tolerant of symptoms associated with laxity (80). Mobile bearing components have been associated with revision for bearing "spin-out" and dislocation in the first 3 months (36). Surgery to treat instability most commonly involved insert exchange, followed in frequency by a total knee revision in the AOANJRR and the KPJRR, but the order of these 2 was reversed in Sweden. Where total knee revisions were performed between 30 and 45% of revisions used FS or hinge components.

An expanded discussion of instability is possible in light of the findings from Paper V, in which 2605 revisions for instability were studied. As shown in Papers II and IV instability was a common cause of revision and was increasing in frequency. It was unclear why this is so, as there have been changes to prostheses and implantation techniques that have occurred which theoretically should improve stability results. These include the addition of more conforming designs of insert (e.g., AS, DD and MPD designs), introduction of single millimeter increments in insert thickness and the introduction of assistive technologies, such as computer navigation and robotic assistance that should improve precision of component insertion (41,42,81). The increase in revision for instability despite these factors may be explained by increased awareness of certain forms of instability, with the concept and dissemination of information regarding mid-flexion instability occurring during the last decade (82). Alternatively, revisions that previously had been considered due to pain of unknown origin may increasingly be classified as due to instability (83,84).

A difficulty encountered when studying instability relates to its' classification. "Instability", includes degrees of instability from mild to severe and, by definition, includes the extreme forms of bearing dislocation and prosthesis dislocation. It also includes several types, categorized by the knee position where instability is noticed (flexion, extension, hyper-extension and mid-flexion). Although grouping instability as a single entity may be a criticism, any information gained in attempt to explain this poorly understood condition should be considered helpful.

The use of data just from the AOANJRR allowed for a more detailed investigation of instability, particularly regarding the finer details of the insert thickness and conformity. Like the findings of Paper IV, instability revision risk was higher in young patients and those with mobile bearings (for the first 3 months). Additional risk factors were female sex, not using a MS design, insert thickness of >14mm in the primary and UHMWPE use (for the first 6 months only).

Gender differences may relate to increased generalized ligament laxity, or possibly higher self-reported rates of instability seen in females or a comparative difference in muscular strength seen with males (85-87). MS designs have less inherent constraint but both PS and MPD designs require Posterior Cruciate Ligament (PCL) sacrifice, and this may not only alter sagittal stability but also diminish proprioception. Insert thickness of >14mm may indicate difficult initial knee pathology requiring a low tibial resection, or one that needs extensive ligament releases, but may be associated with some loss of PCL function (88). The lower rate of revision for instability seen with XLPE in the first 6 months could be explained by the association of the introduction of this polyethylene type with the "new" technologies and prosthesis options.

Surgery to treat instability was by insert exchange in 55% of revisions, often using inserts with greater thickness and, at times, increased conformity. Although these actions seem logical for the management of instability, with CR or PS knees there was no difference found in 2nd revision rate when the amount of insert thickness change was studied, nor were there differences noticed if a CR design was continued with, compared to when a change in conformity was made to an AS or DD design. Perhaps the numbers for analysis were too small to detect any differences.

There was a lower rate of 2nd revision where a total knee revision was performed compared to an insert exchange. Changing both major components allows the use of a more constrained prosthesis. When PS primaries were revised for instability a lower rate of 2nd revision was found when more constrained devices were used in the revision procedure, but with MS primaries this was a non-significant trend.

A final comment at the end of Paper V was that, unfortunately, after revision for instability 24% had undergone a 2nd revision at 14 years, with recurrent instability as the most common reason for the repeat procedure. This implies that there is a great deal more to be gained by an enhanced comprehension of instability and an understanding of how best to treat it.

The same inference could be made with respect to other common reasons for TKR revision, which are all deserving of similar detailed analyses. Within the limitations mentioned earlier, further use of registry data should enable that knowledge expansion, advise of associations with the different reasons for revision, assess best practice, and thereby provide an evidence base to guide future knee replacement surgery.

Summary and conclusions

1. The increase in primary and revision knee replacement (particularly in Sweden and Australia) is not as great as previously predicted.

2. Primary knee replacement increased at a faster rate than revision knee replacement.

3. EDGs can be used to compare and combine registry data.

4. Infection, loosening and instability were the most common reasons for knee replacement revision.

5. Revision for infection increased in all contributing registries.

6. Practice variations exist between knee replacement surgeons of Sweden, Australia and KP, and many have changed with time.

7. Meta-analytic approaches can be used to combine and summarise aggregate registry data.

8. Prosthesis attributes (prosthesis constraint, bearing mobility and fixation method) effect all-cause revision rates.

9. Selecting specific prosthesis factors (MS, cemented, fixed bearing, and patella component use) can lower revision risk for individual reasons for revision.

10. Insert exchange was the most common method used for revising for wear, instability, arthrofibrosis and infection, while TKR was most common for treatment of fracture and loosening, and patella revision was used for revising for patella reasons.

11. Revision for instability has increased.

12. Patient and prosthesis factors (female, younger age, non-MS, mobile bearing, thick inserts) were associated with instability revision.

13. Exchange to a thicker, more conforming insert was a common treatment method for instability.

14. Further instability was the most frequent reason for requiring a 2nd revision after treatment of instability.

15. Major revision to a more constrained prosthesis (FS or Hinge) decreased the risk of 2nd revision when treating instability.

Clinical implications

- Monitoring knee replacement procedure numbers provides information for predicting future demands, which has implications for surgical training and is vital for allocating health resources.

- The finding of a universal increase in revision for infection requires further research as to why, and immediate action to mitigate this development.

- Practice variations can occur and change with time, and continuous monitoring of the effects on revision is needed.

- Appropriate selection of lower risk prosthesis attributes can improve revision-related outcomes.

- Understanding what contributes to instability after TKR may help decrease revisions for this reason.

- Analysis of revision procedures for the common reasons for revision, by determining the CP2R, can advise surgeons of the utility of different approaches.

Future research

Impact of COVID-19 on predictions of TKR rates and outcomes

While the study of previous years knee replacement surgery can be helpful to project future expectations, a serious and unforeseen interruption to world-wide elective surgery occurred with the onset of the COVID-19 pandemic in 2020. This disruption has caused failure of predictive models (as well as to PhD study plans!). Elective surgery, such as TKR, was ceased for varying times in different countries, causing delays for many to have their procedures (89,90). Even when re-allowed, there may have been some initial reluctance for patients to attend hospital due to fear of obtaining infection. In some health systems there is little capability to cope with the backlog of patients requiring surgery, due to staff and capacity limits. Delays are likely to be associated with an increase in the severity of knee disease and with further deconditioning of patients prior to surgery (91). Restrictions on socialization may negatively affect rehabilitation (92). These factors, and possibly many more, have implications for the outcome of TKR (93,94). There may be many aspects of a long-lasting COVID-19 effect, which require further analyses.

Expanding EDGs to further harmonize registry data

As mentioned earlier in this thesis summary, one of the main goals of the International Society of Arthroplasty Registries (ISAR) is to foster international data sharing and collaborative projects with the aim of improving outcomes of joint replacement patients world-wide. Some work has been done already in recommendation of benchmarking standards, international signal detection for under-performing implants (95), co-ordination of PROM instrument usage and times for collection (96), and creation of the international prosthesis library. Equating data from one registry to another can be problematic as there are differences in terminology and a lack of consensus in determining modes of failure. Expansion of the EDG principle (and perhaps also the concept of a diagnosis hierarchy) would enable easier inter-registry collaboration in the future.

Need for a better understanding of periprosthetic infection

One of the undeniable findings of this research is the increase in revisions for infection shown in all registries studied. This has also been the experience of others (97). It has been said that registries understate periprosthetic infections, as some procedures don't have components revised (washouts or debridement alone, or amputations), surgery can occur in emergency settings and miss routine data collection, or be misinterpreted as loosening or synovitis if cultures are negative (43,98,99). Periprosthetic infection occurs as a complex interaction of factors relating to the patient, the surgeon, the prosthesis and the pathogen. In addition, there is a lack of consensus of how best to treat peri-prosthetic infections when they occur (100). As there is an urgent need to better understand these infections, the creation of a joint replacement infection registry with expanded data collection for these cases (including systemic and laboratory findings, treatment methods and timings), may help in that regard. As infection (thankfully) is relatively rare, international co-operation would allow more rapid data acquisition, and hopefully improved comprehension of this complex but vitally important problem.

Detailed assessment of revision diagnoses and treatment strategies

As mentioned in the concluding paragraph of the discussion section, a similar approach used for the study of instability in Paper V, should be undertaken to allow a "deeper dive" into the factors associated with other frequent reasons for revision. Building on the findings of Paper IV, this would allow even better understanding of the patient and prosthesis characteristics associated with each revision diagnosis. Additionally, at present we know relatively little about the outcomes of the revision procedures used. Study of the rates of 2nd revision for each common reason for 1st revision by procedure type, as has been done in Paper V, is required to inform surgeons of the best surgical approach to take to minimise the risk of even further surgery.

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"One can state, without exaggeration, that the observation of and the search for similarities and differences are the basis of all human knowledge."

Alfred Nobel

Paper I

OPEN ACCESS

Increases in the rates of primary and revision knee replacement are reducing: a 15-year registry study across 3 continents

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Background and purpose — Rates of knee replacement (KR) are increasing worldwide. Based on population and practice changes, there are forecasts of a further exponential increase in primary knee replacement through to 2030, and a corresponding increase in revision knee replacement. We used registry data to document changes in KR over the past 15 years, comparing practice changes across Sweden, Australia, and the United States. This may improve accuracy of future predictions.

Patients and methods — Aggregated data from the Swedish Knee Arthroplasty Register (SKAR), the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR), and the Kaiser Permanente Joint Replacement Registry (KPJRR) were used to compare surgical volume of primary and revision KR from 2003 to 2017. Incidence was calculated using population census statistics from Statistics Sweden and the Australian Bureau of Statistics, as well as the yearly active membership numbers from Kaiser Permanente. Further analysis of KR by age < 65 and ≥ 65 years was carried out.

Results — All registries recorded an increase in primary and revision KR, with a greater increase seen in the KPJRR. The rate of increase slowed during the study period. In Sweden and Australia, there was a smaller increase in revision surgery compared with primary procedures. There was consistency in the mean age at surgery, with a steady small decrease in the proportion of women having primary KR. The incidence of KR in the younger age group remained low in all 3 registries, but the proportional increases were greater than those seen in the ≥ 65 years of age group.

Interpretation — There has been a generalized deceleration in the rate of increase of primary and revision KR. While there are regional differences in KR incidence, and rates of change, the rate of increase does not seem to be as great as previously predicted.

Knee replacement (KR) has a favorable survival rate with cumulative revision as low as 3% at 10 years (AOANJRR 2018, SKAR 2018) and this result appears to be improving with time as wear-related revisions become less common (Sharkey et al. 2014, Koh et al. 2017, Postler et al. 2018).

Throughout the last decade, national joint replacement registries have recorded increasing yearly volumes of KR (AOANJRR 2018, NJR 2018, SKAR 2018). The reasons for this increase in procedure numbers are proposed to be increased surgeon and patient acceptance of KR (Hamilton et al. 2015), improved longevity (Patel et al. 2015), increasing incidence of osteoarthritis (OA), and use of KR in younger patients (Weinstein et al. 2013, Leyland et al. 2016, Karas et al. 2019).

With increasing primary KR use it is predicted that the numbers of revision procedures will also rise (Kumar et al. 2015, Patel et al. 2015). Not only are more people receiving a KR, but some of the factors driving increased primary usage of KR also contribute to increased failure. These include longer life-expectancy, whereby patients with a KR have more time to be revised, and use in young and obese patients who place higher demands on their KR (Hamilton et al. 2015). Counterbalancing this trend, to a small extent, is improved prosthesis performance (Pitta et al. 2018).

There is international variation in the use of KR (Kurtz et al. 2011). In a comparative study of 18 countries in 2008, Kurtz et al. (2011) found a range of 8.6 to 213 primary procedures /100,000 population, and a range of 0.2 to 28 revision procedures/100,000 population, but they could not determine if the observed variation related to healthcare systems, access to care, number and distribution of orthopedic surgeons, or the prevalence of joint disease. There are expectations of exponential increases for both primary and revision KR. However, predictions of revision KR in the year 2030 compared with 2005 levels vary widely, from a 75% increase in Taiwan to a 600% increase in the USA and a similar increase in the UK

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Table 1. Yearly totals of knee replacement (KR) procedures recorded in the SKAR, AOANJRR, and KPJRR

KR type [a]	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Sweden															
Primary	8,832	9,195	9,797	10,691	10,527	11,004	12,841	12,848	12,845	13,411	13,361	13,145	12,924	14,053	14,964
Uni	982	892	928	916	728	712	693	689	594	536	494	465	648	984	1169
PF	11	16	21	9	12	17	37	31	52	43	56	58	65	52	48
Total	7,339	8,287	8,848	9,766	9,787	10,275	12,111	12,228	12,198	12,832	12,808	12,622	12,206	13,008	13,743
Revision	596	625	650	650	657	702	758	860	845	869	1002	959	936	934	945
All	9,428	9,820	10,447	11,341	11,184	11,706	13,599	13,708	13,690	14,280	14,363	14,104	13,860	14,987	15,909
Australia															
Primary	26,008	7,540	30,409	31,231	33,064	36,160	37,683	40,838	43,051	44,839	46,903	49,813	53,578	55,878	59,002
Uni	4,109	3,730	3,382	3,628	2,502	3,225	3,087	2,615	2,411	21,46	2,137	2,270	2,557	3,056	3,652
PF	151	180	174	181	195	232	229	268	247	225	246	234	248	307	298
Total	21,735	23,603	26,337	27,376	29,294	32,622	34,307	37,922	40,375	42,453	44,495	47,288	50,763	52,510	55,077
Revision	2,314	2,663	2,721	2,826	2,994	3,250	3,294	3,716	3,894	3,910	4,173	4,301	4,447	4,559	4,791
All	28,322	30,203	33,130	34,057	36,058	39,410	40,977	44,554	46,945	48,749	51,076	54,114	58,025	60,437	63,793
Kaiser Permanente															
Primary	4,271	5,824	7,050	8,255	9,283	10,234	10,806	12,904	13,495	14,084	15,445	17,796	18,324	20,093	20,672
Uni	144	234	210	212	200	330	448	420	371	439	522	631	602	563	579
PF	7	6	6	14	10	24	27	35	38	30	44	57	54	65	84
Total	4,120	5,584	6,834	8,029	9,073	9,880	10,331	12,449	13,086	13,616	14,879	17,109	17,669	19,465	20,009
Revision	274	363	456	556	627	773	766	850	981	1,021	1,091	1,173	1,267	1,305	1,309
All	4,545	6,187	7,506	8,810	9,910	11,007	11,572	13,754	14,476	15,106	16,536	18,969	19,592	21,398	21,981

[a] Uni = unicompartmental; PF= patellofemoral
Note: A small number of other primary knee replacement (unispacer, partial resurfacing, bicompartmental) are included in primary knee totals.

(Kurtz et al. 2007, Kumar et al. 2015, NJR 2018). A further study comparing 24 OECD countries' KR utilization predicted a 400% increase by 2030 (Pabinger et al. 2015). There are other predictive models with a more conservative forecast for the United States (Inacio et al. 2017).

We performed a multi-country comparison of KR, comparing the changing procedure volume and incidence of primary and revision KR using data from the Swedish Knee Arthroplasty Register (SKAR), the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR), and the Kaiser Permanente Joint Replacement Registry (KPJRR) over a 15 year period (2003–2017).

Patients and methods

Data were obtained for the period January 1, 2003 until December 31, 2017 for KR procedures recorded in the SKAR, AOANJRR, and the KPJRR. Primary KR procedures were defined as all initial unicompartmental, patellofemoral, and total KR. Where replacements were bilateral, both knees were included. Revision KR included all revision procedures of a previous replacement (partial or total) where 1 or more components were added, removed, or exchanged, regardless of whether this was the 2nd or subsequent procedure in chronology. The capture rate of these registries exceeds 95% and loss to follow-up was less than 8% over the study period. Validation and quality control methods of these registries have been published previously (Paxton et al. 2010, Robertsson et al. 2014, AOANJRR 2018).

There were 1,133,079 KR included in this analysis. The SKAR contributed 199,020 KR (186,473 primary and 12,547 revision procedures), there were 732,521 KR from the AOANJRR (674,045 primary and 58,476 revision procedures), and 201,350 KR from the KPJRR (188,538 primary and 12,812 revision procedures) (Table 1).

Statistics

Aggregated data regarding type of procedure as well as patient age and sex were obtained. Population data were obtained from Statistics Sweden and the Australian Bureau of Statistics, as well as the yearly active membership numbers from Kaiser Permanente.

Comparisons were made between countries for yearly procedure volume for both primary and revision KR, as well as yearly incidence per 100,000 population. Stratified analysis for ages < 65 and ≥ 65 years was also carried out. Inclusion of bilateral procedures and multiple revisions was thought to affect each country's analysis similarly. Mean age and sex tables were compiled and the proportions by ages < 65 and ≥ 65 years for both primary and revision KR were included.

Annual percentage change in procedure volume for both primary and revision KR was calculated and the mean for each of the 3 5-year time periods was derived, as described by Patel et al. (2015), to summarize trends in these procedures over time and across countries.

Ethics, funding, and conflicts of interest

Ethics approval covering the SKAR data use was approved by the Ethics Board of Lund University (LU20-02). The AOAN-

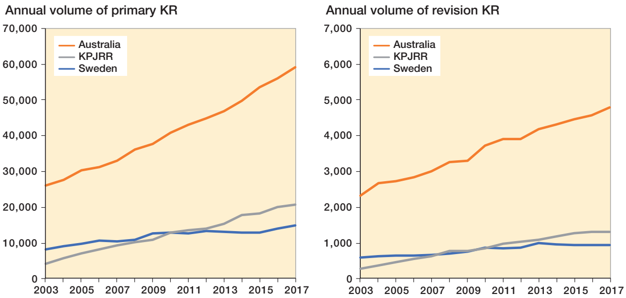

Figure 1. Yearly procedure volume of primary KR (left panel) and revision KR (right panel) recorded by the SKAR, AOANJRR, and KPJRR from 2003 to 2017.

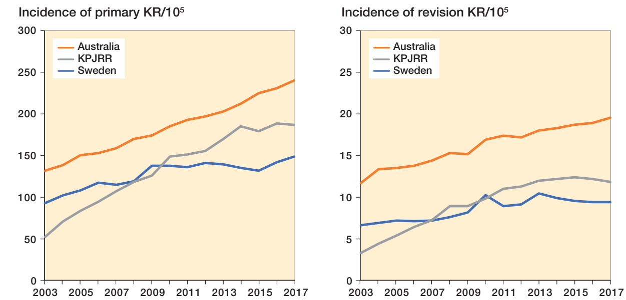

Figure 2. Yearly incidence of primary KR (left panel) and revision KR (right panel) per 10^5 population recorded by the SKAR, AOANJRR, and KPJRR from 2003 to 2017.

JRR is a declared Commonwealth of Australia Quality Assurance Activity under section 124X of the Health Insurance Act, 1973. All AOANJRR studies are conducted in accordance with ethical principles of research (Helsinki Declaration II). Approval for inclusion of data from the Kaiser Permanente Joint Replacement Registry Institutional Review Board approval (#5488) was granted on November 15, 2018.

There was no funding. There are no conflicts of interest.

Results

Throughout the 15 years from 2003 to 2017, annual primary KR procedure volume increased from 8,832 in 2003 to 14,964 in 2017 in Sweden, from 26,008 to 59,002 in Australia, and from 4,271 to 20,672 in the KPJRR. The proportion of total KR rose in both Sweden and Australia from 83.1% and 83.6% to 91.8% and 93.3%, respectively, while the volume of unicompartmental KR reduced. This contrasts with the KPJRR, which had a more constant proportion of total KR remaining around 96% for the entire period. In all 3 registries, the proportion of patellofemoral KR remained low (less than 1%). Over the study period, revision KR procedure volume increased from 596 in Sweden to 945, from 2,314 in Australia to 4,791, and from 274 in the KPJRR to 1,309 (Figure 1). Primary KR volume increases were 79% in Sweden, 127% in Australia, and 384% in the KPJRR. During the same time period, revision KR procedure volume increases were 59% in Sweden, 107% in Australia, and 378% in the KPJRR.

The incidence of primary KR per 100,000 population over this same time span in Sweden increased from 73 to 131 and revision KR incidence increased from 6.6 to 9.4, while in Australia primary KR incidence rose from 132 to 240 and revision KR incidence increased from 11.7 to 19.5. In the KPJRR cohort primary KR incidence/10^5 insured increased from 52 to 187 and revision KR from 3.3 to 11.8 (Figure 2). By this measure, primary KR incidence increased from 2003 to 2017 by 79% in Sweden, 102% in Australia, and 258% in the KPJRR, while over this same time revision KR incidence increased by 42% in Sweden, 63% in Australia, and 255% in the KPJRR. When stratified by age < 65 and ≥ 65 years, the annual incidence/10^5 population for the younger group remained less than 90 for primary KR and less than 8 for revision KR in all 3 registries, while the older cohort from the KPJRR showed the largest increases (from 320 to 884 for primary KR and from 21 to 57 for revision KR) (Figure 3). While the incidence/10^5 in the younger age group remained low, the proportional change over the 15 years in this group for primary KR was 76%, 141%, and 276% for Sweden, Australia, and the KPJRR, respectively, while it was 35%, 58%, and 177% for the ≥ 65 years age group. Over the same time period the increases for revision KR incidence for the < 65 years age group were 39%, 85%, and 277%, and for the ≥ 65 years age group 26%, 32%, and 171% in Sweden, Australia, and the KPJRR, respectively.

When the mean change for each of the 3 5-year periods was calculated for primary and revision KR, all regions showed a deceleration in the increase. The exception is an increase in revision in Sweden between the periods 2003–2007 to 2008–2012 (Figure 4).

During the study period, the mean age of primary and revision KR patients remained stable in all countries (Table 2). The proportion of patients aged < 65 years for both primary and revision KR varied in a narrow range for each registry, peaking in the years 2008–2012 and decreasing again in all instances toward the end of the study period (Table 2). The proportion of women undergoing primary KR decreased in all countries over this 15-year period. The proportion of women undergoing revision KR was lower than in primary KR in all countries and showed little change with time (Table 2).

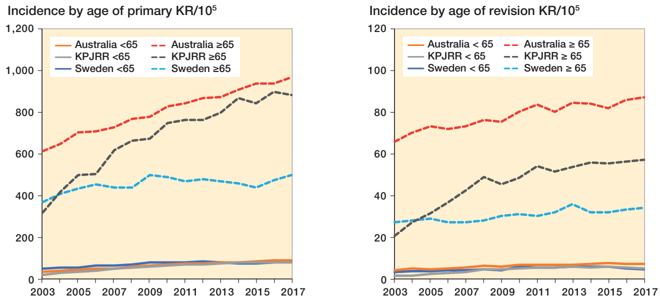

Figure 2. Yearly incidence of primary KR (left panel) and revision KR (right panel) by patient age < 65 and ≥ 65 years per 10^5 population recorded by the SKAR, AOANJRR, and KPJRR from 2003 to 2017.

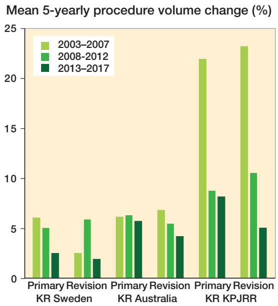

Figure 4. Mean 5-yearly percentage increases in procedure volume in SKAR, AOANJRR, and KPJRR.

Table 2. Yearly mean ages, percentage women, and proportion age < 65 years for primary and revision KR by registry

Factor	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Sweden															
Primary KR															
mean age	69.6	69.5	69.6	69.3	69.3	68.9	69.0	68.8	68.7	68.6	68.6	68.8	68.6	68.9	68.9
women (%)	61.0	61.9	60.0	59.5	60.0	59.3	58.3	58.4	58.2	57.7	57.0	57.2	57.0	56.0	55.7
age < 65 (%)	31.3	31.1	31.0	33.1	32.9	34.3	34.4	34.1	34.7	34.7	33.9	32.9	33.9	33.7	33.2
Revision KR															
mean age	70.7	70.5	70.5	69.9	69.9	69.8	69.2	68.7	68.5	69.4	68.8	68.3	68.5	69.4	69.9
women (%)	58.2	61.0	59.2	61.5	57.5	54.0	61.1	56.6	56.1	55.5	55.5	51.9	54.2	54.6	53.2
age < 65 (%)	29.0	28.9	30.9	35.1	34.2	33.7	33.6	36.7	36.1	33.3	33.5	35.9	34.6	30.9	27.9
Australia															
Primary KR															
mean age	68.7	68.7	68.8	68.6	68.4	68.2	68.1	68.0	67.9	68.1	68.0	68.0	67.9	67.8	67.9
women (%)	56.3	56.8	57.2	56.6	56.9	56.5	56.5	56.3	55.9	56.1	56.4	55.7	55.4	55.5	54.8
age < 65 (%)	32.2	32.4	32.7	33.5	34.2	35.6	35.9	36.2	36.7	35.2	35.6	34.8	35.1	35.4	34.5
Revision KR															
mean age	69.9	68.8	69.5	69.0	69.1	68.7	68.9	68.4	68.6	68.5	68.7	68.6	68.2	68.9	68.9
women (%)	51.6	51.8	50.5	51.5	52.7	51.9	50.8	52.2	50.7	52.3	51.2	52.4	51.3	50.0	51.1
age < 65 (%)	28.7	32.5	29.7	32.4	33.0	34.4	33.9	35.5	33.8	34.2	32.8	34.6	31.3	31.3	30.3
Kaiser Permanente															
Primary KR															
mean age	67.8	67.8	67.8	67.7	67.1	67.1	67.0	67.3	67.3	67.3	67.3	67.3	67.3	67.4	67.5
women (%)	64.4	63.0	64.6	63.4	62.4	61.2	61.7	60.9	61.1	60.6	61.0	60.2	61.5	60.9	60.3
age < 65 (%)	35.8	37.3	36.8	37.2	40.5	41.5	41.3	39.9	40.7	38.8	38.4	38.4	38.0	36.9	36.9
Revision KR															
mean age	68.0	68.0	67.6	66.2	67.5	66.7	66.4	67.3	66.7	66.7	67.1	67.2	66.9	67.5	67.7
women (%)	48.9	54.5	53.3	55.5	53.9	52.8	58.9	55.5	53.0	57.9	53.4	56.9	56.9	53.8	54.8
age < 65 (%)	35.4	34.7	37.9	41.1	39.9	43.9	44.1	43.4	42.1	43.2	41.4	39.7	41.8	39.4	35.7

Discussion

Through the last 15 years, primary and revision KR have increased in all 3 countries studied. Suggested reasons for this widespread change are the increase in the prevalence of knee OA, or increased recognition of the utility of KR by surgeons and the community (Weinstein et al. 2013, Hamilton et al. 2015). The growth in KR in the KPJRR was greater than that seen in the other 2 registries with no clear reason for this difference. This may indicate a previously unmet demand is being filled in this population or be due to local market conditions in the USA. A previous population predictive study has suggested that the rising rate of KR is linked to increasing community obesity (Culliford et al. 2015).

As population profiles may vary both between countries and over time, perhaps a better measure for comparison is incidence/10^5 population. Australia has a higher incidence of both primary and revision KR/10^5 but the incidence in the KPJRR is approaching that of Australia in primary KR. Incidence changes show a parallel increase in primary and revision KR in the KPJRR, while revision incidence growth in both Sweden and Australia has been proportionately less than that of primaries. Incidence increases in the KPJRR cohort were less than the changes in procedure numbers, indicating a larger rise in the population with this insurance.

There has been little change in the mean age of patients receiving either a primary or revision KR in all countries, and little variation in the proportions of KR for patients aged < 65 years. Increases in the use of KR in younger patients are therefore balanced by a comparable increase in the ≥ 65 years age group. This counters the suggestion that KR has been proportionally more frequently used for younger patients over this time (Karas et al. 2019). While the proportion of younger to older KR patients remained stable, the percentage increases in incidence/10^5 in the younger group were greater, a finding consistent with others (Weinstein et al. 2013, Pabinger et al. 2015). In all 3 registries over the study period, there is an increase in the proportion of males receiving a primary KR, and as there are proportionately more males requiring revision (Table 2) this trend may increase future revision rates.

Variation in rates of KR among countries may be due to local economic concerns and health policy, differences in rates of OA, availability of pre-surgical treatments for OA, and access to KR, as well as surgeon availability and variation in thresholds for suitability for operative treatment. The higher incidence of revision KR in Australia compared with the other countries may simply mirror the higher incidence of primary surgery or be due to differences in surgical practice (such as the proportional use of patella resurfacing or cementless fixation) but could also be related to less restricted prosthesis choice in this country.

Part of the reason for a smaller rate of increase in revision KR when compared with primary KR in Sweden and Australia may be due to the decrease in proportion of unicompartmental KR in these countries, as partial KR has more than 2.5 times the rate of revision of total KR at 10 years (AOANJRR 2018). This change may also reflect improved prosthesis performance during this time span, related to factors such as the introduction of more component sizing options or highly cross-linked polyethylene (de Steiger et al. 2015, Turnbull et al. 2016). Alternatively, the relative slowing of revision compared with primary KR may be due to the presence of a time lag between increased numbers of primaries and when they will require revision.

When analysis was carried out by 5-year time periods the increase in both primary and revision surgery decelerated in all countries over the duration of this study, with the only exception being the increase in revision KR in Sweden in 2008–2012 when compared with the earlier period. From our findings, we contend that previous studies predicting an exponential increase in primary and revision KR are incorrect and that a universal deceleration of the growth in primary KR has been experienced, with an even greater slowing in growth of revision KR being evident (Kurtz et al. 2007, Kumar et al. 2015, Patel et al. 2015). However, there is quite a large variation between countries, with the KPJRR cohort showing the greatest percentage increase in both of these procedure types, while Australia and Sweden have a lower growth rate and increasing disparity between primary and revision rates with time. The variations between countries seen in this study over this time period show that predictive models of future demands for 1 region may not translate to others. Our findings also imply that more conservative future estimates would potentially be more accurate, as suggested by Inacio et al. (2017). While there has been a slowing of the increase in the rate of KR in all 3 countries, our findings may not be generalizable to other countries, where different health systems are in place. A limitation of our study is its retrospective nature, which may have little bearing on future trends. In addition, the study is a simple overview of population changes with time, which can be influenced by many factors, and little or no detail as to the reasons for changes is revealed. This area could be the subject of further analysis. Caution should be used in extrapolating the findings of the cohort from the KPJRR as these may not be representative of the changes found elsewhere in the United States. In addition, revision incidence would be overestimated as it has been calculated irrespective of multiple surgeries for the same patient or knee. These methodological limitations are expected to affect each registry similarly and be consistent throughout the study period. There may also be other unknown influences, such as the introduction of new technologies or changing health policies and economics, which can affect each country differently, and these have not been examined in this study.

Conclusion

While there has been an increase in both primary and revision KR across all 3 countries during the past 15 years, the rate of increase has slowed. While there are regional differences in KR incidence, and also differences in rates of change, the rate of increase, particularly in Sweden and Australia, does not seem to be as great as previously predicted. Additionally, the rate of increase in revision KR in these 2 countries is less than the increase in primary KR.

PL: conception of study, statistical analysis, interpretation of data, and manuscript preparation; AWD, MS, OR, EP, HP, and SG: interpretation of data and manuscript preparation.

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Paper II

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Variation and trends in reasons for knee replacement revision: a multi-registry study of revision burden

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Background and purpose — Studies describing time-related change in reasons for knee replacement revision have been limited to single regions or institutions, commonly analyze only 1st revisions, and may not reflect true caseloads or findings from other areas. We used revision procedure data from 3 arthroplasty registries to determine trends and differences in knee replacement revision diagnoses.

Patients and methods — We obtained aggregated data for 78,151 revision knee replacement procedures recorded by the Swedish Knee Arthroplasty Register (SKAR), the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR), and the Kaiser Permanente Joint Replacement Registry (KPJRR) for the period 2003–2017. Equivalent diagnosis groups were created. We calculated the annual proportions of the most common reasons for revision.

Results — Infection, loosening, and instability were among the 5 most common reasons for revision but magnitude and ranking varied between registries. Over time there were increases in proportions of revisions for infection and decreases in revisions for wear. There were inconsistent proportions and trends for the other reasons for revision. The incidence of revision for infection showed a uniform increase.

Interpretation — Despite some differences in terminology, comparison of registry-recorded revision diagnoses is possible, but defining a single reason for revision is not always clear-cut. There were common increases in revision for infection and decreases in revision for wear, but variable changes in other categories. This may reflect regional practice differences and therefore generalizability of studies regarding reasons for revision is unwise.

Although the survivorship of knee arthroplasty has improved over the last 15 years, the increased volume of primary knee replacement has led to growing numbers of revision procedures (Kumar et al. 2015, Patel et al. 2015). A prior study we undertook outlined changes in the volume and incidence of revision rates in Sweden, Australia, and the Kaiser Permanente registry from the USA (Lewis et al. 2020b).

Factors influencing revision change with time. Patient factors may affect the rate of primary procedures, such as rising patient and surgeon acceptance of knee replacement (Hamilton et al. 2015), increasing rates of osteoarthritis (Hunter and Bierma-Zeinstra 2019), growing use in younger patients (Leyland et al. 2016, Karas et al. 2019), and also survivorship, such as longer life expectancy, increasing obesity, and higher physical activity of those receiving a replacement (Hamilton et al. 2015). In addition, prosthesis designs change to improve perceived shortcomings such as wear, instability, and patellofemoral pain and tracking (Lewis et al. 2020a). Methods to improve surgical precision, such as computer navigation (Jones and Jerabek 2018), image-derived instrumentation (Kizaki et al. 2019), and robotic assistance (Jacofsky et al. 2016) may decrease revision requirements (Price et al. 2018)

These changing factors alter the reasons for revision. Previous studies observed a decrease in revisions for wear and loosening (Sharkey et al. 2014, Thiele et al. 2015), and related this to improved prosthesis design and materials. Other studies note infection is now the most common reason for revision (Koh et al. 2017, Postler et al. 2018). Studies of changing knee replacement failure modes are limited by being derived from single institutions or regions and may not accurately reflect what is occurring elsewhere (Sharkey et al. 2014, Thiele et al. 2015, Dyrhovden et al. 2017, Koh et al. 2017, Lum et al. 2018,

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Postler et al. 2018). Additionally, these studies do not show the true revision burden as they are restricted to 1st revision procedures, or only revisions of previous total knee replacements (TKR), and do not include revisions of partial knee replacement procedures.

Combining registry data can be difficult due to inconsistency in the definition of revision (Liebs et al. 2015), and lack of consensus in defining modes of failure, with different terminologies used (Niinimaki 2015, Siqueira et al. 2015). Some have attempted to overcome this by defining equivalent diagnoses (Havelin et al. 2011, Paxton et al. 2011, Rasmussen et al. 2016).

We determined variations and trends in reasons for knee replacement revision using data on all knee arthroplasty revision procedures from the national registries of Sweden and Australia and the institutional registry of Kaiser Permanente in the USA by using equivalent diagnosis groups (Table 1, see Supplementary data).

Patients and methods

We obtained data for the period January 1, 2003 until December 31, 2017 for all revision knee replacement procedures recorded in the Swedish Knee Arthroplasty Register (SKAR), Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR), and the Kaiser Permanente Joint Replacement Registry (KPJRR).

Revision knee replacements included all revision procedures of a previous replacement where 1 or more components were added, removed, or exchanged, regardless of whether this was the 2nd or subsequent procedure in chronology. Revisions of all types of knee replacement were included irrespective of whether the arthroplasty was a partial or total knee replacement. Where knee revisions were bilateral, both knees were included and recorded separately. The capture rate or completeness of these registries exceeds 95% and loss to follow-up was less than 8% over the study period. Validation and quality control methods of these registries have been published (Paxton et al. 2010, Robertsson et al. 2014, AOANJRR 2019).

In all registries the reason for revision was determined from the revision diagnosis selected by the surgeon at the time of the revision procedure from a predetermined list, or specifically added. Multiple reasons could be listed. In Sweden all operative reports were methodically read and from these the primary reason for revision was interpreted by registry staff. In the AOANJRR and KPJRR, when multiple reasons for revision were recorded, a diagnosis hierarchy was used to determine the most important reason for revision. In this study only one reason for revision was permitted for each revision procedure.

We included 78,151 revision knee replacement procedures. The SKAR contributed 12,612 revision procedures, the AOANJRR 53,853 revisions, and the KPJRR 11,686 revisions.

Using the categories from the SKAR as a basis, a table of equivalent diagnoses was created. For each registry the reasons for revision were then reclassified according to the "harmonized diagnosis" category.

Statistics

Aggregated data regarding procedure numbers, patient age, and sex were obtained for each registry (Table 2, see Supplementary data). After categorization using the equivalent diagnosis method, the number of revisions for each of the 10 most common reasons was determined and the remainder classed as "other" (Table 3, see Supplementary data). The "other" category also included a small percentage of missing data (1.1% or 137 procedures) from Sweden. The "other" group from the KPJRR contained those with a recorded diagnosis of "failed TKR," which contributed between 3.3% and 12% of all revisions each year.

For all registries the annual proportions of each harmonized revision diagnosis were calculated. For further analysis of revision for infection, the incidence per 100,000 was calculated from population data obtained from Statistics Sweden and the Australian Bureau of Statistics, as well as the yearly active membership numbers from Kaiser Permanente.

Ethics, funding, and conflicts of interest

Ethics approval covering the SKAR data use was issued by the Ethics Board of Lund University (LU20-02). The AOANJRR is a declared Commonwealth of Australia Quality Assurance Activity under section 124X of the Health Insurance Act, 1973. All AOANJRR studies are conducted in accordance with the ethical principles of research (Helsinki Declaration II). Approval for inclusion of data from the Kaiser Permanente Joint Replacement Registry Institutional Review Board r(#5488) was granted on November 15, 2018.

There was no funding. There are no conflicts of interest.

Results

Considering all revisions during the entire time period, infection was the most frequent revision diagnosis in the SKAR and KPJRR while loosening was most common in the AOANJRR. Instability, patellar causes, progression of disease, wear, and pain showed variable proportions across the registries (Figure 1.)

The number of revisions and yearly proportions for each of the 10 most common reasons for revision are given in Table 3 (see Supplementary data) and a graphical representation of the proportions to highlight trends is shown in Figure 2.

In all registries, there was an increase in the proportion of revisions for infection through the study period rising from 20%, 16%, and 22% in the Swedish, Australian, and KP registries in 2003 to 35%, 30%, and 43% in 2017, respectively. To determine whether this was a true rise, not just a propor-

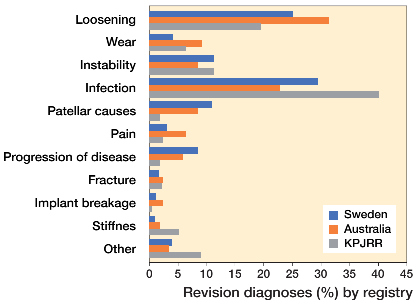

Figure 1. Overall revision diagnoses shown as a proportion for each registry.

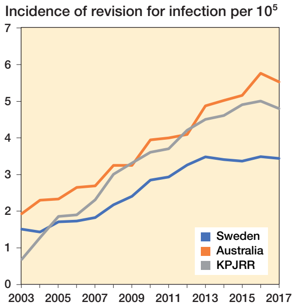

Figure 3. Yearly incidence of revision knee replacement for infection per 100,000 population for the SKAR, AOANJRR, and KPJRR.

tionate increase, the yearly incidence of revision procedures for infection was calculated. This also increased in all registries (Figure 3.) Revision for loosening fell from 41% in 2003 to 13% in 2017 in the AOANJRR but a smaller decline was seen in the SKAR (27% to 23%), while the proportion in the KPJRR fell from 27% in 2003 to 14% 2008 but then rose and remained around 20% from 2011 to 2017. There was a universal decrease in revisions for wear with the proportions declining from 6.5% to 1.5% in Sweden, 13% to 5.3% in Australia, and 21% to 4.8% in the KPJRR. Instability as a revision diagnosis showed a trend for increase in Sweden and Australia, but fluctuated in the KPJRR. Revisions for patellar reasons contributed to a higher proportion of revisions in Sweden than Australia, showing a modest increase in these 2 countries while this diagnosis was infrequent in the KPJRR. Stiffness contributed proportionally more as a revision diagnosis in the

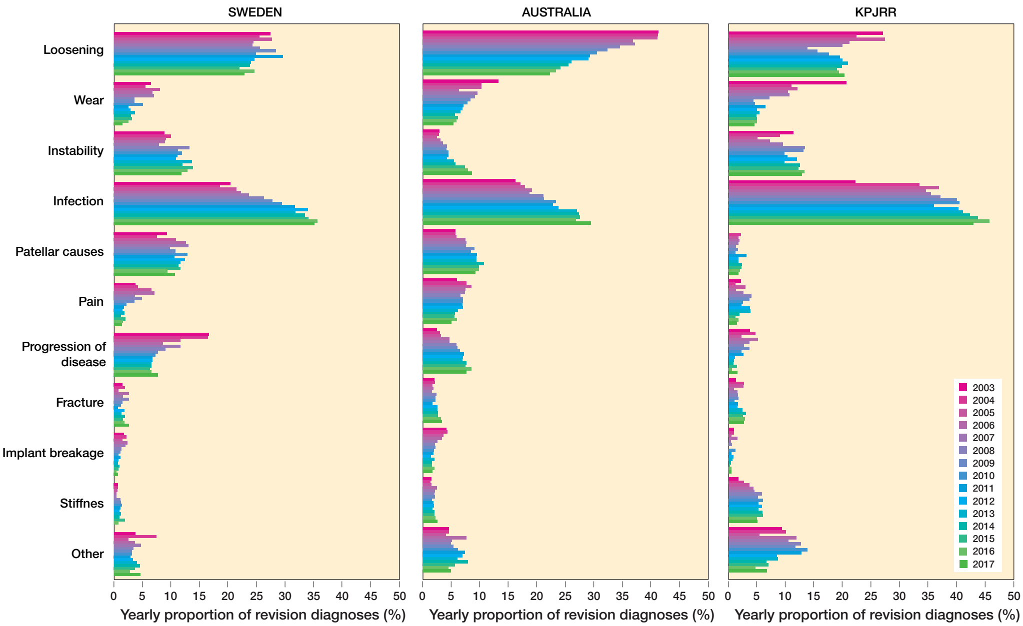

Figure 2. Yearly proportions of knee replacement revision recorded in the SKAR, the AOANJRR, and the KPJRR, respectively.

KPJRR, where this reason showed a small increase with time. There was a general tendency for fewer revisions for pain throughout all registries toward the end of the time period. Progression of disease decreased over time in both Sweden and the KPJRR while it increased in Australia as a reason for revision. Fracture and implant breakage were uncommon causes of revision in all registries.

Discussion

We have previously shown a decrease in all-cause revision rates in all 3 of these registries, but the reasons for revision were not studied (Lewis et al. 2020b). In the present study, when considering the entire study period, infection, loosening, and instability were among the 5 most common reasons for revision in all 3 registries; however, ranking and proportions of these varied. Over time, reasons for knee replacement revision changed, and while there were some similarities in rising proportions of revisions for infection, and decreasing proportions for wear, there were also differences between registries in 8 of the 10 most common revision reasons. These findings suggest revision reasons are partially dependent on factors specific to each healthcare system, and while variation in prosthesis use may be a major cause, analysis of this aspect is the subject of a further study.

A limitation of this study is that categorizing revision diagnoses can be subjective. While many diagnoses are self-evident, in a knee replacement with pronounced wear, loosening, instability, and prosthesis breakage it can be difficult to determine which is the main cause of failure. This choice may vary between surgeons. There may be differences in interpretation: where one surgeon may nominate “progression of disease” as the reason for revision, another may record “patella erosion” for the same clinical findings. These interpretive differences can exist both within and between registries. A technique to limit the effect of this would be to correlate the revision diagnosis with the revision procedure.

Using the method of equivalent diagnoses, we created a “cross-walk” between reported reasons for revision in each of the registries. Most categorizing of revision reasons is straightforward but in a few instances creation of a format to compare registry results is also open to subjectivity. For example, the diagnosis of “inflammatory arthritis” in the KPJRR has been considered as “progression of disease” but may be the equivalent to the AOANJRR diagnosis of “synovitis,” which has been classed as “other.” While malalignment is a revision diagnosis in the AOANJRR, neither the SKAR nor the KPJRR record this specific diagnosis separately, and therefore these are included in the “other” category. Registries may also have “systematic” differences in ranking of relative importance where more than 1 diagnosis is reported. These classification and ranking issues are likely to have only a small effect on the overall results.

A further limitation is that while we included all knee revision procedures to compare revision burdens and changing reasons for revision with time, we could not determine whether these changes relate to the first or subsequent revisions. However, previous registry analyses have shown that 60–85% of annual revisions are first revisions (AOANJRR 2019). There was a universal increase in proportion and yearly incidence of revisions for infection in the 3 registries studied. The reason for this worrying widespread increase is not clear, but is consistent with the findings of others (Sharkey et al. 2014, Dyrhovden et al. 2017, Koh et al. 2017). It has been suggested that debridement, antibiotics, and implant retention with only polyethylene insert exchange (DAIR) is being increasingly and more aggressively used for the treatment of periprosthetic infection (Kunutsor et al. 2018).

Increases in revisions for infection are even more concerning as registries under-report infection, particularly missing non-revision episodes of treatment that do not have a prosthetic component removed or replaced (Witsø 2015, Zhu et al. 2016). In the AOANJRR, where the reason for revision is recorded at the time of operation, there may be under-reporting of infection where delayed culture results are returned as positive and, similarly, there may be a small proportion of over-reporting where a suspicion of infection is not supported by microbiological results. This type of inaccuracy would be lower in the SKAR and KPJRR as these registries can postoperatively modify the recorded diagnosis of infection on the basis of microbiological results (SKAR 2019).

Revisions for wear decreased in all 3 registries, which is also a finding reported by others (Le et al. 2014, Sharkey et al. 2014, Thiele et al. 2015). Proposed reasons for this decrease are improvements in polyethylene by modified sterilization and packaging methods (Faris et al. 2006), increased use of highly cross-linked polyethylene (de Steiger et al. 2015), increased bearing conformity (Zhang et al. 2019), altered knee kinematics with femoral component design changes (Gilbert et al. 2014), or decreased tibial baseplate roughness and improved polyethylene locking mechanisms (Sisko et al. 2017).

Loosening decreased as a reason for revision in both the SKAR and AOANJRR but remained unchanged in the KPJRR. The SKAR can determine which components have loosened from the operative records, but in the other 2 registries this is not possible. While an impression may be obtained by correlation with the components changed in the revision procedures, this may not be precise as, for example, if tibial loosening alone is present, both major components may be revised to allow for increased stability in the revision prosthesis configuration. Late loosening is thought to be related to wear and its consequence of osteolysis (Holt et al. 2007) and would be expected to decrease as polyethylene wear decreases. Early loosening, in contrast, most likely relates to a lack of initial fixation and is greater where cementless prostheses are used with the intent of biological fixation (Aprato et al. 2016). While our study did not explore prostheses attributes, the inter-registry differences in loosening may relate to the proportional use of cementless implants or factors such as different bone cements and cementing techniques or types of polyethylene inserts used.

The Swedish and Australian registries showed an increase in proportion of revision for instability. While this finding supports previous reports (Thiele et al. 2015, Dyrhovden et al. 2017), it contrasts with another where a decrease has been shown (Sharkey et al. 2014). An explanation for this change could be an increase in recognition of instability, where revisions that were once diagnosed as pain of unknown origin have increasingly been interpreted as pain due to instability (Firestone and Eberle 2006, Grayson et al. 2016). Another possibility is the development of new knowledge, with the dissemination and acceptance of the concept of mid-flexion instability during the study period (Ramappa 2015, Longo et al. 2020). There may also be a link between instability revisions and the use of posterior cruciate substituting prostheses (Hino et al. 2013).

Patellar causes for revision made up a consistently higher proportion of revisions in Sweden, followed by Australia and then the KPJRR. While revisions in this category predominantly involve secondary insertion of a patellar component in a previously un-resurfaced patella and much of this difference may relate to the use of patellar components at the time of primary surgery, it also includes patellar component revisions and even patellectomy. In 2018 in Sweden there was a 3% rate of primary patellar component use (SKAR 2019), in Australia the rate of use has climbed from 42% in 2005 to 69% in 2018 (AOANJRR 2019), while in the KPJRR patellar component use has been reported at 98% (Paxton et al. 2011). Leaving the patella unresurfaced allows the potential need for a secondary resurfacing procedure. Additionally, there may be differences relating to the prostheses used with respect to generation of anterior knee pain or other patellar complications such as maltracking.

While there were no consistent trends in revision for progression of disease or for pain, these 2 categories are more difficult to understand. Revision for progression of disease was higher in Sweden than in the other 2 registries, and may, in part, be explained by the possible inclusion of patellar erosion or patellar degenerative change of an un-resurfaced patella as diagnoses in this category. The proportion of knees revised for progression of disease in Sweden decreased with time, and may mirror the fall in proportional use of unicompartmental knee replacement (from 13% of primary knee replacement in 2003 to 9% in 2017) (Lewis et al. 2020b) . However, these factors cannot explain the increase in revision for progression of disease in Australia, where there has been a decrease in use of unicompartmental knee replacement (from 15% of primary knee replacement in 2003 to 6% in 2017) with an increase in patellar component use (from 41% of primary TKR in 2005 to 67% in 2017) (AOANJRR 2019). Similarly, this cannot explain the decline in the KPJRR where unicompartmental knee use and patellar resurfacing remained constant (at 4% and 98% respectively) (Lewis et al. 2020b, Paxton et al. 2011). (The annual procedure numbers of partial and total knee replacement for each registry have been described in our previous paper—Lewis et al. 2020b). Other covert factors, such as the inclusion of revisions of knee replacements from the time prior to the commencement of this study where the proportions of unicompartmental or patellar prosthesis use are unknown, may contribute to these findings.

The revision diagnoses of fracture, stiffness, and component breakage occurred infrequently. Fracture as a reason for revision showed a small increase, which is possibly related to a globally ageing and more osteoporotic knee replacement population (Johnson et al. 2019). Revision for fracture would understate the frequency of periprosthetic fracture, as many of these are treated by means other than revision, such as fracture fixation alone. Stiffness or true arthrofibrosis is rare, and there can be cultural differences in patients, and possibly even their surgeons, proceeding to revision surgery for this reason (Springer et al. 2012). Similar to fracture, registry data does not reflect the true incidence of stiffness, as non-revision treatment methods, such as manipulation under anesthetic, are not included. A decline in implant breakage may reflect improved component durability.

Of concern is the "other" diagnosis category from the KPJRR, which included a diagnosis of "failed TKR." The true reason for revision in these procedures is unclear, but the proportion in the "other" group decreased over the study period, indicating improving precision of revision diagnosis records in this registry. The influence of this is difficult to determine.

In conclusion, we have shown that despite some differences in terminology it is possible to compare registry data regarding reasons for revision. Defining a single reason for knee replacement revision is not always clear-cut. While infection, loosening, and instability are within the 5 most common reasons for revision for all 3 registries studied, their magnitude and ranking varied through the period. There were consistent increases in revision for infection, and decreases in revision for wear, but variable changes in other categories. Findings from the 3 registries studied differed, which may reflect regional differences in patient, prosthesis, or technique characteristics, and further study is required to define these practice variations. Widespread generalizability of studies regarding reasons for knee replacement revision may not be prudent. There may also be a place for defining the revision diagnoses by an international consensus, in the method Kalson et al. (2016) used for arthrofibrosis, which would give clarity, consistency, and better understanding of this area.

Supplementary data

Tables 1–3 are available as supplementary data in the online version of this article, http://dx.doi.org/10.1080/17453674.2020.1853340

PL: conception of study, statistical analysis, interpretation of data, manuscript preparation. AWD, OR, and HP: statistical analysis, interpretation of data, manuscript preparation. SG, EP: interpretation of data and manuscript preparation.

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Supplementary data

Table 1. Table of equivalent diagnoses for each registry

Harmonized diagnosis	Sweden diagnoses	Australian diagnoses	KP diagnoses
1. Loosening	Loosening	Loosening	Aseptic loosening Ingrowth failure
2. Wear	Implant wear	Wear tibial insert Lysis Metal related pathology Wear tibia Wear patella Wear femur	Poly liner wear Osteolysis Implant wear
3. Instability	Instability Dislocated polyethylene	Instability Bearing dislocation Prothesis dislocation	Instability
4. Infection	Infection	Infection	Infection wound drainage
5. Patellar causes	Patellar causes	Patellofemoral pain Patellar erosion Patellar maltracking	Patellofemoral joint malfunction Failed extensor mechanism Patellar causes
6. Pain	Pain	Pain	Pain
7. Progression of disease	Progress of disease	Progression of disease	Osteoarthritis Inflammatory arthritis Old rheumatoid Posttraumatic arthritis
8. Fracture	Bone fracture	Fracture	Fracture
9. Implant breakage	Implant fracture	Implant breakage tibial insert Implant breakage tibia Implant breakage patella Implant breakage femur	Component fracture/breakage
10. Stiffness	Stiffness	Arthrofibrosis	Arthrofibrosis/stiffness
11. Other	Other Tumor Surgical error Missing	Malalignment Incorrect sizing Synovitis Osteonecrosis Tumor Heterotopic bone Incorrect side Other	Failed TKR Failed UKA Failed Unispacer AVN Synovial impingement Hematoma Other
12. Excluded (non-revision procedures)	Gangrene Cement/free body		Wound dehiscence Failed ORIF

Table 2. Yearly procedure numbers, mean ages, and percentage of females for revision knee replacement 2003– 2017 by registry

Registry	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Sweden															
Revisions, n	657	686	715	698	698	757	801	904	870	903	1,043	980	962	966	972
Mean age	70.7	70.5	70.5	69.9	69.9	69.8	69.2	68.7	68.5	69.4	68.8	68.3	68.5	69.4	69.9
Female sex (%)	58.2	61.0	59.2	61.5	57.5	54.0	61.1	56.6	56.1	55.5	55.5	51.9	54.2	54.6	53.2
Australia															
Revisions, n	2,314	2,663	2,721	2,826	2,994	3,250	3,294	3,716	3,984	3,910	4,173	4,301	4,447	4,559	4,791
Mean age	69.9	68.8	69.5	69	69.1	68.7	68.9	68.4	68.6	68.5	68.7	68.6	68.2	68.9	68.9
Female sex (%)	51.6	51.8	50.5	51.5	52.7	51.9	50.8	52.2	50.7	52.3	51.2	52.4	51.3	50	51.1
Kaiser Permanente															
Revisions, n	247	338	423	473	556	704	706	780	908	947	992	1,051	1,148	1,177	1,236
Mean age	68.0	67.7	67.5	66.2	67.9	66.6	66.5	67.4	66.6	66.8	67.1	67.2	67.1	67.4	67.7
Female sex (%)	47.4	53.9	53.2	55.6	54.0	54.1	58.4	55.5	53.0	58.6	52.8	56.0	56.5	52.8	54.6

Table 3a. Yearly number and proportions of reasons for revision — Sweden

Reason for revision	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Loosening, n	180	176	189	171	170	194	228	225	258	224	251	235	213	238	224
%	*27.4*	*25.5*	*27.7*	*24.4*	*24.3*	*25.6*	*28.4*	*24.9*	*29.6*	*24.6*	*24.0*	*23.9*	*22.0*	*24.6*	*22.9*
Wear, n	43	38	58	47	49	27	29	46	22	26	39	30	30	24	15
%	*6.5*	*5.5*	*8.1*	*6.7*	*7.0*	*3.6*	*3.6*	*5.1*	*2.5*	*2.9*	*3.7*	*3.0*	*3.1*	*2.5*	*1.5*
Instability, n	58	69	65	62	55	100	90	108	97	99	144	118	134	125	116
%	*8.8*	*10.0*	*9.1*	*8.9*	*7.9*	*13.2*	*11.2*	*11.9*	*11.1*	*10.9*	*13.7*	*12.0*	*13.9*	*12.9*	*11.8*
Infection, n	135	128	154	156	166	199	223	266	276	309	333	330	329	345	345
%	*20.4*	*18.6*	*21.5*	*22.2*	*23.7*	*26.3*	*27.8*	*29.4*	*31.7*	*34.0*	*31.8*	*33.5*	*34.1*	*35.7*	*35.2*
Patellar causes, n	61	52	78	88	91	74	87	117	92	113	122	111	112	90	105
%	*9.3*	*7.5*	*10.9*	*12.6*	*13.0*	*9.8*	*10.8*	*12.9*	*10.6*	*12.4*	*11.6*	*11.3*	*11.6*	*9.3*	*10.7*
Pain, n	25	29	47	50	26	37	29	20	15	14	19	12	19	15	14
%	*3.8*	*4.2*	*6.6*	*7.1*	*3.7*	*4.9*	*3.6*	*2.2*	*1.7*	*1.5*	*1.8*	*1.2*	*2.0*	*1.6*	*1.4*
Progr. of disease, n	109	114	84	60	81	68	62	66	59	61	68	65	61	64	75
%	*16.6*	*16.5*	*11.7*	*8.6*	*11.6*	*9.0*	*7.7*	*7.3*	*6.7*	*6.7*	*6.6*	*6.6*	*6.3*	*6.6*	*7.7*
Fracture	10	13	6	18	11	20	12	11	6	16	14	19	15	17	25
%	*1.5*	*1.9*	*0.8*	*2.6*	*1.6*	*2.6*	*1.5*	*1.2*	*0.7*	*1.8*	*1.3*	*1.9*	*1.6*	*1.8*	*2.6*
Implant breakage, n	11	15	11	16	14	10	9	7	10	7	7	9	8	4	7
%	*1.7*	*2.2*	*1.5*	*2.3*	*2.0*	*1.3*	*1.1*	*0.8*	*1.1*	*0.8*	*0.7*	*0.9*	*0.8*	*0.4*	*0.7*
Stiffness, n	0	5	5	4	3	3	9	11	12	10	9	12	9	18	8
%	*0*	*0.7*	*0.7*	*0.6*	*0.4*	*0.4*	*1.1*	*1.2*	*1.4*	*1.1*	*0.9*	*1.2*	*0.9*	*1.9*	*0.8*
Other, n	25	47	18	26	32	25	23	27	23	24	37	39	32	26	38
%	*3.8*	*7.4*	*2.5*	*3.7*	*4.7*	*3.4*	*3.1*	*3.1*	*2.9*	*3.3*	*4.0*	*4.5*	*3.7*	*2.8*	*4.6*
Total, n	657	686	715	698	698	757	801	904	870	903	1,043	980	962	966	972

Table 3b. Yearly number and proportions of reasons for revision — Australia

Reason for revision	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Loosening, n	957	1,099	1,122	1,043	1,113	1,124	1,067	1,133	1,145	1,133	1,091	1,097	1,078	1,070	1,068
%	*41.4*	*41.3*	*41.2*	*36.9*	*37.2*	*34.6*	*32.4*	*30.5*	*29.4*	*29*	*26.1*	*25.5*	*24.2*	*23.4*	*22.3*
Wear, n	307	274	281	179	288	295	274	290	275	269	277	240	278	263	254
%	*13.3*	*10.3*	*10.3*	*6.3*	*9.6*	*9.1*	*8.3*	*7.8*	*7.1*	*6.9*	*6.6*	*5.6*	*6.2*	*5.8*	*5.3*
Instability, n	68	75	66	87	104	136	135	168	175	164	227	145	326	361	413
%	*2.9*	*2.8*	*2.4*	*3.1*	*3.5*	*4.2*	*4.1*	*4.5*	*4.5*	*4.2*	*5.4*	*5.7*	*7.3*	*7.9*	*8.6*
Infection	378	456	468	540	559	688	701	869	892	930	1,127	1,179	1,227	1,228	1,413
%	*16.3*	*17.1*	*17.9*	*19.1*	*18.7*	*21.2*	*21.3*	*23.4*	*22.9*	*23.8*	*27.0*	*27.4*	*27.6*	*26.9*	*29.5*
Patellar causes, n	129	150	156	207	229	244	295	312	368	369	392	462	436	436	442
%	*5.7*	*5.7*	*5.8*	*7.4*	*7.6*	*7.5*	*9.0*	*8.4*	*9.5*	*9.4*	*9.4*	*10.7*	*9.8*	*9.8*	*9.2*
Pain, n	137	202	230	209	218	213	232	260	269	275	257	239	246	275	241
%	*5.9*	*7.6*	*8.5*	*7.4*	*7.3*	*6.6*	*7.0*	*7.0*	*6.9*	*7.0*	*6.2*	*5.6*	*5.5*	*6.0*	*5.0*
Progr. of disease, n	55	80	88	133	141	187	201	242	281	274	290	330	328	386	367
%	*2.4*	*3.0*	*3.2*	*4.7*	*4.7*	*5.8*	*6.1*	*6.5*	*7.2*	*7.0*	*6.9*	*7.7*	*7.4*	*8.5*	*7.7*
Fracture, n	47	55	46	51	49	74	71	82	66	97	105	113	122	144	157
%	*2.0*	*2.1*	*1.7*	*1.8*	*1.6*	*2.3*	*2.2*	*2.2*	*1.7*	*2.5*	*2.5*	*2.6*	*2.7*	*3.2*	*3.3*
Implant breakage, n	94	115	97	92	76	67	73	70	69	56	82	68	70	90	82
%	*4.1*	*4.3*	*3.6*	*3.3*	*2.5*	*2.1*	*2.2*	*1.9*	*1.8*	*1.4*	*2.0*	*1.6*	*1.6*	*2.0*	*1.7*
Stiffness, n	35	35	41	69	63	64	70	59	70	73	70	88	88	99	120
%	*1.5*	*1.3*	*1.5*	*2.4*	*2.1*	*2.0*	*2.1*	*1.6*	*1.8*	*1.9*	*1.7*	*2.0*	*2.0*	*2.2*	*2.5*
Other, n	107	122	108	216	154	158	175	231	284	270	255	340	248	207	234
%	*4.6*	*4.6*	*4.0*	*7.6*	*5.1*	*4.9*	*5.3*	*6.2*	*7.3*	*6.9*	*6.1*	*7.9*	*5.6*	*4.5*	*4.9*
Total, n	2,314	2,663	2,721	2,826	2,994	3,250	3,294	3,716	3894	3,910	4,173	4,301	4,447	4,559	4,791

Table 3c. Yearly number and proportions of reasons for revision — Kaiser Permanente

Reason for revision	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Loosening, n	67	76	116	100	111	97	110	137	177	189	208	208	218	227	251
%	*27.1*	*22.5*	*27.4*	*21.1*	*20.0*	*13.8*	*15.6*	*17.6*	*19.5*	*20.0*	*21.0*	*19.8*	*19.0*	*19.3*	*20.3*
Wear, n	51	37	51	49	59	50	30	36	58	46	54	50	56	57	56
%	*20.7*	*11.0*	*12.1*	*10.4*	*10.6*	*7.1*	*4.3*	*4.6*	*6.4*	*4.9*	*5.4*	*4.8*	*4.9*	*4.8*	*4.5*
Instability, n	28	30	21	34	53	94	92	76	93	113	96	131	141	156	159
%	*11.3*	*8.9*	*5.0*	*7.2*	*9.5*	*13.4*	*13.0*	*9.7*	*10.2*	*11.9*	*9.7*	*12.5*	*12.3*	*13.3*	*12.9*
Infection, n	55	113	156	164	197	262	283	316	328	382	408	445	502	539	531
%	*22.3*	*33.4*	*36.9*	*34.7*	*35.4*	*37.2*	*40.1*	*40.5*	*36.1*	*40.3*	*41.1*	*42.3*	*43.7*	*45.8*	*43.0*
Patellar causes, n	0	7	7	9	9	9	11	9	28	16	16	24	25	23	21
%	*0.0*	*2.1*	*1.7*	*1.9*	*1.6*	*1.3*	*1.6*	*1.2*	*3.1*	*1.7*	*1.6*	*2.3*	*2.2*	*2.0*	*1.7*
Pain, n	5	4	12	6	14	28	25	19	20	35	37	19	13	20	17
%	*2.0*	*1.2*	*2.8*	*1.3*	*2.5*	*4.0*	*3.5*	*2.4*	*2.2*	*3.7*	*3.7*	*1.8*	*1.1*	*1.7*	*1.4*
Progr. of disease, n	9	16	9	24	20	19	25	17	23	10	8	8	15	6	18
%	*3.6*	*4.7*	*2.1*	*5.1*	*3.6*	*2.7*	*3.5*	*2.2*	*2.5*	*1.1*	*0.8*	*0.8*	*1.3*	*0.5*	*1.5*
Fracture, n	3	9	11	4	8	11	12	7	14	14	23	31	28	32	33
%	*1.2*	*2.7*	*2.6*	*0.9*	*1.4*	*1.6*	*1.7*	*0.9*	*1.5*	*1.5*	*2.3*	*3.0*	*2.4*	*2.7*	*2.7*
Implant breakage, n	2	3	2	7	2	4	0	9	4	7	6	4	2	5	6
%	*0.8*	*0.9*	*0.5*	*1.5*	*0.4*	*0.6*	*0.0*	*1.2*	*0.4*	*0.7*	*0.6*	*0.4*	*0.2*	*0.4*	*0.5*
Stiffness, n	4	9	15	20	25	41	36	47	47	55	51	62	69	57	61
%	*1.6*	*2.7*	*3.6*	*4.2*	*4.5*	*5.8*	*5.1*	*6.0*	*5.2*	*5.8*	*5.1*	*5.9*	*6.0*	*4.8*	*4.9*
Other, n	23	34	23	56	58	89	82	107	116	80	85	69	79	55	83
%	*9.3*	*10.1*	*5.4*	*11.8*	*10.4*	*12.6*	*11.6*	*13.7*	*12.8*	*8.5*	*8.6*	*6.6*	*6.9*	*4.7*	*6.7*
Total, n	247	338	423	473	556	704	706	780	908	947	992	1,051	1,148	1,177	1,236

Paper III

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The effect of patient and prosthesis factors on revision rates after total knee replacement using a multi-registry meta-analytic approach

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† Otto Robertsson died October 2nd 2021. Dr Michael Dunbar, an old friend to Otto, wrote an obituary for the Knee Society, see postscript on page 293.

Background and purpose — Characteristics of patients receiving total knee arthroplasty (TKA) and prostheses used vary between regions and change with time. How these practice variations influence revision remains unclear. We combined registry data for better understanding of the impact of variation, which could potentially improve revision rates.

Patients and methods — We used data from 2003 to 2019 for primary TKA from arthroplasty registries of Sweden (SKAR), Australia (AOANJRR), and Kaiser Permanente (KPJRR). We included 1,072,924 TKA procedures for osteoarthritis. Factors studied included age, sex, ASA class, BMI category, prosthesis constraint, fixation, bearing mobility, patellar resurfacing, and polyethylene type. Cumulative percentage revision (CPR) was calculated using Kaplan–Meier estimates, and unadjusted Cox hazard ratios were used for comparisons. Random-effects generic inverse-variance meta-analytic methods were used to determine summary effects.

Results — We found similarities in age and sex, but between-registry differences occurred in the other 7 factors studied. Patients from Sweden had lower BMI and ASA scores compared with other registries. Use of cement fixation was similar in the SKAR and KPJRR, but there were marked differences in patellar resurfacing and posterior stabilized component use. Meta-analysis results regarding survivorship favored patients aged ≥ 65 years and minimally stabilized components. There were inconsistent results with time for sex, fixation, and bearing mobility, and no differences for the patellar resurfacing or polyethylene type comparisons.

Interpretation — Marked practice variation was found. Use of minimally stabilized and possibly also cemented and fixed bearing prostheses is supported.

Total knee arthroplasty (TKA) prosthesis survivorship is > 95% at 10 years (1-3). TKA revision rates vary according to the region (4,5) and over time (1,6). However, how these differences affect revision rates remains unclear, or whether improvement is possible choosing certain TKA attributes.

Patient factors that influence TKA survivorship include age (5,7), sex (8), obesity (9,10), and comorbidity (11,12). Key prosthesis factors are prosthesis constraint (13,14), bearing mobility (15,16), fixation method (17,18), patellar resurfacing (19,20), and polyethylene type (21,22).

Randomized trials are unsuitable for studying these factors, as strict inclusion/exclusion criteria and use of standardized prostheses may complicate generalizability. Registry studies are limited by prosthesis choice confounding, and difficulty in assessing each factor's influence. Propensity score matching and instrumental variable analysis are methods to reduce selection bias, but these may still not control for unmeasured confounding, or fit the assumption of instrument and outcome independence (23,24).

Considerable practice variability exists among specialist TKA surgeons both within and between countries (25,26). An example is patellar resurfacing rates, which varied from 4% in Norway to 82% in the USA (27). These differences provide opportunity to explore variables that may influence prosthesis survivorship (a "natural experiment") (28). Combining data may balance distortions resulting from differential prosthesis use, enhancing understanding of the relationship between these factors and revision rates. Sharing even de-identified patient data is often not possible due to data ownership regulations and concerns regarding privacy and data security. Using a meta-analytic approach to pool registry data has proven utility, being shown to be similar to individual patient-level data analysis (29).

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In a previous study we found inter-registry differences regarding reasons for knee replacement revision and theorized this was related to patient selection and prosthesis choice (30). This study (i) documents regional and temporal variation in primary TKA practice across 3 registries between 2003 and 2019 and (ii) uses a meta-analytic technique to determine the influence of each factor on the risk of revision.

Patients and methods

We obtained aggregate annual data for the period January 1, 2003 until December 31, 2019 for all primary TKA procedures recorded in the Swedish Knee Arthroplasty Register (SKAR), the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR), and the Kaiser Permanente Joint Replacement Registry (KPJRR). Only TKA for osteoarthritis (OA) was included. Partial knee arthroplasties, revision TKA, and TKA for pathologies other than OA were excluded. The completeness of these registries exceeds 95% and loss to follow-up was less than 8% over the study period. Validation and quality control methods of these registries have been published (2,31,32).

There were 1,072,924 primary TKA for OA included (188,290 from the SKAR, 663,982 from the AOANJRR, and 220,652 from the KPJRR). Patient factors recorded were age, sex, ASA score, and body mass index (BMI). As the SKAR and AOANJRR began collecting ASA and BMI data at later time points, these categories permitted limited analyses.

We analyzed 5 prosthesis factors. Prosthesis constraint was divided into minimally stabilized (MS) (those that have a flat or dished tibial articulation, regardless of congruency), posterior stabilized (PS) (implants that provide posterior stability using a peg and box design), fully stabilized (FS) (implants with a large peg and box design designed to give some collateral as well as posterior stability), and hinged (implants with a hinge mechanism to link the femoral and tibial components). Fixation was cemented (both femoral and tibial components cemented), cementless (both components inserted without cement), and hybrid (tibial or femoral component only cemented). Bearing mobility was either mobile (inserts designed to move relative to the tibial base-plate) or fixed (components designed not to move relative to the tibial base-plate). Patellar resurfacing components were either used or not used. Polyethylene type was ultra-high molecular weight polyethylene (UHMWPE), highly cross-linked (XLPE, classified as ultrahigh molecular weight polyethylene that has been irradiated by high dose (> 50 kGy) gamma or electron beam radiation) and highly cross-linked polyethylene with antioxidant (combining vitamin E and Covernox; DePuy Synthes. Warsaw, IN, USA) (XLPE + AntiOx). The proportions of the alternatives for these categories were calculated and trends assessed over time.

For the meta-analyses, either the measure was dichotomized or, if there were more than 2 alternatives for a factor, the 2 most common categories were selected for analysis. This approach minimized the number of comparisons. Age was divided into < 65 years and compared with ≥ 65 years of age. For analysis of ASA, scores 1 and 2 were combined to compare those with no or mild systemic disease with those with severe disease (ASA scores 3 and over). For BMI, the non-obese group (with a BMI < 30) were compared with the obese (BMI ≥ 30). For the analyses of prosthesis constraint, minimally stabilized were compared with posterior stabilized (as fully stabilized and hinged prostheses made up less than 1% of primary TKA), cement fixation was compared with cementless fixation (as hybrid fixation was rarely used in the SKAR and KPJRR), and for polyethylene type XLPE and XLPE + AntiOx were combined for comparison with UHMWPE.

Statistics

Kaplan–Meier estimates of survivorship were used to report the time to revision, with censoring at the time of death and closure of each dataset at the end of December 2019. Patients in the KPJRR were also censored if they ended membership with the healthcare plan. The cumulative percentage revision (CPR) rates, with 95% confidence intervals (CI), were calculated using point-wise Greenwood estimates. For each registry, hazard ratios (HR) were calculated from Cox models to compare the rate of revision between groups. In order to combine the hazards, knowing that these ratios can vary with time, we used unadjusted ratios calculated for each pair of variables of interest at 5, 10, and 15 years from surgery. All tests were two-tailed and 0.05 was the significance threshold. Analyses were performed using SAS version 9.4 (33) for the AOANJRR and KPJRR data, and STATA release 15 (34) for the Swedish data.

We used software from R (Version V.3.1.2) (35) using the General Package for Meta-analysis for the generic inverse-variance method for calculating a total treatment effect at each time-point for each variable. The random-effects models were used for all analyses and 95% confidence intervals (CI) are presented as are 95% prediction intervals. Heterogeneity was determined by both Tau^2 and I^2.

Ethics, data sharing, funding, and potential conflicts of interest

Ethics approval covering the SKAR data use was approved by the Ethics Board of Lund University (LU20-02). The AOANJRR is a declared Commonwealth of Australia Quality Assurance Activity under section 124X of the Health Insurance Act, 1973. All AOANJRR studies are conducted in accordance with ethical principles of research (Helsinki Declaration II). Approval for inclusion of data from the Kaiser Permanente Joint Replacement Registry Institutional Review Board (#5488) was granted on November 15, 2018. A data sharing agreement for the purpose of this study was finalized on December 10, 2020 by the directors of the SKAR, AOANJRR, and KPJRR. There was no funding. There are no conflicts of interest.

Table 1. Summary of patient factors for TKA for OA 2003–2019 by registry. Values are count (%) unless otherwise specified

	SKAR n = 188,290	AOANJRR n = 663,982	KPJRR n = 220,652
Sex			
Males	79,230 (42)	291,208 (44)	84,937 (38)
Females	109,060 (58)	372,774 (56)	135,715 (62)
Mean age (SD)	69.5 (8.9)	68.5 (9.1)	67.6 (8.9)
Age groups			
< 55	11,164 (5.9)	43,508 (6.6)	15,915 (7.2)
55–64	47,111 (25)	177,066 (27)	65,693 (30)
65–74	74,830 (40)	263,105 (40)	88,065 (40)
≥ 75	55,185 (29)	180,303 (27)	50,979 (23)
ASA	from 2009	from 2013	from 2003
1	24,112 (18)	20,306 (5.7)	3,431 (1.6)
2	88,804 (65)	188,640 (53)	124,206 (56)
3	22,426 (16)	128,551 (36)	73,502 (33)
4	249 (0.2)	3,672 (1.0)	1,769 (0.8)
5	9 (0.0)	10 (0.0)	13 (0.0)
Missing	1,348 (1.0)	14,891 (4.2)	17,731 (8.0)
BMI	from 2009	from 2015	from 2003
Underweight	214 (0.2)	439 (0.2)	393 (0.2)
Normal	24,483 (18)	25,581 (9.6)	25,849 (12)
Pre-obese	58,839 (43)	77,407 (29)	69,110 (3.1)
Obese 1	38,000 (28)	76,861 (29)	66,968 (30)
Obese 2	11,565 (8.4)	42,505 (16)	37,882 (17)
Obese 3	2,436 (1.8)	26,499 (10)	14,524 (6.6)
Missing	1,411 (1.0)	16,641 (6.3)	5,926 (2.7)

Table 2. Summary of prosthesis factors for TKA for OA by registry. Values are count (%)

	SKAR n = 188,290	AOANJRR n = 663,982	KPJRR n = 220,652
Prosthesis constraint			
Minimally stabilized	175,667 (93)	487,626 (73)	66,489 (30)
Posterior stabilized	11,340 (6.0)	172,530 (26)	146,780 (67)
Fully stabilized	758 (0.4)	2,519 (0.4)	3,210 (1.4)
Hinged	470 (0.2)	1,133 (0.2	64 (0.0)
Missing	55 (0.0)	174 (0.0)	5,009 (2.3)
Fixation			
Both cemented	180,220 (96)	389,650 (59)	208,391 (94)
Both cementless	7,424 (3.9)	120,616 (18)	3,746 (1.7)
Tibia only cemented	136 (0.1)	147,232 (22)	6,387 (2.9)
Femur only cemented	277 (0.1)	6,484 (1.0)	357 (0.2)
Missing	233 (0.1)	0 (0)	1,771 (0.8)
Bearing mobility			
Fixed	186,680 (99)	539,194 (81)	202,426 (92)
Mobile	1,461 (0.8)	124,614 (19)	13,208 (6.0)
Missing	149 (0.1)	174 (0.0)	5,018 (2.3)
Patellar component			
Used	7,975 (4.2)	375,409 (57)	215,924 (98)
Not used	180,315 (96)	288,573 (44)	4,728 (2.1)
Polyethylene type			
UHMWPE	162,648 (86)	395,665 (60)	147,384 (67)
XLPE	24,473 (13)	230,781 (35)	36,750 (17)
XLPE + AntiOx.	495 (0.3)	37,255 (5.6)	24,156 (11)
Missing	674 (0.4)	281 (0.0)	12,362 (5.6)

Results

Overall results

The age and sex of TKA patients were similar between registries. There was a higher proportion of TKA patients in Sweden with no or mild systemic disease and without obesity (Table 1).

Prosthesis factors showed greater variation. Minimally stabilized prostheses were used in 93% of TKA in Sweden, 73% in Australia, but in only 30% in the KPJRR. Surgeons in the KPJRR preferred PS prostheses in 67% of TKA. Cement fixation of both components was favored in 96% and 94% of procedures in the SKAR and KPJRR, but in only 59% in the AOANJRR. The remaining cases in Australia were hybrid (tibial component cemented) (22%) or cementless (18%). All registries had over 80% fixed bearing use. Patellar resurfacing showed greatest variation: 4% in the SKAR, 98% in the KPJRR, and 57% in the AOANJRR. UHMWPE was used in the majority of procedures in all countries (Table 2).

Time-related trends

In all registries, the mean age of TKA recipients initially showed a small decline but a minor increase in the last 3–4 years. There was a reduction in the percentage of females in all registries with time (Figure 1).

The major difference between Sweden and the KPJRR for the use of MS TKA persisted with little change, while the proportion in Australia varied from 67% to 83%. The use of PS TKA varied between 57% and 70% in the KPJRR, rose from 17% to 32% in Australia until 2010 but declined to 19% in 2019, while in Sweden PS use remained below 9% for the entire period. Cement fixation was consistently used in > 93% and > 88% of TKA in the SKAR and the KPJRR respectively, while increasing in the AOANJRR from 44% to 68%.

Mobile bearing prostheses have never been popular in Sweden, used in a maximum of 2% of procedures, while a decline in the use with time was observed in both Australia and the KPJRR. The patellar resurfacing tendency remained low in Sweden (11% falling to 2%), while in the KPJRR patellar component use was consistently high (over 97%). In Australia, patellar resurfacing rose from 44% to 73%. There was a trend for increased use of XLPE (Figure 2).

Meta-analysis of patient and prosthesis factors

Meta-analysis showed a higher revision risk associated with age < 65 years, with increasing summary hazard ratios over time (HR 1.6 at 5 years, HR 2.0 at 10 years, and HR 2.2 at 15 years). Males showed a higher risk of revision compared with females in the first 5 years (HR 1.2), but after this no difference was observed. Patients with severe systemic disease showed a higher risk of revision at 5 years compared with patients with no or mild systemic disease (HR 1.3), as did obese patients when compared with non-obese (HR 1.2). The prediction interval for each of these analyses contained 1 (Figure 3, see Supplementary data).

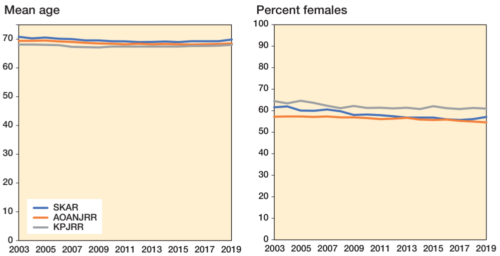
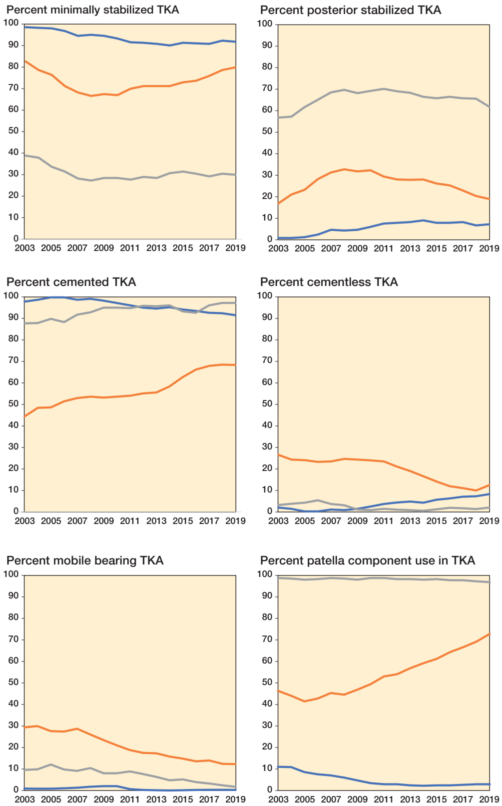


Figure 1. Time-related trends in patient factors in TKA for OA for each registry.

Prosthesis factor meta-analysis showed a higher risk of revision for PS TKA compared with MS (HR 1.4 at 5 years and HR 1.3 at both 10 years and 15 years) at all time-point comparisons. Cementless fixation gave a higher risk of revision compared with cemented fixation (HR 1.3 at both 5 years and 15 years) but no risk difference at 10 years. Mobile bearing TKA had a higher risk of revision compared with fixed bearing at 5 years (HR 1.6) but at 10 and 15 years there was no observed difference. Analysis of patellar component use showed no observed difference in risk of revision with or without patellar resurfacing. There was no revision risk difference associated with the use of XLPE when compared with UHMWPE, but limited data allowed analysis only to 10 years. Only for the analysis of fixation at 5 years did the prediction interval not include 1 (Figure 4, see Supplementary data).



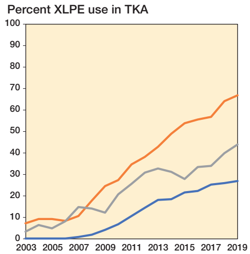


Figure 2. Time-related trends in prosthesis factors in TKA for OA for each registry. For color codes, see Figure 1.

Discussion

We described the international and time-related similarities and differences in primary TKA surgery between 3 distinct registries. Similarities were seen with age and sex, but between-registry differences occurred in the other 7 factors studied, with prosthesis constraint and patellar component use showing the greatest diversity. There were common trends over time for increased use of fixed bearing prostheses and XLPE inserts. Meta-analysis showed consistent findings for survivorship favoring patients aged ≥ 65 years and minimally stabilized components. There were findings favoring female sex, cement fixation, and fixed bearing components at some of the time comparisons, and no differences at any time were shown with analyses of patellar component use or polyethylene type.

Previous studies comparing registry-recorded characteristics have been limited to a comparison of 2 areas (**36**), or a localized region, such as the Nordic Arthroplasty Register Association (**37,38**). Others have extracted data from the annual reports from different registries (**39**) or used a distributed data network (**14,15**). Previous meta-analytic approaches using registry data have been used to assess the overall revision rate (**40**) or individual factors such as fixation (**41**), but there has been no previous study of multiple factors.

The patient-related meta-analytic summary findings regarding lower revision risk favored age ≥ 65 years, those with no or mild systemic disease, and those considered non-obese. The concordance of individual registry results for these factors suggests reliability of these findings. Younger age is a known risk for TKR revision. Obesity was shown in a systematic review to have a higher all-cause and septic revision risk (9). The relationship of comorbidity to revision has been shown to relate not just to obesity, but also to iron-deficiency anemia and liver disease (11). We found female sex was associated with a lower risk of revision at 5 years, consistent with studies showing males with a higher early risk of revision related to infection (8,42).

The finding in favor of lower risk of revision using MS components was strongest in Sweden where these designs were used for over 90% of TKA. A higher rate of revision with PS prostheses was also seen in the KPJRR where PS components were far more popular, and in Australia where there was mixed use of both constraint types. The similarity of the findings despite the usage differences increases the weight of this evidence. While there has been persistent debate regarding prosthetic constraint, with some claiming no difference in revision rate (43), our results are consistent with the claim of superiority of the MS designs (13,44).

Cement fixation gave a lower risk of revision when compared with cementless fixation at 5 and 15 years. Cement may protect against early migration and revision for loosening (45). Cement fixation for TKA has been termed the "gold standard" and has consistently been reported to be superior to cementless fixation (18,37,46). However, there has been support for the contrary viewpoint (17).

While there were differences between registries, mobile bearing prostheses overall had a higher risk of revision compared with fixed bearing at 5 years, but showed no difference at 10 and 15 years. This difference may be explained by bearing dislocation and instability that occur early in the mobile group (47). Mobile bearings were used in less than 20% of TKA in all registries during the study period. Our study endorses the trend to declining use of these designs, and confirms the results of previous studies (15,48,49).

Analysis of patellar resurfacing showed divergent usage and revision results. In the KPJRR, where patellar resurfacing is commonplace, revision risk analyses favored patellar component use, but the converse was found in the SKAR where the usual practice of not resurfacing was shown to have lower revision rates. In the AOANJRR, where patellar component use varied, there were lower revision rates at 5 and 10 years with patellar resurfacing, but no difference at 15 years. While some studies have shown lower early revision rates with patellar resurfacing, there are concerns about wear and loosening in the longer term (19,20,50).

XLPE use increased in all registries, but we observed no revision risk difference with its use compared with UHMWPE. Results showed a wide variation at 5 years with XLPE giving a lower revision risk in Australia, but UHMWPE gave better revision results in Sweden. These analyses most likely reflect results of limited prostheses that offer XLPE. Of note is the increased use, which seems to be market-driven, rather than a response to registry-recorded outcomes. A "no difference" finding for all-cause revision is consistent with other studies (51,52).

With some analyses, low usage of certain types of prostheses resulted in higher revision rates with that choice, and this may reflect selective use in difficult or specific clinical settings, limited prosthesis selection, or lack of familiarity with the procedure. This could explain some of the differences in the magnitude of hazard ratios.

Among the registries studied there was considerable heterogeneity, as in all but 2 of the 22 meta-analyses the measure of heterogeneity (I^2) was 70 or above. As each registry uses similar approaches to data collection and analysis, there is little methodological difference, and so the heterogeneity seen in this study would relate to clinical diversity. According to Cochrane methodology (53), heterogeneity should diminish the certainty of the findings. However, we argue that where there are consistent findings despite differences in populations studied this should strengthen the validity of the results. The finding of heterogeneity also led to use of the random-effects models for meta-analysis. An advantage of the random-effects model, when compared with the fixed-effects model, is that the number of procedures each registry contributes has a smaller influence on the results, diminishing potential inequality from the larger volume Australian registry. For comparisons (other than fixation at 5 years) the prediction interval assessments cast some uncertainty on the findings. This interpretation suggests that there may be circumstances in which the alternative to a favored factor has the better outcome.

There are a number of limitations of this study. Only 3 registries were included, and more robust conclusions could be drawn by the inclusion of even more data. Analysis of observational data can be affected by unmeasured confounding. We studied only 9 factors relating to TKA surgery, and there are other factors, such as patient activity levels or surgeon experience, that influence revision rates in addition those studied. Each factor was analyzed independently but there may be interaction between the factors studied, such as different rates of revision with PS and MS prostheses without patellar component use. Also, consistent with other registry studies, revision was the chosen outcome measure, but different results might have been found with other measures, such as those assessing function or satisfaction. We have used all-cause revision rates, and it is possible that if more focused reasons for revision were used (such as revision for loosening when analyzing fixation) different results could be found. Also, the comparisons considered prosthesis factors as distinct groups, but there are known prosthesis-specific performance differences (54). In addition, with some factors studied there was insufficient follow-up to allow analysis at all time points.

Why surgeons use specific prostheses for knee replacement surgery is poorly understood. A multi-national survey of TKA surgeons found "lowest registry revision risk" only rated 10th out of 17 attributes regarding prosthesis choice (26). It is hoped that, as evidence regarding the factors related to TKA revision increases, there will be a parallel increase in the influence that registry results have on surgeon choices.

In conclusion, while patient factors have little potential for change, altered prosthesis selection can possibly increase TKA survivorship. Our study suggests that the use of minimally stabilized, and possibly also fixed bearing prostheses, used with cement fixation result in a lower risk of revision. These styles are already common in the SKAR, but patients from the AOANJRR and the KPJRR may benefit from increased choice of these designs. Further study is required to assess the influence of patellar resurfacing and XLPE use.

PLL: literature search, study design, methodology determination, data collection, data analysis, data synthesis, manuscript writing. AWD: Study design, interpretation of data, manuscript preparation. OR: Methodology advice, data analysis, interpretation of data, manuscript preparation. ML: Data analysis, methodology advice. HAP: Data analysis, manuscript preparation. SEG: Interpretation of data, manuscript preparation. EWP: Interpretation of data, manuscript preparation.

The authors would like to thank the patients and surgeons who contribute their valuable data to the SKAR, AOANJRR, and KPJRR, without which studies such as this would not be possible. They also acknowledge the valuable assistance given by Dr Sophie Rainbird and Dr David Campbell to aid finalization of this manuscript.

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Supplementary data

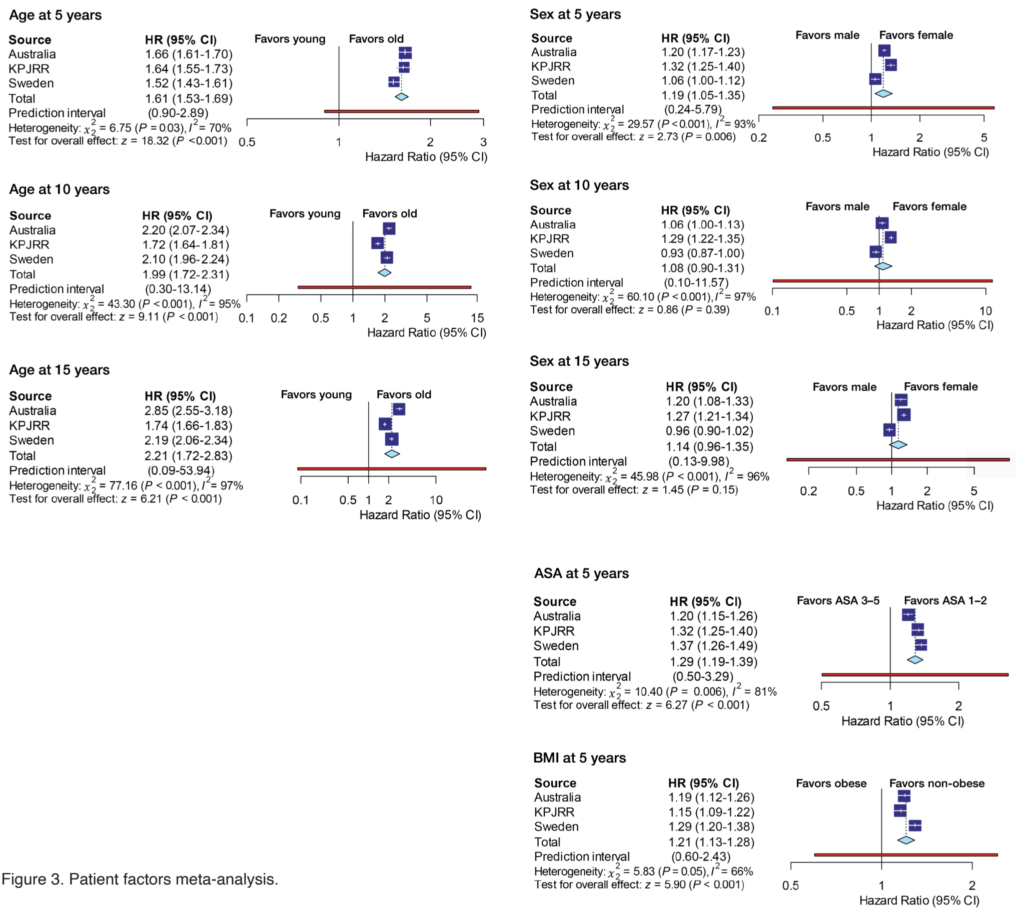

Figure 3. Patient factors meta-analysis.

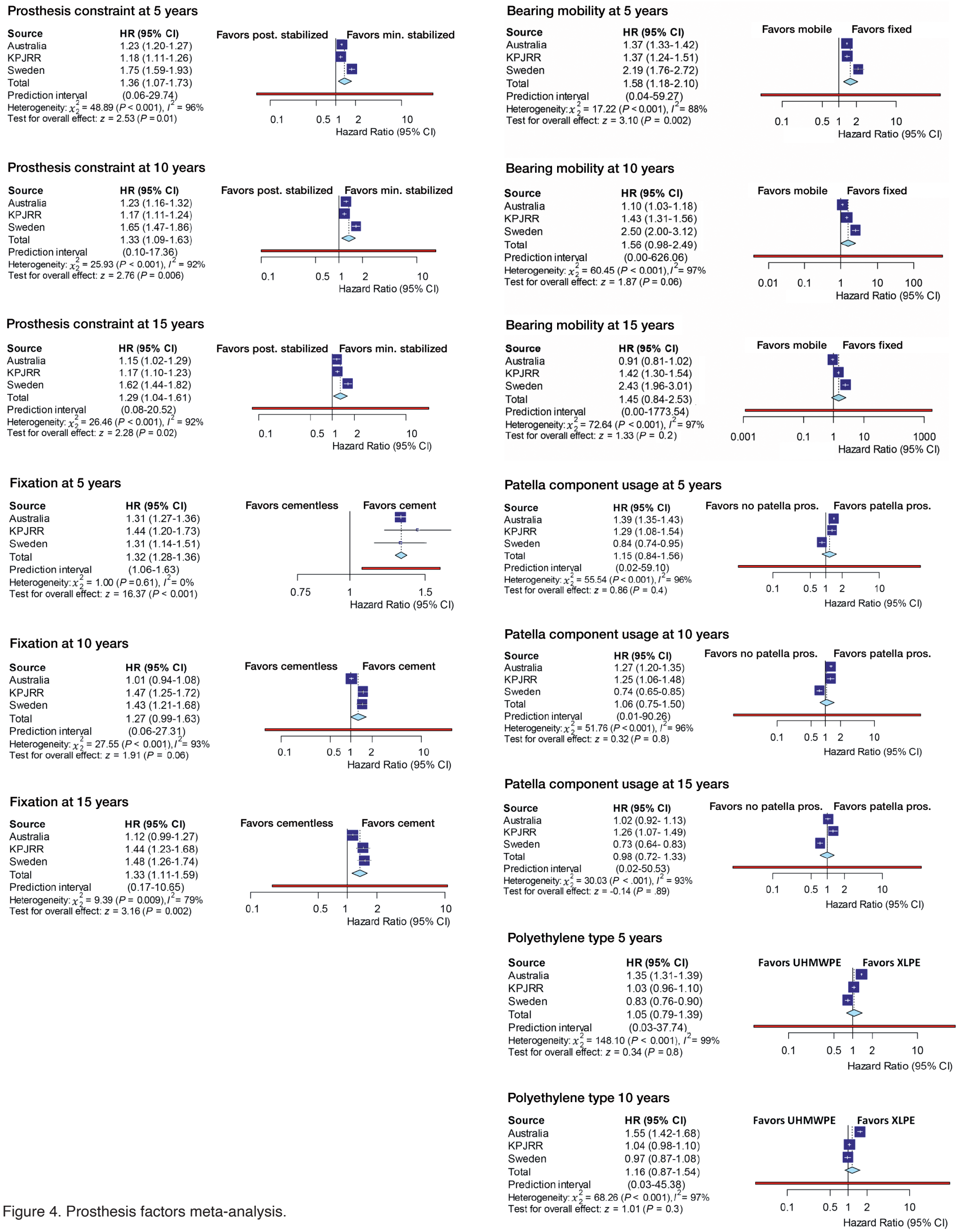

Figure 4. Prosthesis factors meta-analysis.

Dear colleagues and friends of the Knee Society

It is with a sad heart that I am writing to inform you of the passing of my friend and mentor, Otto Robertsson. Otto passed away suddenly in his home town of Reykjavik, Iceland, on Saturday, October 2nd. He was 68 years old and is survived by his dear wife Elin, his three daughters, and his four grandchildren, all of whom he adored.

Otto attended medical school in Aarhus, Denmark, from which he graduated as an MD in 1982. After returning to Iceland for a few years he then moved to Sweden for specialist training and received authorization as an orthopaedic surgeon in 1989. He started working at the University Hospital in Lund in 1990 and soon became involved in the Swedish Knee Arthroplasty Register (SKAR). Otto managed the SKAR, since 1996, for almost 25 years. Under his leadership the register became a well-respected and preeminent arthroplasty register with international recognition. As early as 1997, Otto was a pioneer in initiating PROMs data collection in the SKAR. It was with these efforts that I first met Otto and had the great privilege to study at his side. We published numerous papers together under his vision and direction.

Otto was the general secretary of the Icelandic Orthopaedic Society in 2003-2011, represented Iceland in EFORT and was the congress president of both the Nordic Orthopaedic Federation and the 7th congress of International Society of Arthroplasty Registries (ISAR) in Reykjavik 2018. Otto was a founding member and passionate supporter of ISAR. His efforts and outstanding contributions were recognized in 2020 when he received the ISAR Lifetime Achievement Award; a fitting recognition of his lasting and impactful contributions to registry science.

In 2000 Otto defended his doctoral thesis (PhD) "The Swedish Knee Arthroplasty Register – Validity and Outcome" at Lund University. He authored over 100 publications, mostly based on register work, many of them in high impact journals. Otto was a frequent lecturer at national and international orthopaedic conferences. He was involved in several PhD studies including SKAR data over the years. Otto was internationally well respected and was granted membership in the Knee Society in 2012.

Otto had a deep knowledge of modern statistical methods and was an excellent scientific writer, only accepting perfection before submitting a study for publication. He was a rigorous methodologist, a keen debater, and frankly, a brilliant mind. Despite his most impressive accomplishments, he shunned the spotlight and accolades and was a role model of humility.

Otto smoking salmon in his smoke house at his summer home in Iceland, August, 2021.

Otto loved his family summer house in Iceland where he shared time with his beloved family and friends. He was well known for his smoked salmon that he caught in the glacial river by his summer house and hay smoked on his property. He enjoyed nature and sharing a good whiskey or cognac with friends, ideally shared with his salmon or a roasted leg of Icelandic lamb.

Otto was a gracious and generous friend with a huge heart. I, like so many others, will miss him deeply for having left us too soon but my heart swells and a smile comes to my face when I reflect back on the many great moments we shared. I am a better person for having known him and I will personally remember him by doubling my efforts to be a better surgeon-scientist, and more importantly, a better friend.

Please take the time to spare a moment of reflection for Otto. Also, take a moment to reach out and say hi to your friends as life is short and friends are so precious. I miss you deeply and will remember you always, my dear friend.

Michael Dunbar

Paper IV

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Impact of patient and prosthesis characteristics on common reasons for total knee replacement revision: a registry study of 36,626 revision cases from Australia, Sweden, and USA

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Background and purpose — Total knee replacement (TKR) studies usually analyze all-cause revision when considering relationships with patient and prosthesis factors. We studied how these factors impact different revision diagnoses.

Patients and methods — We used data from 2003 to 2019 of TKR for osteoarthritis from the arthroplasty registries of Sweden, Australia, and Kaiser Permanente, USA to study patient and prosthesis characteristics for specific revision diagnoses. There were 1,072,924 primary TKR included and 36,626 were revised. Factors studied included age, sex, prosthesis constraint, fixation method, bearing mobility, polyethylene type, and patellar component use. Revision diagnoses were arthrofibrosis, fracture, infection, instability, loosening, pain, patellar reasons, and wear. Odds ratios (ORs) for revision were estimated and summary effects were calculated using a meta-analytic approach.

Results — We found between-registry consistency in 15 factor/reason analyses. Risk factors for revision for arthrofibrosis were age < 65 years (OR 2.0; 95% CI 1.4–2.7) and mobile bearing designs (MB) (OR 1.7; CI 1.1–2.5), for fracture were female sex (OR 3.2; CI 2.2–4.8), age ≥ 65 years (OR 2.8; CI 1.9–4) and posterior stabilized prostheses (PS) (OR 2.1; CI 1.3–3.5), for infection were male sex (OR 1.9; CI 1.7–2.0) and PS (OR 1.5; CI 1.2–1.8), for instability were age < 65 years (OR 1.5; CI 1.3–1.8) and MB (OR 1.5; CI 1.1–2.2), for loosening were PS (OR 1.5; CI 1.4–1.6), MB (OR 2.2; CI 1.6–3.0) and use of ultra-high molecular weight polyethylene (OR 2.3; CI 1.8–2.9), for patellar reasons were not resurfacing the patella (OR 13.6; CI 2.1–87.2) and MB (OR 2.0; CI 1.2–3.3) and for wear was cementless fixation (OR 4.9; CI 4.3–5.5).

Interpretation — Patients could be counselled regarding specific age and sex risks. Use of minimally stabilized, fixed bearing, cemented prostheses, and patellar components is encouraged to minimize revision risk.

More than 100,000 annual total knee replacement (TKR) procedures are recorded by the combined arthroplasty registries of Sweden, Australia, and Kaiser Permanente from the USA (1). Although survivorship of TKR is over 95% at 10 years, the frequency of the procedure creates a considerable number requiring revision (2,3).

Data from large arthroplasty registries is useful for studying TKR revision, and this gives "real-world" assessments as it describes community experience rather than that of a tertiary referral service (4). Combining data from multiple registries can not only increase the number available to study, but also reduce practice variation limitations and increase generalizability (1). Although individual patient data is ideal, there can be difficulties obtaining this due to patient privacy regulations and data security and ownership concerns, so, alternatively, summary data can be obtained and combined using meta-analytic techniques (1,5).

Studies of patient and prosthesis characteristics affecting TKR revision usually analyze all-cause revision (1,6). While there have been summaries of common revision diagnoses, including arthrofibrosis (7,8), fracture (9,10), infection (11,12), instability (13,14), loosening (15,16), pain (17,18), patellar pain (19,20), and wear (21,22), how patient and prosthesis factors relate to these different reasons for revision remains unclear.

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In a previous study using a multi-registry approach we found characteristics associated with overall revision rates of primary TKR (1). Now we analyze patient and prosthesis factors in relation to each common reason for revision.

Patients and methods

We obtained aggregate annual data for the period January 1, 2003 to December 31, 2019 for all first revision TKR procedures recorded in the Swedish Knee Arthroplasty Register (SKAR), the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR), and the Kaiser Permanente Joint Replacement Registry (KPJRR). We included revision TKR only where the primary TKR procedure was recorded in the study period (between 2003 and 2019) and the initial diagnosis was osteoarthritis (OA). Revisions of partial knee arthroplasties, revisions of primary TKR for pathologies other than OA, with primary procedures prior to 2003 or subsequent revisions of a previous revision, were excluded. The completeness of these registries exceeds 95% and loss to follow-up was less than 8% over the study period. Validation and quality control methods of these registries have been published (2,23,24).

During this period, there were 1,072,924 primary TKRs for OA recorded (188,290 from the SKAR, 663,982 from the AOANJRR, and 220,652 from the KPJRR). Of these, 36,626 were revised (5,613 from the SKAR, 24,931 from the AOANJRR, and 6,082 from the KPJRR) and this constitutes the study group. Revision knee replacements included revision procedures of a previous total knee replacement where 1 or more components were added, removed, or exchanged.

The reason for revision was determined from the revision diagnosis selected by the surgeon at the time of the revision procedure from a predetermined list, or specifically added. Multiple reasons could be listed. In Sweden, all operative reports were methodically read and from these the primary reason for revision was interpreted by registry staff. In the AOANJRR and KPJRR, when multiple reasons for revision were recorded, a diagnosis hierarchy was used to determine the most important reason for revision. In this study only 1 reason for revision was permitted for each revision procedure. Revision diagnoses were classified by a previously created harmonized table of equivalent diagnosis groups (25).

Patient factors recorded (for both primary and revision procedures) were age, sex, ASA class, and BMI. As the SKAR and AOANJRR began collecting ASA and BMI data at later time points, these categories permitted limited analyses. We analyzed 5 prosthesis factors: (i) Prosthesis constraint was divided into minimally stabilized (MS) (those that have a flat or dished tibial articulation, regardless of congruency), posterior stabilized (PS) (implants that provide posterior stability using a peg and box design), fully stabilized (FS) (implants with a large peg and box design designed to give some collateral as well as posterior stability), and hinged (implants with a hinge mechanism to link the femoral and tibial components); (ii) Fixation was cemented (both femoral and tibial components cemented), cementless (both components inserted without cement), and hybrid (tibial or femoral component only cemented); (iii) Bearing mobility was either mobile (inserts designed to move relative to the tibial base-plate) or fixed (inserts designed not to move relative to the tibial base-plate); (iv) Patellar resurfacing components were either used or not used; (v) Polyethylene type was ultra-high molecular weight polyethylene (UHMWPE), highly cross-linked (XLPE, classified as ultrahigh molecular weight polyethylene that has been irradiated by high dose [> 50 kGy] gamma or electron beam radiation) and highly cross-linked polyethylene with antioxidant (combining the anti-oxidants vitamin E and Covernox [DePuy Synthes. Warsaw, IN, USA]) (XLPE + AntiOx).

For the patient and prosthesis factor comparisons the 2 most common categories were selected for analysis. Age was divided into < 65 years and compared with ≥ 65 years of age. For the analyses of prosthesis constraint, MS were compared with PS, cement fixation was compared with cementless fixation, and for polyethylene type XLPE and XLPE + AntiOx were combined for comparison with UHMWPE.

Statistics

Proportions of the individual registry's reasons for revision and revision procedures were determined and compared. Mean time to revision for each reason was calculated.

As time-to-event data was not available for this study, categorical data was used to calculate odds ratios (OR) with 95% confidence intervals (CI) for patient and prosthesis factors for each reason for revision using the on-line GIGAcalculator (26). The number revised was considered with respect to the total number of primary procedures having that factor. Where the odds ratios for each registry were concordant and all either above or below 1, and the confidence interval did not contain 1 (i.e., a consistent and statistically significant association was found), these were chosen for meta-analysis. The Mantel–Haenszel random-effects method was used due to the event rate being low and the presence of inter-registry heterogeneity. RevMan version 5.4 (27) was used for the calculations. Heterogeneity was determined by I^2.

Ethics, data sharing, funding, and potential conflicts of interest

Ethics approval covering the SKAR data use was approved by the Ethics Board of Lund University (LU20-02). The AOANJRR is a declared a Commonwealth of Australia Quality Assurance Activity under section 124X of the Health Insurance Act, 1973. All AOANJRR studies are conducted in accordance with ethical principles of research (Helsinki Declaration II). Approval for inclusion of data from the Kaiser Permanente Joint Replacement Registry Institutional Review Board approval (#5488) was granted on August 18, 2021. A

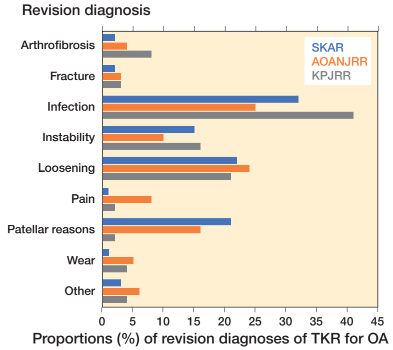


Figure 1. Proportions of revision diagnoses of TKR for OA.

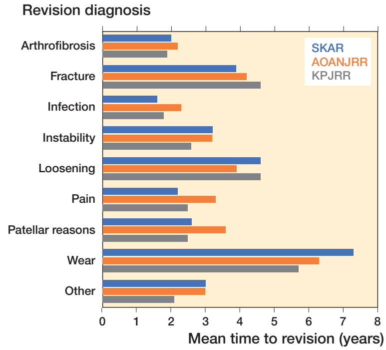


Figure 2. Mean time to revision (years) by revision reason.

data sharing agreement for the purpose of this study was finalized on December 10, 2020 by the directors of the SKAR, AOANJRR, and KPJRR. There was no funding. There are no conflicts of interest.

Results

The mean patient ages of primary TKR were similar to those revised, while there were marginally greater proportions of males undergoing revision compared with primary TKR. ASA status and BMI for revised patients both showed a small shift in proportion to higher categories. Prosthetic factor comparisons between primary TKR and those revised showed small increases in proportions of PS components revised, mobile-bearing (MB) prostheses, and those using UHMWPE, but no consistent differences regarding fixation type or patellar component use (Table 1, see Supplementary data).

Reasons for revision

Infection, loosening, patellar reasons, and instability were the most common reasons for revision, except for the KPJRR where revisions for patellar reasons were infrequent (Figure 1). The mean times to revision were shortest for infection and arthrofibrosis and longest for wear, loosening, and fracture (Figure 2).

Patient factors for each of the more common reasons for revision were analyzed (Table 2). The mean age at time of revision ranged from 64 to 77 years, being lowest for revisions for arthrofibrosis and highest for revisions for fracture. The

Table 2. Patient factors for all primary TKR for OA 2003–2019 and their revisions

	Total	Female n (%)	Mean age (SD)	Years to revision (SD)	ASA 1–2 n (%)	BMI > 30 n (%)
SKAR						
All primaries	188,290	109,060 (58)	70 (9)		112,916 (83)	52,001 (38)
Revised for						
Arthrofibrosis	86	43 (50)	65 (11)	2.0 (2.2)	64 (89)	25 (28)
Fracture	105	92 (88)	73 (9)	3.9 (4.3)	50 (59)	29 (35)
Infection	1,812	771 (43)	70 (9)	1.6 (2.7)	873 (61)	605 (44)
Instability	857	572 (67)	67 (9)	3.2 (2.9)	553 (77)	299 (41)
Loosening	1,246	769 (62)	69 (9)	4.6 (3.6)	817 (76)	512 (47)
Pain	72	48 (67)	66 (9)	2.2 (1.6)	16 (77)	10 (48)
Patellar reasons	1,205	755 (63)	69 (9)	2.6 (2.4)	735 (80)	386 (42)
Wear	32	15 (47)	66 (8)	7.3 (3.9)	22 (76)	14 (48)
AOANJRR						
All primaries	663,982	372,774 (56)	69 (9)		208,946 (59)	145,865 (55)
Revised for						
Arthrofibrosis	926	503 (54)	66 (9)	2.2 (2.1)	325 (61)	225 (24)
Fracture	781	594 (76)	73 (10)	4.2 (4.2)	180 (35)	194 (54)
Infection	6,128	2,401 (39)	69 (10)	2.3 (2.9)	1,299 (35)	1,387 (60)
Instability	2,437	1,464 (60)	67 (10)	3.2 (3.1)	864 (51)	829 (63)
Loosening	5,888	3,342 (57)	67 (9)	3.9 (3.4)	1,664 (52)	1,470 (64)
Pain	2,040	1,165 (57)	68 (9)	3.3 (2.8)	610 (57)	500 (63)
Patellar reasons	4,003	2,297 (57)	69 (9)	3.6 (3.1)	1,292 (56)	954 (60)
Wear	1,159	650 (56)	68 (9)	6.3 (4.1)	336 (50)	308 (61)
KPJRR						
All primaries	220,652	135,715 (61)	68 (8)		127,637 (58)	119,374 (54)
Revised for						
Arthrofibrosis	495	296 (60)	64 (9)	1.9 (1.8)	296 (67)	255 (52)
Fracture	164	138 (84)	77 (10)	4.6 (4.1)	46 (32)	76 (47)
Infection	2,469	1,180 (48)	69 (10)	1.8 (2.5)	715 (37)	1,330 (54)
Instability	979	622 (64)	65 (9)	2.6 (2.5)	492 (56)	562 (58)
Loosening	1,256	788 (63)	66 (9)	4.6 (3.3)	630 (54)	795 (63)
Pain	146	94 (64)	66 (9)	2.5 (2.1)	83 (65)	81 (56)
Patellar reasons	126	78 (62)	67 (9)	2.5 (2.2)	64 (57)	75 (60)
Wear	197	114 (58)	67 (9)	5.7 (4.2)	96 (51)	114 (58)

Note: Mean age (at time of revision) in years, proportions for ASA and BMI exclude missing values.

Table 3. Prosthesis factors for all primary TKR for OA 2003–2019 and their revisions. Values are count (%)

	Total	MS	PS	Cemented	Cementless	Hybrid	Fixed bearing	UHMWPE	XLPE	Patellar resurfacing
SKAR										
All primaries	188,290	175,667 (94)	11,340 (6)	180,220 (96)	7,424 (4)	136 (0)	186,680 (99)	162,648 (86)	24,968 (13)	7,975 (4)
revised for										
Arthrofibrosis	86	73 (85)	11 (13)	81 (94)	5 (6)	0 (0)	82 (95)	67 (78)	18 (21)	10 (12)
Fracture	105	86 (82)	15 (14)	103 (98)	2 (2)	0 (0)	104 (99)	96 (91)	9 (9)	10 (10)
Infection	1,812	1,576 (87)	194 (11)	1,724 (95)	81 (4)	0 (0)	1,780 (98)	1,525 (84)	284 (15)	107 (6)
Instability	857	772 (90)	76 (9)	782 (91)	70 (8)	2 (0)	843 (98)	745 (87)	106 (12)	39 (5)
Loosening	1,246	1,110 (89)	123 (10)	1,220 (98)	18 (1)	4 (0)	1,206 (97)	1,143 (92)	99 (8)	139 (11)
Pain	72	69 (96)	1 (1)	69 (96)	2 (3)	1 (1)	72 (100)	71 (99)	1 (1)	5 (7)
Patellar reasons	1,205	1,120 (93)	76 (6)	1,143 (95)	61 (5)	0 (0)	1,175 (98)	1,086 (89)	133 (11)	15 (1)
Wear	32	32 (100)	0 (0)	26 (81)	6 (19)	0 (0)	32 (100)	26 (81)	6 (19)	8 (25)
AOANJRR										
All primaries	663,982	487,626 (73)	172,530 (26)	389,650 (59)	120,616 (18)	147,232 (23)	539,194 (81)	395,665 (60)	268,036 (41)	375,409 (57)
revised for										
Arthrofibrosis	926	644 (70)	281 (30)	508 (55)	238 (26)	169 (18)	712 (77)	632 (68)	294 (32)	490 (53)
Fracture	781	503 (64)	256 (33)	413 (53)	185 (24)	168 (22)	606 (78)	583 (75)	198 (25)	431 (53)
Infection	6,128	3,948 (64)	2,062 (34)	3,853 (63)	1,011 (16)	1,186 (19)	4,916 (80)	3,994 (65)	2,133 (35)	3,564 (58)
Instability	2,437	1,693 (69)	720 (30)	1,131 (55)	527 (22)	549 (23)	1904 (78)	1,736 (71)	701 (29)	1,368 (56)
Loosening	5,888	3,839 (65)	2,025 (34)	3,095 (52)	1,570 (27)	1,143 (19)	4,117 (70)	4,725 (80)	1,159 (20)	3,169 (54)
Pain	2,040	1,419 (70)	613 (30)	1,072 (53)	483 (24)	447 (22)	1,524 (75)	1,564 (77)	474 (23)	632 (31)
Patellar reasons	4,003	2,940 (73)	1,050 (26)	1,879 (97)	1,138 (28)	903 (23)	2,970 (74)	3,174 (79)	829 (20)	91 (2)
Wear	1,159	950 (82)	208 (18)	386 (33)	574 (50)	187 (16)	671 (58)	1,027 (89)	132 (11)	555 (48)
KPJRR										
All primaries	220,652	66,489 (30)	146,780 (67)	208,391 (94)	3746 (2)	6,387 (3)	202,426 (92)	147,384 (67)	60,906 (28)	215,924 (98)
revised for										
Arthrofibrosis	495	179 (36)	304 (61)	467 (94)	11 (2)	12 (2)	434 (88)	354 (72)	123 (25)	486 (98)
Fracture	164	22 (13)	132 (80)	151 (92)	3 (2)	5 (3)	148 (90)	128 (78)	22 (13)	162 (99)
Infection	2,469	639 (26)	1,727 (70)	2,344 (95)	39 (2)	60 (2)	2,226 (90)	1,762 (71)	615 (25)	2,419 (98)
Instability	979	287 (29)	659 (67)	912 (93)	20 (2)	34 (3)	845 (86)	670 (68)	268 (27)	960 (98)
Loosening	1,256	296 (24)	936 (75)	1,150 (92)	46 (4)	50 (4)	1,092 (87)	1,022 (81)	189 (15)	1,239 (99)
Pain	146	46 (32)	95 (65)	130 (89)	12 (8)	3 (2)	123 (84)	106 (73)	29 (20)	137 (94)
Patellar reasons	126	34 (27)	91 (72)	113 (90)	6 (5)	6 (5)	107 (85)	92 (73)	30 (24)	102 (81)
Wear	197	72 (37)	118 (60)	174 (88)	17 (9)	4 (2)	172 (87)	133 (68)	55 (28)	194 (98)

Note: MS = minimally stabilized; PS = Posterior stabilized. XLPE includes XLPE and XLPE with antioxidant. Patellar resurfacing is patellar resurfacing component used.

proportion of females revised ranged from 39% to 88%, being lowest for revisions for infection and highest for revisions for fracture.

Prosthesis factors for the individual reasons for revision are presented in Table 3. These are the characteristics of the components used in the primary procedure that was revised. For each registry, the number and proportions for these factors for all primary procedures from which these revisions were derived are also listed for comparison. The proportions of revised TKR to primary TKR in each registry were compared for the 8 revision diagnoses, giving 24 comparisons. The proportion of revised compared with primary TKR using UHMWPE was higher in 21 of 24 comparisons, for both cementless and PS prostheses in 15 comparisons, while use of a fixed bearing was only higher in 2 comparisons.

Association of prosthesis factors with reasons for revision

Odds ratio determinations for individual reasons for revision showed that there was inconsistency between registries for many of the factors studied (Table 4, see Supplementary data). There was insufficient data for analysis of ASA or BMI. Where consistency was found, a summary effect for revision risk was determined by meta-analysis (Table 5).

Analysis of arthrofibrosis showed that young age (OR 2.0; CI 1.4–2.7) and MB designs (OR 1.7; CI 1.1–2.5) were risk factors for revision. Higher odds for revision for fracture were seen for females (OR 3.2; CI 2.2–4.8), age 65 years and over (OR 2.8; CI 1.9–4), and with PS prostheses (OR 2.1; CI 1.3–3.5). Factors affecting revision for infection were male sex (OR 1.9; CI 1.7–2.1), and PS components (OR 1.5; CI 1.2–1.8). Younger age (OR 1.5; CI 1.3–1.8) and MB designs (OR 1.5; CI 1.1–2.2) had higher odds for revision for instability, while PS (OR 1.5; CI 1.4–1.6), as well as MB designs (OR 2.2; CI 1.6–3) and UHMWPE inserts (OR 2.3; CI 1.8–2.9) had higher odds for revision for loosening. There was no consistency found when factors were assessed with regard to revision for pain. MB components (OR 2.0; CI 1.2–3.3) and not using a patellar component (OR 13.6; CI 2.1–87.2) increased odds for revision for patellar reasons. Cementless fixation (OR 4.9; CI 4.3–5.5) increased the odds for revision for wear. The meta-analyses showed substantial or considerable statis-

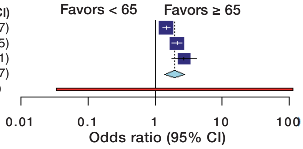
Table 5. Meta-analysis of odds ratios for the selected patient and prosthesis factors for each reason for revision, using the Mantel–Haenszel random-effects method

1. Arthrofibrosis

Age and revision for arthrofibrosis

	< 65		≥ 65		
Source	Events	Total	Events	Total	OR (95% CI)
AOANJRR	389	220,574	537	443,408	1.5 (1.3–1.7)
KPJRR	274	81,608	221	139,044	2.1 (1.8–2.5)
SKAR	47	58,275	39	130,015	2.7 (1.8–4.1)
Total		360,457		712,247	1.9 (1.4–2.7)
Predicition interval					(0.0–112.2)

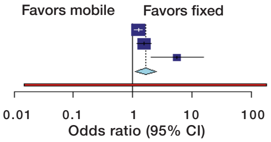
Heterogeneity: χ^2_2 = 15.7 (p < 0.001), I^2 = 87%
Test for overall effect: z = 3.87 (p < 0.001)



Bearing mobility and revision for arthrofibrosis

	Mobile		Fixed		
Source	Events	Total	Events	Total	OR (95% CI)
AOANJRR	214	129,788	712	539,194	1.2 (1.1–1.5)
KPJRR	61	18,226	434	202,426	1.6 (1.2–2.0)
SKAR	4	1,610	82	186,680	5.7 (2.1–16)
Total		149,624		928,300	1.7 (1.1–2.5)
Predicition interval					(0.0–184.3)

Heterogeneity: χ^2_2 = 9.97 (p = 0.007), I^2 = 80%
Test for overall effect: z = 2.38 (p = 0.02)

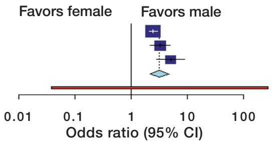


2. Fracture

Sex and revision for fracture

	Female		Male		
Source	Events	Total	Events	Total	OR (95% CI)
AOANJRR	594	372,774	187	291,208	2.5 (2.1–2.9)
KPJRR	138	135,715	26	84,937	3.3 (2.2–5.1)
SKAR	92	109,060	13	79,240	5.1 (2.9–9.2)
Total		617,549		455,385	3.2 (2.2–4.8)
Predicition interval					(0.0–276.1)

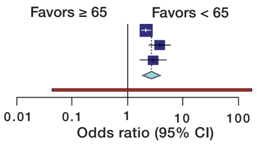
Heterogeneity: χ^2_2 = 6.67 (p = 0.04), I^2 = 70%
Test for overall effect: z = 5.85 (p < 0.001)



Age and revision for fracture

	< 65		≥ 65		
Source	Events	Total	Events	Total	OR (95% CI)
AOANJRR	146	220,574	635	443,408	2.2 (1.8–2.6)
KPJRR	22	81,608	142	139,044	3.8 (2.4–5.9)
SKAR	14	58,275	91	130,015	2.9 (1.7–5.1)
Total		360,457		712,467	2.7 (1.9–4.0)
Predicition interval					(0.0–174.5)

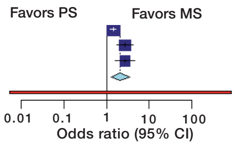
Heterogeneity: χ^2_2 = 5.69 (p = 0.06), I^2 = 65%
Test for overall effect: z = 5.29 (p < 0.001)



Constraint and revision for fracture

	MS		PS		
Source	Events	Total	Events	Total	OR (95% CI)
AOANJRR	256	172,530	503	487,626	1.4 (1.2–1.7)
KPJRR	132	146,780	22	664,489	2.7 (1.7–4.3)
SKAR	15	11,340	86	175,667	2.7 (1.6–4.7)
Total		330,650		729,782	2.1 (1.3–3.5)
Predicition interval					(0.0–839.0)

Heterogeneity: χ^2_2 = 10.7 (p = 0.05), I^2 = 81%
Test for overall effect: z = 2.89 (p = 0.004)

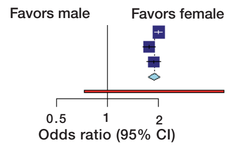


3. Infection

Sex and revision for infection

	Female		Male		
Source	Events	Total	Events	Total	OR (95% CI)
AOANJRR	2,401	372,774	3,727	291,208	2.0 (1.9–2.1)
KPJRR	1,180	135,715	1,289	84,937	1.8 (1.6–1.9)
SKAR	771	109,060	1,041	79,230	1.9 (1.7–2.1)
Total		617,549		455,375	1.9 (1.7–2.0)
Predicition interval					(0.0–4.9)

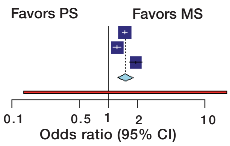
Heterogeneity: χ^2_2 = 7.49 (p = 0.02), I^2 =73%
Test for overall effect: z = 15.0 (p < 0.001)



Constraint and revision for infection

	PS		MS		
Source	Events	Total	Events	Total	OR (95% CI)
AOANJRR	2,062	172,530	3,948	478,626	1.5 (1.4–1.6)
KPJRR	1,727	146,780	639	66,489	1.2 (1.1–1.3)
SKAR	194	11,340	1,576	175,667	1.9 (1.7–2.2)
Total		330,650		729,782	1.5 (1.2–1.8)
Predicition interval					(0.1–17.0)

Heterogeneity: χ^2_2 = 27.1 (p < 0.001), I^2 = 93%
Test for overall effect: z = 4.11 (p < 0.001)



tical heterogeneity for all but 2 measures (fixation and revision for wear and prosthesis constraint and revision for loosening). It was only for the analysis of fixation for revision for wear that the prediction interval did not contain 1.

Discussion

We found infection, loosening, instability, and patellar reasons were the most common diagnoses for revision of TKR for OA in all 3 registries, with the only difference seen in the KPJRR where 98% of TKR had a primary patellar resurfacing and patellar causes for revision were rare. These findings, along with the timing of these revisions, are consistent with previous studies (25,28,29). When patient and prosthesis factors for revision reasons were studied, 15 of 56 possible factor/reason combinations showed between-registry consistency, varying from 3 concordant factors for each of revision for fracture and loosening, and no factor consistency for revision for pain.

Where discrepancy in odds ratio was found, this could mean that there is no link between the factor and revision reason (such as patellar component use and revision for instability), the numbers revised were too small to detect a difference (such as revisions for wear in the SKAR), or there may have been practice variations and individual prosthesis performance differences within the factor studied. There may also be between-surgeon differences in selecting revision diagnoses (for instance, due to multiple failure mechanisms being present, loosening recorded when a low-grade infection is detected later, or distinguishing between pain and patellar pain).

Younger age and MB designs were risk factors for revision for arthrofibrosis. Arthrofibrosis, or postoperative stiffness, is poorly understood but thought to involve an exaggerated soft tissue inflammation (8). While there is

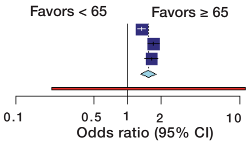
Table 5 continued

4. Instability

Age and revision for instability

Source	< 65 Events	Total	≥ 65 Events	Total	OR (95% CI)
AOANJRR	974	220,574	1,463	443,408	1.3 (1.2–1.5)
KPJRR	489	81,608	490	139,044	1.7 (1.5–1.9)
SKAR	362	58,275	495	130,015	1.6 (1.4–1.9)
Total		360,457		712,467	1.5 (1.3–1.8)
Predicition interval					(0.2–11.3)

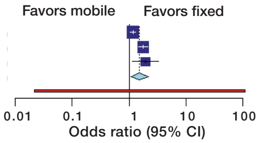
Heterogeneity: χ^2_2 = 12.7 (p = 0.002), I^2 = 84%
Test for overall effect: z = 5.16 (p < 0.001)



Bearing mobility and revision for instability

Source	Mobile Events	Total	Fixed Events	Total	OR (95% CI)
AOANJRR	533	129,788	1,904	539,194	1.2 (1.1–1.3)
KPJRR	134	18,226	845	202,426	1.8 (1.5–2.1)
SKAR	14	1,610	843	186,680	1.9 (1.1–3.3)
Total		149,624		928,300	1.5 (1.1–2.2)
Predicition interval					(0.0–107.7)

Heterogeneity: χ^2_2 = 18.0 (p < 0.001), I^2 = 89%
Test for overall effect: z = 2.30 (p = 0.02)

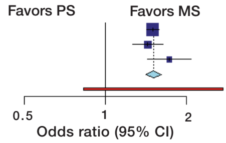


5. Loosening

Constraint and revision for loosening

Source	PS Events	Total	MS Events	Total	OR (95% CI)
AOANJRR	2,025	172,530	3,839	478,626	1.5 (1.4–1.6)
KPJRR	936	146,780	296	66,489	1.4 (1.3–1.6)
SKAR	123	11,340	1,110	175,667	1.7 (1.4–2.1)
Total		330,650		729,782	1.5 (1.4–1.6)
Predicition interval					(0.8–2.7)

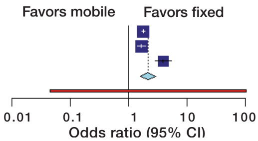
Heterogeneity: χ^2_2 = 2.57 (p < 0.3), I^2 = 22%
Test for overall effect: z = 11.9 (p < 0.001)



Bearing mobility and revision for loosening

Source	Mobile Events	Total	Fixed Events	Total	OR (95% CI)
AOANJRR	1,771	129,788	4,117	539,194	1.8 (1.7–1.9)
KPJRR	164	18,226	1,092	202,426	1.7 (1.4–2.0)
SKAR	40	1,610	1,206	186,680	3.9 (2.8–5.4)
Total		149,624		928,300	2.2 (1.6–3.0)
Predicition interval					(0.0–103.3)

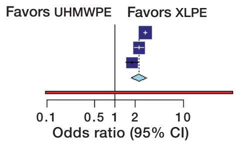
Heterogeneity: χ^2_2 = 23.4 (p < 0.001), I^2 = 91%
Test for overall effect: z = 4.85 (p < 0.001)



Polyethylene type and revision for loosening

Source	UHMWPE Events	Total	XLPE Events	Total	OR (95% CI)
AOANJRR	4,725	395,665	1,159	268,036	2.8 (2.6–3.0)
KPJRR	1,022	147,384	189	60,906	2.2 (1.9–2.6)
SKAR	1,143	162,648	99	24,968	1.8 (1.4–2.2)
Total		705,697		353,910	2.3 (1.8–2.9)
Predicition interval					(0.0–53.6)

Heterogeneity: χ^2_2 = 20.8 (p < 0.001), I^2 = 90%
Test for overall effect: z = 6.27 (p < 0.001)

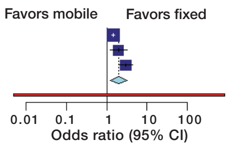


6. Patellar reasons

Bearing mobility and revision for patella reasons

Source	Mobile Events	Total	Fixed Events	Total	OR (95% CI)
AOANJRR	1,033	129,788	2,970	539,194	1.4 (1.3–1.6)
KPJRR	19	18,226	107	202,426	2.0 (1.2–3.2)
SKAR	30	1,610	1,175	186,680	3.0 (2.1–4.3)
Total		149,624		928,300	2.0 (1.2–3.3)
Predicition interval					(0.0–838,4)

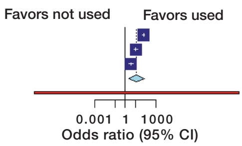
Heterogeneity: χ^2_2 = 15.9 (p < 0.001), I^2 = 87%
Test for overall effect: z = 2.75 (p = 0.006)



Patella usage and revision for patella reasons

Source	Not used Events	Total	Used Events	Total	OR (95% CI)
AOANJRR	3,912	258,573	2,970	375,409	63 (52–78)
KPJRR	24	4,728	102	215,924	11 (6.9–17)
SKAR	1,190	180,315	15	7,975	3.5 (2.1–5.9)
Total		149,624		599,308	14 (2.2–82)
Predicition interval					(0.0–15^{10})

Heterogeneity: χ^2_2 = 136 (p < 0.001), I^2 = 99%
Test for overall effect: z = 2.84 (p = 0.004)



no consensus regarding the influence of age on postoperative stiffness shown in a systematic review (7), arthrofibrosis was the most frequent cause for revision in a recent MB study (30).

Higher likelihood for revision for fracture was seen with female sex and age ≥ 65 years, consistent with previous findings (31), and the association with PS components has been related to excessive or eccentric "box" cuts and increased internal prosthetic constraint compared with cruciate-retaining designs (10,32).

The odds ratio for revision for infection was higher for males, as has previously been described (11,33). The increase in revision for infection with PS components has been reported (12,34), attributed to polyethylene debris and the associated joint response seen with these designs (34).

Revision for instability was associated with younger age, consistent with other results (13,14), while instability with MB prostheses has been described (35,36). Due to inter-registry differences in the odds ratios (which may relate to prosthesis use patterns) prosthesis constraint was not a factor chosen for further analysis for instability.

The fixation method had inconsistent odds ratios for revision for loosening, but there were associations identified with factors relating to the bearing. UHMWPE showed higher odds for revision for loosening than XLPE, while there was a greater risk with PS and MB designs. Previous studies have been variable, with some showing no difference between "conventional" polyethylene and XLPE (37), while others report findings similar to ours that may relate to biological reactions to wear products (16). Osteolysis may also be a common mechanism to explain the association of loosening with PS and MB components (21,38), which others claim relates simply to component design (39).

Odds ratio summaries showed no factor consistency in the analysis of revision for pain. Post-TKR pain is considered multifactorial, and often related to systemic conditions such as depression and catastrophizing (17), and it is not surprising that prosthesis factors showed no association in this study.

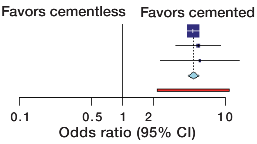
Table 5 continued

7. Wear

Fixation and revision for wear

	Cementless		Cemented		
Source	Events	Total	Events	Total	OR (95% CI)
AOANJRR	574	120,616	386	389,650	4.8 (4.2–5.5)
KPJRR	17	3,746	174	208,391	5.5 (3.3–9.0)
SKAR	6	7,424	26	180,220	5.6 (2.3–14)
Total		131,786		778,261	4.9 (4.3–5.5)
Predicition interval					(2.2–10.9)

Heterogeneity: χ^2_2 = 0.32 (p = 0.9), I^2 = 0%
Test for overall effect: z = 25.,1 (p < 0.001)



The strongest association between prosthesis factors and revision was shown in the analysis of patellar component use and revision for patellar reasons, where not using a patellar component showed much higher odds for revision for these diagnoses. Although some controversy may remain around function and pain relief regarding patellar component use (**40**), there seems less doubt that using a patellar component leads to a lower rate of revision for this reason (**41**). The finding that MB prostheses also showed higher odds for revision for patellar reasons is contrary to a study from the New Zealand Joint Registry that found fixed-bearing PS prostheses had a higher rate of secondary patellar resurfacing than mobile-bearing designs (**42**). This difference may relate to the specific prostheses used in each registry, or possibly to the common "gap balancing" technique for implantation, where femoral component rotation is determined after ligament releases (**43**).

Prostheses with cementless fixation had higher odds for revision for wear compared with cemented components. While there seems no direct link of the implant–bone interface to the bearing, cementless fixation may have been selected for more active patients (**44**). Surgeons may also have difficulty deciding between wear and loosening as the primary mechanism leading to revision (**25**). The lack of further associations with wear may be due to the relative rarity of revisions for this diagnosis, particularly in Sweden.

This study has a number of limitations. Despite the study design that included large data sets from each registry, some revision reasons still have only small numbers for analysis and more robust conclusions would require the inclusion of data from more registries. Only 7 patient and prosthesis factors were included, and there may be other influences on revision. We used a categorical distinction of revised/not revised as the outcome measure, and perhaps more detail could have been obtained had time-to-event data been available. In addition, odds ratios for each reason for revision were considered separately, comparing the number revised for that diagnosis with the number not revised, and this method does not take into account TKR revised for other competing reasons, or those who died. Additionally, the number revised for each reason most likely understates the true number of revisions as, in order to assess the proportion of primary TKRs revised, toward the censoring endpoint some TKRs were included that did not have time to be revised. This aspect would have a greater effect on those reasons with longer times to revision. Each factor was analyzed independently and there may be interactions between factors. We used categories for each prosthesis factor analyzed and there may be prosthesis performance differences within these categories. We used the Mantel–Haenszel method for calculating a summary effect size, and this is known to become less accurate with small event rates (**45**).

In summary, age < 65 years was associated with lower odds of revision for fracture but higher odds of revision for arthrofibrosis and instability. Females had higher odds of revision for fracture, but lower odds of revision for infection. PS prostheses had a higher likelihood of revision for infection, fracture, and loosening, while MB prostheses had higher odds of revision for arthrofibrosis, instability, and for patellar reasons, cementless fixation showed higher odds of revision for wear, and not using a patellar component increased the likelihood of revision for patellar reasons.

Patients could be counselled regarding specific risks for their age and sex, while the use of minimally stabilized, fixed-bearing, cemented prostheses and patellar components is encouraged to minimize revision risk. However, the final choice of implant characteristics may need to be modified according to specific patient circumstances.

PLL: Literature search, study design, methodology determination, data collection, data analysis, data synthesis, manuscript writing. AWD: Study design, interpretation of data, manuscript preparation. OR: Data analysis. HAP: Data analysis, manuscript preparation. SEG: Interpretation of data, manuscript preparation.

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Supplementary data

Table 1. Summary of patient and prosthesis factors for primary and revised TKR for OA 2003–2019 by registry. Values are count (%) unless otherwise specified

	Primary SKAR	Primary AOANJRR	Primary KP	Revised SKAR	Revised AOANJRR	Revised KP
Total number of TKR	188,290	663,982	220,652	5,613	24,931	6,082
Patient factors						
Sex						
Males	79,230 (42)	291,208 (44)	84,937 (38)	2,430 (43)	11,683 (47)	2,641 (43)
Females	109,060 (58)	372,774 (56)	135,715 (62)	3,183 (57)	13,248 (53)	3,441 (57)
Mean age (SD)	69.5 (8.9)	68.5 (9.1)	67.6 (8.9)	69.2 (9.3)	68.2 (9.4)	67.1 (9.6)
Age groups						
< 55	11,164 (6)	43,508 (7)	15,915 (7)	411 (7)	1,886 (8)	594 (10)
55–64	47,111 (25)	177,066 (27)	65,693 (30)	1,436 (26)	6,698 (27)	1,850 (30)
65–74	74,830 (40)	263,105 (40)	88,065 (40)	2,141 (38)	9,850 (40)	2,220 (37)
≥ 75	55,185 (29)	180,303 (27)	50,979 (23)	1,625 (29)	6,497 (26)	1,418 (23)
ASA from year	2009	2013	2003	2009	2013	2003
ASA 1	24,112 (13)	20,306 (3)	3,431 (2)	525 (11)	524 (4)	34 (1)
ASA 2	88,804 (47)	188,640 (28)	124,206 (56)	2,728 (56)	6,507 (45)	2,504 (41)
ASA 3	22,426 (12)	128,551 (19)	73,502 (33)	1,193 (25)	7,002 (48)	2,527 (42)
ASA 4	249 (0)	3,672 (1)	1,769 (1)	33 (1)	527 (4)	138 (2)
ASA 5	9 (0)	10 (0)	13 (0)	0 (0)	6 (0)	5 (0)
Missing	1,348 (1)	14,891 (2)	17,731 (8)	363 (7)	0 (0)	874 (14)
Total	136,948	356,070	220,652	4,842	14,566	6,082
BMI from year	2009	2015	2003	2009	2015	2003
Underweight (< 18.5)	214 (0)	439 (0)	393 (0)	7 (0)	29 (0)	20 (0)
Normal (18.5–24.9)	24,483 (13)	25,581 (4)	25,849 (12)	751 (15)	964 (9)	752 (12)
Pre-obese (25.0–29.9)	58,839 (31)	77,407 (12)	69,110 (31)	1,762 (36)	2,940 (29)	1,846 (30)
Obese 1 (30.0–34.9)	38,000 (20)	76,861 (12)	66,968 (30)	1,318 (27)	3,121 (31)	1,767 (29)
Obese 2 (35.0–39.9)	11,565 (6)	42,505 (6)	37,882 (17)	481 (10)	1,863 (18)	1,068 (18)
Obese 3 (≥ 40.0)	2,436 (1)	26,499 (4)	14,524 (7)	126 (3)	1,242 (12)	583 (10)
Missing	1,411 (1)	16,641 (3)	5,926 (3)	462 (9)	0 (0)	46 (1)
Total	136,948	265,933	220,652	4,907	10,159	6,082
Prosthesis factors						
Prosthesis constraint						
Minimally stabilized	175,667 (93)	487,626 (73)	66,489 (30)	5,025 (90)	16,973 (68)	1,643 (27)
Posterior stabilized	11,340 (6)	172,530 (26)	146,780 (67)	504 (9)	7,725 (31)	4,232 (70)
Fully stabilized	758 (0)	2,519 (0)	2310 (1)	38 (1)	139 (1)	91 (1)
Hinged	470 (0)	1,133 (0)	64 (0)	41 (1)	86 (0)	5 (0)
Missing	55 (0)	174 (0)	5,009 (2)	5 (0)	8 (0)	111 (2)
Fixation						
Both cemented	180,220 (96)	389,650 (59)	208,391 (94)	5,336 (95)	13,353 (54)	5,671 (93)
Both cementless	7,424 (4)	120,616 (18)	3,746 (2)	254 (5)	6,130 (25)	163 (3)
Tibia only cemented	136 (0)	147,232 (22)	6,387 (3)	7 (0)	5,050 (20)	183 (3)
Femur only cemented	277 (0)	6,484 (1)	357 (0)	7 (0)	398 (2)	15 (0)
Missing	233 (0)	0 (0)	1,771 (1)	9 (0)	0 (0)	50 (1)
Bearing mobility						
Fixed	186,680 (99)	539,194 (81)	202,426 (92)	5,489 (98)	18,575 (75)	5,371 (88)
Mobile	1,461 (1)	124,614 (19)	13,208 (6)	116 (2)	6,348 (25)	600 (10)
Missing	149 (0)	174 (0)	5,018 (2)	8 (0)	8 (0)	111 (2)
Patellar component						
Used	7,975 (4)	375,409 (57)	215,924 (98)	345 (6)	11,252 (45)	5,941 (98)
Not used	180,315 (96)	288,573 (43)	4,728 (2)	5,268 (94)	13,679 (55)	141 (2)
Polyethylene type						
UHMWPE	162,648 (86)	395,665 (60)	147,384 (67)	4,920 (88)	18,569 (74)	4,448 (73)
XLPE	24,473 (13)	230,781 (35)	36,750 (17)	665 (12)	5,788 (23)	1,002 (16)
XLPE + AntiOx.	495 (0)	37,255 (6)	24,156 (11)	10 (0)	567 (2)	387 (6)
Missing	674 (0)	281 (0)	12,362 (6)	18 (0)	7 (0)	245 (4)

Table 4. Odds ratios with 95% confidence intervals for each reason for revision

	Patient factors			Prosthesis factors			
	Sex F vs. M	Age < 65 vs. ≥ 65	Constraint PS vs. MS	Cement no vs. yes	Bearing mobility Mobile vs. fixed	Poly type UHMWPE:XLPE	Patellar component used no vs. yes
Arthrofibrosis							
SKAR	0.7 (0.5–1.1)	2.7 (1.8–4.1) [a]	2.3 (1.2–4.4) [a]	1.5 (0.6–3.7)	5.7 (2.1–16) [a]	0.6 (0.4–1.0)	0.3 (0.2–0.7) [b]
AOANJRR	0.7 (0.6–0.8) [b]	1.5 (1.3–1.7) [a]	1.2 (1.1–1.4) [a]	1.5 (1.3–1.8) [a]	1.3 (1.1–1.5) [a]	1.5 (1.3–1.7) [a]	1.6 (1.0–2.3)
KPJRR	0.9 (0.8–1.1)	2.1 (1.8–2.5) [a]	0.8 (0.6–0.9) [b]	1.3 (0.7–2.4)	1.6 (1.2–2.0) [a]	1.2 (1.0–1.5)	0.9 (0.4–1.6)
Fracture							
SKAR	5.1 (2.9–9.2) [a]	0.3 (0.2–0.6) [b]	2.7 (1.6–4.7) [a]	0.5 (0.1–1.9)	1.1 (0.2–8.0)	1.6 (0.8–3.2)	0.4 (0.2–0.8) [b]
AOANJRR	2.5 (2.1–2.9) [a]	0.5 (0.4–0.6) [b]	1.4 (1.2–1.7) [a]	1.5 (1.2–1.7) [a]	1.2 (1.0–1.4)	2.0 (1.7–2.4) [a]	1.2 (1.0–1.4)
KPJRR	3.3 (2.2–5.0) [a]	0.3 (0.2–0.4) [b]	2.7 (1.7–4.3) [a]	1.1 (0.4–3.5)	1.2 (0.7–2.0)	2.4 (1.5–3.8) [a]	0.6 (0.1–2.3)
Infection							
SKAR	0.5 (0.5–0.6) [b]	0.8 (0.7–0.9) [b]	1.9 (1.7–2.2) [a]	1.1 (0.9–1.4)	2.1 (1.5–3.0) [a]	0.8 (0.7–0.9) [b]	0.7 (0.6–0.9) [b]
AOANJRR	0.5 (0.5–0.5) [b]	0.9 (0.9–1.0)	1.5 (1.4–1.6) [a]	0.9 (0.8–0.9) [b]	1.0 (1.0–1.1)	1.0 (0.9–1.0)	1.0 (1.0–1.1)
KPJRR	0.6 (0.5–0.6) [b]	0.9 (0.8–0.9) [b]	1.2 (1.1–1.3) [a]	0.9 (0.7–1.3)	1.2 (1.1–1.4) [a]	1.2 (1.1–1.3) [a]	0.9 (0.7–1.3)
Instability							
SKAR	1.5 (1.3–1.7) [a]	1.6 (1.4–1.9) [a]	1.5 (1.2–1.9) [a]	2.2 (1.7–2.8) [a]	1.9 (1.1–3.3) [a]	1.1 (0.9–1.3)	0.9 (0.7–1.3)
AOANJRR	1.2 (1.1–1.3) [a]	1.3 (1.2–1.5) [a]	1.2 (1.1–1.3) [a]	1.5 (1.4–1.7) [a]	1.2 (1.1–1.3) [a]	1.7 (1.5–1.8) [a]	1.1 (1.1–1.2) [a]
KPJRR	1.1 (1.0–1.2)	1.7 (1.5–1.9) [a]	1.0 (0.9–1.2	1.2 (0.8–1.9)	1.8 (1.5–2.1) [a]	1.0 (0.9–1.2)	0.9 (0.6–1.4)
Loosening							
SKAR	1.2 (1.1–1.3) [a]	1.2 (1.0–1.3)	1.7 (1.4–2.1) [a]	0.4 (0.2–0.6) [b]	3.9 (2.9–5.4) [a]	1.8 (1.4–2.2) [a]	0.4 (0.3–0.4) [b]
AOANJRR	1.0 (1.0–1.1)	1.2 (1.2–1.3) [a]	1.5 (1.4–1.6) [a]	1.7 (1.6–1.8) [a]	1.8 (1.7–1.9) [a]	2.8 (2.6–3.0) [a]	1.3 (1.2–1.3) [a]
KPJRR	1.1 (0.9–1.2)	1.3 (1.1–1.4) [a]	1.4 (1.3–1.6) [a]	2.2 (1.7–3.0) [a]	1.7 (1.4–2.0) [a]	2.2 (1.9–2.6) [a]	0.6 (0.4–1.0)
Pain							
SKAR	1.5 (0.9–2.4)	3.0 (1.9–4.7) [a]	0.2 (0.0–1.6)	0.7 (0.2–2.9)	n.a.	11 (1.5–79) [a]	0.1 (0.0–0.1) [b]
AOANJRR	1.0 (1.0–1.1)	1.0 (0.9–1.1)	1.2 (1.1–1.3) [a]	1.5 (1.3–1.6) [a]	1.4 (1.3–1.6) [a]	2.2 (2.0–2.5) [a]	3.3 (3.0–36) [a]
KPJRR	1.1 (0.8–1.6)	1.6 (1.1–2.2) [a]	0.9 (0.7–1.3)	5.2 (2.9–9.3) [a]	2.1 (1.3–3.3) [a]	1.5 (1.0–2.3)	3.0 (1.5–5.9) [a]
Patellar reasons							
SKAR	1.2 (1.1–1.4) [a]	1.1 (1.0–1.3)	1.1 (0.8–1.3)	1.3 (1.0–1.7)	3.0 (2.1–4.3) [a]	1.3 (1.1–1.5) [a]	3.5 (2.1–5.9) [a]
AOANJRR	1.1 (1.0–1.1)	1.0 (0.9–1.0)	1.0 (1.0–1.1)	2.0 (1.8–2.1) [a]	1.5 (1.4–1.6) [a]	2.6 (2.4–2.8) [a]	63 (52–78) [a]
KPJRR	1.0 (0.7–1.5)	1.2 (0.8–1.7)	0.4 (0.3–0.5) [b]	3.0 (1.3–6.7) [a]	2.0 (1.2–3.2) [a]	1.3 (0.8–1.9)	11 (6.9–17) [a]
Wear							
SKAR	0.6 (0.3–1.3)	2.0 (1.0–3.9)	n.a.	5.6 (2.3–14) [a]	n.a.	0.7 (0.3–1.6)	0.1 (0.1–0.3) [b]
AOANJRR	1.0 (0.9–1.1)	1.0 (0.9–1.1)	0.6 (0.5–0.7) [b]	4.8 (4.2–5.5) [a]	3.0 (2.7–3.4) [a]	5.3 (4.4–6.3) [a]	1.6 (1.4–1.8) [a]
KPJRR	0.9 (0.7–1.1)	1.1 (0.8–1.4)	0.7 (0.6–1.0)	5.5 (3.3–9.0) [a]	1.6 (1.1–2.5) [a]	1.0 (0.7–1.4)	0.7 (0.2–2.2)

[a] Significant > 1
[b] Significant < 1
n.a. = not applicable (numbers too small to calculate).

Paper V

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Primary Knee

Primary Total Knee Arthroplasty Revised for Instability: A Detailed Registry Analysis

Check for updates

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ABSTRACT

Background: Instability after total knee arthroplasty is a common but poorly understood complication.
Methods: Data from a large national registry was used to study patient and prosthesis characteristics of 2605 total knee arthroplasty revisions for instability. The cumulative percent revision was calculated using Kaplan-Meier estimates, and Cox proportional models used to compare revision rates. The rate of further revision was analyzed with regard to prostheses used in the first revision.
Results: Instability increased from 6% of all first revision procedures in 2003 to 13% in 2019. The revision risk was lower for minimally stabilized prostheses, males, and patients aged ≥65 years. Polyethylene insert exchange was used for 55% of revision procedures, using a thicker insert in 93% and a change in insert conformity in 24% of cruciate-retaining knees. The increase in either thickness or conformity had no effect on the rate of further revision. After a revision for instability, 24% had a second revision by 14 years. Recurrent instability accounted for 32% of further revisions. A lower second revision rate was seen after revision of both femoral and tibial components, and where constrained components were used.
Conclusion: Revision for instability is increasing. Revising both femoral and tibial components led to a lower rate of second revision compared to a change in insert alone. Recurrent instability was common.

Instability after total knee arthroplasty (TKA) is an important cause of revision surgery that is increasing over time. The Australian Orthopedic Association National Joint Replacement Registry (AOANJRR) records instability as the third most common reason for revision accounting for 8.5% of all first revisions [1]. Other registries record revision for instability between 6.0% and 17.7% [2,3]. Clinical series report 10%-26% of revision procedures in primary TKA for instability [4–8].

Revisions for postoperative TKA instability within the first few years are most likely related to technical errors such as poor gap balancing, incorrect component selection or positioning [9–14], trauma to the periprosthetic soft tissues [9,15], or following correction of a severe articular deformity that required extensive ligament releases [16]. Instability can occur with systemic connective tissue disorders or neuromuscular diseases [13,17–19].

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Ethics: The study was approved by the Commonwealth of Australia as a Declaration of Quality Assurance Activity under section 124X of the Health Insurance Act, 1973. All investigations were conducted in accordance with ethical principles of research (the Helsinki Declaration II).

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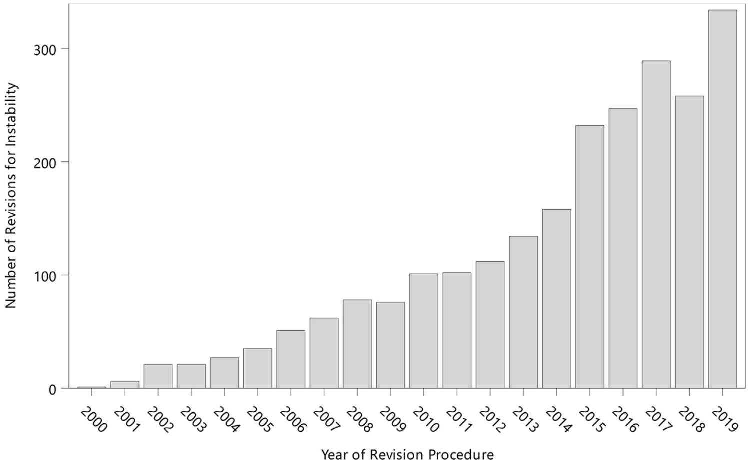


Fig. 1. Annual procedure numbers for revision for instability.

Table 1
Summary of Primary Total Knee Arthroplasty for OA Revised for Instability or Other Reasons or Not Revised.

Variable	Revision for Instability	Other Revision Diagnoses	Not Revised	Total
Follow-up years				
Mean ± SD	3.3 ± 3.4	3.6 ± 3.7	6.6 ± 4.6	6.5 ± 4.6
Median (IQR)	2 (1-4.6)	2.2 (1-5.2)	5.9 (2.8-9.8)	5.7 (2.7-9.7)
Minimum	0	0	0	0
Maximum	17.3	19.8	20.3	20.3
Age at primary				
Mean ± SD	63.9 ± 9.8	64.9 ± 9.3	68.7 ± 9.1	68.6 ± 9.1
Median (IQR)	64 (58-71)	65 (59-71)	69 (62-75)	69 (62-75)
Age group				
<55	427 (16.4%)	3345 (13.4%)	41,879 (6.2%)	45,651 (6.5%)
55-64	946 (36.3%)	8669 (34.7%)	174,903 (26%)	184,518 (26.4%)
65-74	825 (31.7%)	9030 (36.2%)	267,029 (39.8%)	276,884 (39.6%)
≥75	407 (15.6%)	3931 (15.7%)	187,892 (28%)	192,230 (27.5%)
Gender				
Female	1565 (60.1%)	13,084 (52.4%)	377,892 (56.3%)	392,541 (56.1%)
Male	1040 (39.9%)	11,891 (47.6%)	293,811 (43.7%)	306,742 (43.9%)
ASA score				
1	68 (6.7%)	370 (5.7%)	19,868 (6%)	20,306 (6%)
2	568 (55.7%)	3400 (52.1%)	184,672 (55.4%)	188,640 (55.3%)
3	372 (36.5%)	2653 (40.6%)	125,526 (37.6%)	128,551 (37.7%)
4	12 (1.2%)	109 (1.7%)	3551 (1.1%)	3672 (1.1%)
5			10 (0%)	10 (0%)
BMI				
Underweight (<18.50)		6 (0.2%)	433 (0.2%)	439 (0.2%)
Normal (18.50-24.99)	45 (7.4%)	332 (8.5%)	25,204 (10.3%)	25,581 (10.3%)
Preobese (25.00-29.99)	177 (29.2%)	1134 (28.9%)	76,096 (31.1%)	77,407 (31.1%)
Obese class 1 (30.00-34.99)	205 (33.8%)	1199 (30.6%)	75,457 (30.8%)	76,861 (30.8%)
Obese class 2 (35.00-39.99)	117 (19.3%)	714 (18.2%)	41,674 (17%)	42,505 (17.1%)
Obese class 3 (≥40.00)	63 (10.4%)	535 (13.6%)	25,901 (10.6%)	26,499 (10.6%)
Constraint in primary procedure				
Fully stabilized	22 (0.8%)	132 (0.5%)	2472 (0.4%)	2626 (0.4%)
Hinged	4 (0.2%)	82 (0.3%)	1062 (0.2%)	1148 (0.2%)
Medial pivot design	92 (3.5%)	507 (2%)	23,467 (3.5%)	24,066 (3.4%)
Minimally stabilized	1742 (66.9%)	16,897 (67.7%)	475,512 (70.8%)	494,151 (70.7%)
Posterior stabilized	745 (28.6%)	7348 (29.4%)	169,004 (25.2%)	177,097 (25.3%)
Unknown		9 (0%)	186 (0%)	195 (0%)
Age at first revision				
Mean ± SD	67.2 ± 9.8	68.5 ± 9.4		68.4 ± 9.5
Median (IQR)	67 (61-74)	69 (62-75)		69 (62-75)
Total	**2605**	**24,975**	**671,703**	**699,283**

OA, osteoarthritis; SD, standard deviation; IQR, interquartile range; ASA, American Society of Anesthesiologists; BMI, body mass index.

Later instability revisions are more likely due to progressive insufficiency of soft tissues or wear of the polyethylene insert [4,5,20,21].

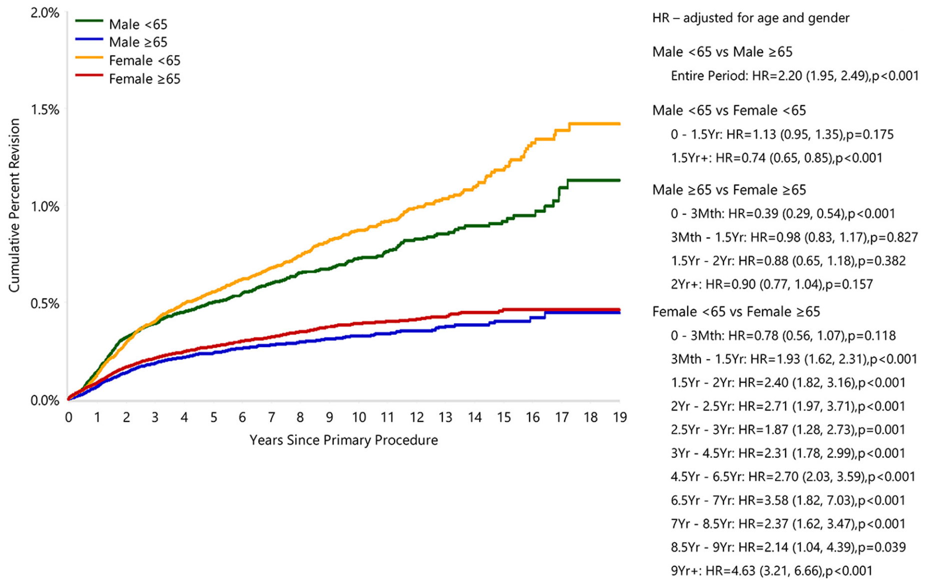
Concepts, classifications, and treatment strategies have been reported [4,7,14,15,22] but the definition and reported frequency of instability are controversial, with some calling it a “wastebasket diagnosis” [23], or a modern-day labeling of pain post-TKA that is otherwise undiagnosed [24].

A better understanding of postoperative instability is needed to reduce revision procedures for this diagnosis [25]. The AOANJRR reports improving all-cause TKA revision rates over time, but infection and instability have increased [1]. A registry study detailing changing reasons for revision over the last 15 years has also highlighted this increase, but the reasons are unclear [26].

The study aims were to: (1) document the frequency of TKA revised for instability, and the patient and prosthesis factors associated with this revision diagnosis; (2) describe the procedures used to treat TKA instability; and (3) compare the outcome of these surgical strategies by calculating the cumulative rate of second revision for primary TKA procedures revised for instability.

Materials and Methods

Using data from the AOANJRR, we studied primary TKA performed until December 31, 2019. AOANJRR data collection commenced in 1999, and includes over 97.8% of arthroplasty procedures undertaken in Australia since 2003. These data are externally validated against patient-level data provided by state and territory health departments. A sequential, multilevel matching process is used to identify any missing data which are subsequently obtained by follow-up with the relevant hospital. All primary procedures are linked to any subsequent revision involving the same patient, joint, and side. Data are also matched biannually to the Australian National Death Index.



Number at Risk		0 Yr	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs	8 Yrs	9 Yrs
Male	<65	104937	94471	84194	74985	66415	58288	50983	44298	37961	31619
	≥65	201805	180930	160997	141629	123626	106469	90502	76117	62923	51120
Female	<65	125232	114359	103137	92454	82205	72556	63680	55092	47275	39727
	≥65	267309	242628	218104	194587	172146	150617	130309	111573	94075	77984

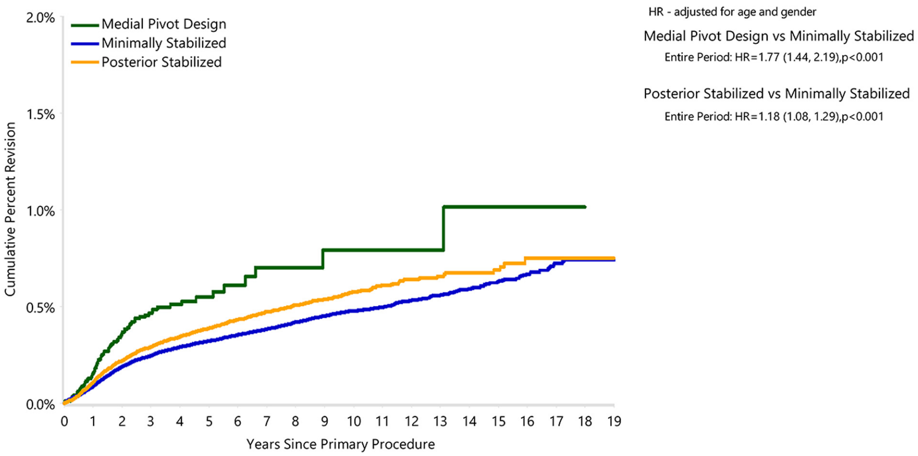
Number at Risk		10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs	16 Yrs	17 Yrs	18 Yrs	19 Yrs
Male	<65	26036	21129	16740	13124	9990	7152	4820	2873	1241	302
	≥65	40693	31835	24233	17856	12603	8454	5238	2842	1133	246
Female	<65	32844	26880	21353	16891	12885	9286	6203	3624	1531	355
	≥65	63366	50516	39331	29580	21536	14553	9203	5081	2106	481

Fig. 2. CPR of primary TKA for OA revised for instability by age and gender. CPR, cumulative percent revision; TKA, total knee arthroplasty; OA, osteoarthritis.

Table 2
Analyses of Patient and Prosthesis Factors of Primary TKA for OA With Regard to Revision for Instability.

	Factor	N at Risk	N Revised for Instability	Comparator	N at Risk	N Revised for Instability	Time Period	Hazard Ratio	Confidence Intervals	*P* Value
Age	<65	230,169	1373	≥65	469,114	1232	0-3 mo	1.02	0.74-1.41	.893
							3-9 mo	1.92	1.54-2.41	**<.001**
							9 mo to 1.5 y	2.24	1.89-2.66	**<.001**
							1.5-2 y	2.32	1.83-2.94	**<.001**
							2-2.5 y	2.07	1.58-2.70	**<.001**
							2.5-4.5 y	2.03	1.68-2.45	**<.001**
							4.5-5 y	3.69	2.20-6.19	**<.001**
							5-6 y	2.22	1.66-2.97	**<.001**
							6.5+ y	3.28	2.68-4.01	**<.001**
Gender	Male	306,742	1040	Female	392,541	1565	Entire	1.17	1.08-1.27	**<.001**
Age and gender	Male <65	104,937	566	Male ≥65	201,805	474	Entire	2.20	1.95-2.49	**<.001**
	Female <65	125,232	807	Female ≥65	267,309	758	0-3 mo	0.78	0.56-1.07	.118
							3 mo to 1.5 y	1.93	1.62-2.31	**<.001**
							1.5-2 y	2.40	1.82-2.16	**<.001**
							2-2.5 y	2.71	1.97-3.71	**<.001**
							2.5-3 y	1.87	1.28-2.73	**<.001**
							3-4.5 y	2.31	1.78-2.99	**<.001**
							4.5-6 y	2.70	2.03-3.59	**<.001**
							6.5-7 y	3.58	1.82-7.03	**<.001**
							7-8.5 y	2.37	1.62-3.47	**<.001**
							8.5-9 y	2.14	1.04-4.39	**.039**
							9+ y	4.63	3.21-6.66	**<.001**
ASA	3-5	132,233	384	1 and 2	208,946	636	Entire	1.15	1.01-1.30	**.036**
BMI	BMI ≥30	145,865	385	BMI <30	103,427	222	Entire	1.08	0.91-1.28	.365
Prosthetic constraint	Posterior stabilized	177,097	745	Minimally stabilized	494,151	1742	Entire	1.18	1.08-1.29	**<.001**
	Medial pivot design	24,066	92	Minimally stabilized	494,151	1742	Entire	1.77	1.44-2.19	**<.001**
	Medial pivot design	24,066	992	Posterior stabilized	177,097	745	Entire	1.50	1.21-1.87	**<.001**
MS insert conformity	Anterior stabilized	8593	31	Cruciate retaining	440,127	1548	Entire	1.21	0.85-1.73	.284
	Deep dish	45,431	163	Cruciate retaining	440,127	1458	Entire	1.07	0.91-1.26	.415
	Anterior stabilized	8593	31	Deep dish	45,431	163	Entire	1.14	0.77-1.67	.515
MS insert thickness	≤14 mm	4,766,780	1605	>14 mm	16,128	132	0-3 mo	0.26	0.16-0.42	**<.001**
							3 mo to 1 y	0.40	0.28-0.55	**<.001**
							1-1.5 y	0.56	0.39-0.80	**.001**
							1.5-2 y	0.64	0.46-0.88	**.006**
							2+ y	0.55	0.44-0.69	**<.001**
PS insert thickness	≤14 mm	169,074	691	>14 mm	7604	50	Entire	0.69	0.52-0.93	**.012**
Bearing mobility	Mobile	134,764	605	Fixed	564,324	2000	0-3 mo	4.81	3.55-6.52	**<.001**
							3+ mo	0.93	0.85-1.03	.162
Polyethylene type	Non-XLPE	430,183	1903	XLPE	268,798	702	0-6 mo	2.16	1.64-2.84	**<.001**
							6+ mo	1.10	1.00-1.20	.054
Fixation	Cemented	405,675	1411	Cementless	128,657	566	Entire	1.02	0.92-1.12	.733
	Cemented	405,675	1411	Hybrid	164,951	628	Entire	1.02	0.93-1.12	.624
	Cementless	128,657	566	Hybrid	164,951	628	Entire	1.01	0.90-1.13	.911

TKA, total knee arthroplasty; OA, osteoarthritis; ASA, American Society of Anesthesiologists; BMI, body mass index; MS, minimally stabilized; PS, posterior stabilized; non-XLPE, non-cross-linked polyethylene; XLPE, cross-linked polyethylene. The values in bold indicate that they are significant at the 5% level (ie, $P < .05$).



Number at Risk	0 Yr	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs	8 Yrs	9 Yrs
Medial Pivot Design	24066	18708	13964	9912	6275	3707	2486	1905	1502	1104
Minimally Stabilized	494151	447048	400531	357238	317274	278540	242136	207904	176048	146659
Posterior Stabilized	177097	163285	149147	134218	118982	104181	89646	76314	63931	52098

Number at Risk	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs	16 Yrs	17 Yrs	18 Yrs	19 Yrs
Medial Pivot Design	839	655	554	455	355	250	176	100	45	4
Minimally Stabilized	120923	98372	78473	61439	46505	32823	21663	12466	5290	1243
Posterior Stabilized	40755	31020	22401	15381	10026	6287	3567	1817	654	134

Fig. 3. CPR of primary TKA for OA revised for instability by prosthesis constraint.

We defined “instability” to include all revisions for instability, bearing dislocation, or arthroplasty dislocation. Dislocations of the polyethylene bearing or knee prosthesis were included as these result from more extreme forms of instability [11,27]. The study inclusion criteria were all TKA procedures with a primary diagnosis of osteoarthritis (OA) revised for instability by this definition.

We calculated the cumulative percent revision as the primary outcome measure, and performed subanalyses for gender, age at

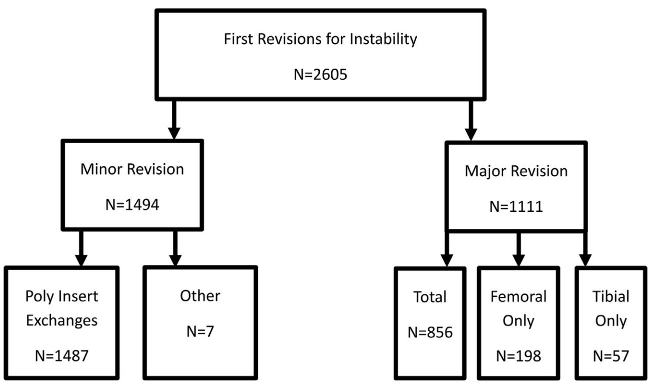


Fig. 4. Flow diagram of revision of primary TKA for instability.

the time of revision surgery, patient comorbidity, and body mass index. Patient comorbidity was assessed by American Society of Anesthesiologists Physical Status Classification System score [28] and body mass index was classified into the World Health Organization categories [29].

Prosthesis characteristics studied included thickness and mobility of the insert, type of fixation (cemented, cementless, and hybrid), and prosthesis constraint. Constraint was classified as minimally stabilized (MS, defined as those that have a flat or dished tibial articulation, regardless of congruency), posterior stabilized (PS, implants that provide additional posterior stability, most commonly using a peg-and-box design), medial pivot design (MPD, arthroplasties that have a ball-and-socket medial portion of the articulation), fully stabilized (FS, implants with a large peg-and-box design designed to give some collateral as well as posterior stability which are also known as varus/valgus constrained components), and hinged (implants which have a hinge mechanism to link the femoral and tibial components).

We further subdivided the MS group used with a cruciate-retaining (CR) femoral component by the conformity of the insert. These were CR, anterior stabilized (AS, defined as inserts with increased anterior conformity intended to provide additional anterior stability), and deep dished (DD, defined as inserts that have an ultracongruent insert that is intended to give additional sagittal stability without the need for a peg-and-box design).

For the outcome of revision TKA for instability, we analyzed the rate of second revision with regard to the level of constraint, thickness, and conformity of the new tibial insert. Also, we divided the type of revision into minor revision and major revision dependent on whether the femoral and tibial components were exchanged. The latter was subdivided into major partial revision (changing femoral or tibial component) and major total revision (changing both components).

Statistical Analysis

Kaplan-Meier estimates of survivorship were used to report the time to revision, with censoring at the time of death and closure of the dataset at the end of December 2019. The cumulative percent revision, with 95% confidence intervals (CIs), was calculated using unadjusted point-wise Greenwood estimates. Age and gender-adjusted hazard ratios (HRs) were calculated from Cox proportional hazard models to compare the rate of revision between groups. The assumption of proportional hazards was checked analytically for each model. If the interaction between the predictor and the log of time was statistically significant in the standard Cox model, then a time-varying model was estimated. Time points were selected based on the greatest change in hazard, weighted by a function of events. Time points were iteratively chosen until the assumption of proportionality was met and HRs were calculated for each selected time period. If no time period was specified, the HR was calculated over the entire follow-up period. All tests were 2-tailed at 5% levels of significance. Statistical analysis was performed using SAS software version 9.4 (SAS Institute Inc, Cary, NC).

Table 3
Types of Revision Procedures for Instability by Primary TKA Prosthesis Constraint.

Constraint Type	Revision Procedure Type	N
Minimally stabilized	Minor	931
	Major	796
Posterior stabilized	Minor	490
	Major	253
Medial pivot design	Minor	51
	Major	40
Fully stabilized	Minor	12
	Major	9
Hinged	Minor	3
	Major	1
Other minor (staple, etc.)		7
Unknown constraint		12
Total		**2605**

TKA, total knee arthroplasty.

Table 4
Minor Revisions for Instability Showing Changes in Polyethylene Insert Thickness by Constraint of Primary TKA.

Thickness Change	Minimally Stabilized		Posterior Stabilized	
	n	%	n	%
Nil	52	6	43	9
1-3 mm	333	38	168	34
3-5 mm	359	40	187	38
>5 mm	136	15	79	16
Thinner	7	1	3	1
Unknown	0	0	10	2
Total	**887**		**490**	

TKA, total knee arthroplasty.

Results

Patient and Prosthesis Characteristics of Primary Total Knee Arthroplasty Revised for Instability

There were 699,283 primary TKAs for OA recorded from 1999 to 2019, and 27,580 of these had undergone a first revision. Instability was the reason for revision in 9.4% (2605/27,580) and was the third most common reason after loosening and infection. The surgeon description was “instability” in 90%, “bearing dislocation” in 7.1%, and “prosthesis dislocation” in 2.9%. The yearly number of revision procedures for instability is shown in Figure 1.

The characteristics of those revised for instability are detailed in Table 1. Females had a higher revision risk for instability compared to males (HR 1.17, 95% CI 1.08-1.27, $P < .001$), and after 3 months patients aged <65 years had a higher risk of revision when compared to patients aged ≥65 years (Fig. 2).

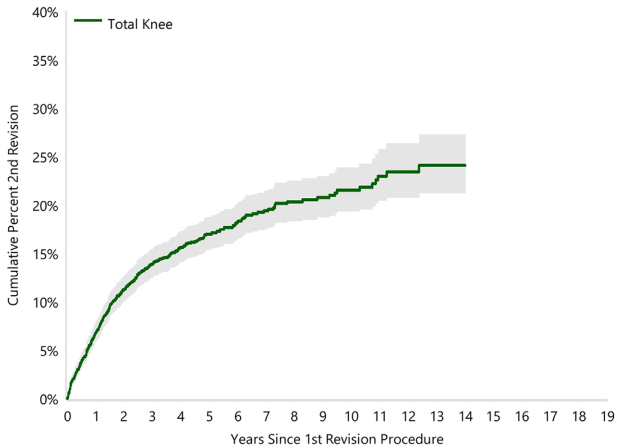
Patient and prosthesis factors regarding revision of primary TKA for instability are summarized in Table 2. Both PS and MPD designs had a higher rate of revision compared to MS prostheses (HR 1.18, 95% CI 1.08-1.29, $P < .001$ and HR 1.77, 95% CI 1.44-2.19, $P < .001$, respectively) (Fig. 3). When comparing the subgroups of primary MS implants, there was no difference among CR, AS, and DD inserts.

Insert thickness >14 mm (for both MS and PS implants) had a higher risk of revision compared to thinner inserts. Those with mobile bearings had a higher risk of revision for instability compared to fixed-bearing prostheses for the first 3 months, after which there was no difference. Procedures using non cross-linked polyethylene (non-XLPE) also had a higher rate of revision for the

Table 5
Minor Revision of Minimally Stabilized TKA for Instability Showing Changes in Polyethylene Insert Conformity and Thickness.

Primary Insert	Revision Insert Conformity						
	Total	CR	%	AS	%	DD	%
Cruciate retaining	**774**	564	73	86	11	124	16
Increased thickness		522	93	83	97	112	90
Anterior stabilized	**17**	2	12	15	88	0	
Increased thickness		2	100	14	93	0	
Deep dish	**96**	7	11	0		89	93
Increased thickness		6	86	0		85	96

CR, cruciate retaining; AS, anterior stabilized; DD, deep dish; TKA, total knee arthroplasty.



Number at Risk	0 Yr	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs	8 Yrs	9 Yrs
Total Knee	2605	2082	1712	1383	1106	872	701	552	447	349

Number at Risk	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs	16 Yrs	17 Yrs	18 Yrs	19 Yrs
Total Knee	261	187	125	83	55	35	24	13	3	1

Fig. 5. Cumulative percent second revision of TKA for OA where first revision was for instability.

first 6 months when compared to XLPE, after this time there was no difference.

Types of Revision Total Knee Arthroplasty Procedures for Instability

A flow diagram of first revisions of primary TKA for instability is shown in Figure 4 and the types of revision by constraint of the primary TKA is shown in Table 3. Minor revisions accounted for 57.4% (1494/2605) of all revision procedures for instability. The polyethylene insert was exchanged in 99.5% (1487/1494), with addition of minor components (staples, screws, and suture anchors) making up the remainder.

For the 887 MS knees that had a minor revision for instability, the amount of insert thickness and conformity change is shown in Tables 4 and 5 Some knee designs do not have options for conformity change. The insert thickness increases in the 480 minor revisions of PS knees is also shown in Table 4, and in 11% (52/480) an FS insert was used in the few designs where this is possible without femoral component exchange.

Table 6
Reasons for Second Revision Following First Revision for Instability.

Second Revision Diagnosis	Number	Percent
Instability	122	32
Loosening	103	27
Infection	78	20
Patella causes	22	6
Pain	17	4
Other	43	11
Total	385	100

With the major revisions there was a tendency to increase prosthetic constraint with the revision procedure. Constraint increased in 87% (954/1099) of major revisions, while in 12% (135/1099) it remained the same and in 2% (21/1099) decreased.

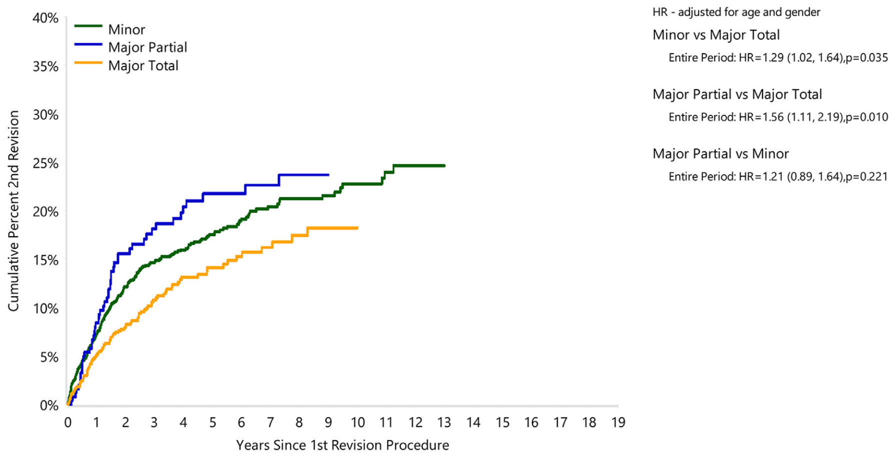
Results of Revision Total Knee Arthroplasty for Instability

Of the 2605 revisions for instability, 385 have required a second revision. There was a cumulative percent second revision of 24% at 14 years (Fig. 5). The most common reason for second revision was further instability (32%) (Table 6).

Where the first revision was a minor revision, there was no difference in second revision rates with insert thickness change. There was also no difference in second revision comparing the insert conformity used within the MS group.

There was a lower rate of second revision when a major total revision was used compared to a minor revision or major partial revisions (HR 1.29, 95% CI 1.02-1.64, $P = .035$ and HR 1.56, 95% CI 1.11-2.19, $P = .010$, respectively) (Fig. 6).

When primary MS knees were revised for instability using a major revision there was no statistical difference with prosthesis constraint used for the revision, but there was a trend for a lower rate of second revision with FS and hinged devices (Fig. 7). When PS knees were revised with a major revision there was a higher rate of second revision using another PS design when compared to an FS design (HR 4.33, 95% CI 1.51-12.41, $P = .006$) (Fig. 8). The results of analyses of prosthesis factors with regard to second revision of primary TKA for OA where the first revision was for instability are presented in Table 7.



Number at Risk	0 Yr	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs	8 Yrs	9 Yrs
Minor	1487	1201	1001	800	648	519	411	328	270	216
Major Partial	255	211	178	154	133	102	87	76	64	45
Major Total	856	668	532	428	324	250	203	148	113	88

Number at Risk	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs	16 Yrs	17 Yrs	18 Yrs	19 Yrs
Minor	164	123	85	54	37	22	15	8	3	1
Major Partial	39	25	16	11	6	5	4	1	0	0
Major Total	58	39	24	18	12	8	5	4	0	0

Fig. 6. Cumulative percent second revision of TKA for OA where first revision was for instability by type of revision.

Discussion

This detailed registry study of instability after TKA describes the patient and prosthesis characteristics of those revised, the procedures used, and the results of revision. Revision for instability increased during the study period. There were diverse approaches to the treatment of instability, but over 50% of revisions were insert exchanges. Revision procedures usually increased insert conformity or prosthetic constraint. However, following revision for instability, there was a high rate of second revision with the most common reason being recurrent instability.

Patient and Prosthesis Factors Related to Revision for Instability

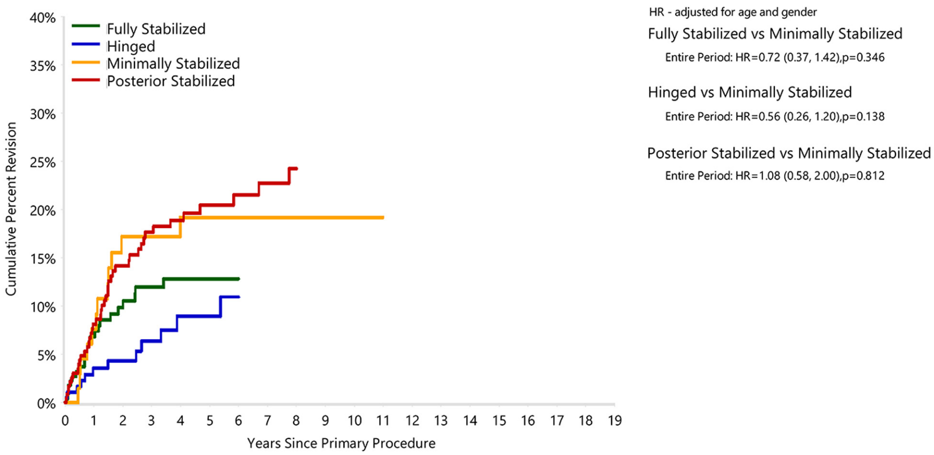
It is unclear why there has been an increase in revision for instability. This has occurred despite changes in prosthetic components that could be expected to lower instability. These include the recent availability of inserts in single millimeter thickness increases [30], more conforming designs (such as AS or DD) [31–33], and the use of assistive technology. The lower rate of revision using XLPE seen before 6 months may be explained by these generalized prosthesis factor changes that have coincided with the introduction of XLPE. However, increasing instability revision with time implies there are other factors involved, for example, increased awareness of certain forms of instability such as mid-flexion instability [9,34]. During the study period, revisions for “pain” decreased, but less than the commensurate increase in instability revisions [26].

The median time to revision was 2 years, suggesting that most instability relates to technical error or incorrect primary prosthetic choice, rather than progressive soft tissue stretching or polyethylene wear. This is consistent with the findings of others [14,35].

Patients <65 years were at increased risk of revision for instability, consistent with previous case series [6,36]. This may be due to the physical demands of the active younger patients. Female patients had a greater risk of instability revisions. Gender differences may relate to increased knee ligament laxity, a comparative difference in muscular strength, or possibly the higher rate of self-reported instability described in females [37–39].

Surprisingly, the MS designs had the lowest revision rates for instability. MS components have less inherent constraint, but both MPD and PS designs require PCL resection and this structure may contribute not only to stability but also to joint proprioception [40]. In addition, a study using intraoperative computer navigation data found more mid-flexion instability with PS than CR prostheses [41]. A recent study of MPD knees has identified a high rate of revisions for instability with this design [42] which is apparent in our analysis.

We found that primary TKA with >14-mm-thick inserts had higher revision rates. This finding has been previously reported [43] although recently disputed [44]. Based on our results, if the primary operative conditions require an insert thickness of >14 mm,



Number at Risk	0 Yr	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs	8 Yrs	9 Yrs
Fully Stabilized	228	166	134	110	86	70	52	38	32	26
Hinged	186	146	106	85	62	49	42	33	20	14
Minimally Stabilized	71	60	51	49	40	34	32	25	23	16
Posterior Stabilized	232	193	158	136	119	85	70	59	49	39

Number at Risk	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs	16 Yrs	17 Yrs	18 Yrs	19 Yrs
Fully Stabilized	19	13	7	7	7	6	5	3	0	0
Hinged	9	6	3	2	1	1	0	0	0	0
Minimally Stabilized	14	9	6	4	2	1	0	0	0	0
Posterior Stabilized	30	21	14	10	5	3	2	1	0	0

Fig. 7. Cumulative percent second revision of minimally stabilized primary TKA for OA where the first revision was for instability, by prosthesis constraint used in the revision.

consideration should be given to changing to a more constrained prosthesis to avoid instability.

A mobile-bearing design was a risk factor for revision for instability only in the first 3 months. In a large cohort of mobile-bearing knees, 15 of 23 cases of bearing "spin-out" occurred during this time period, with claims that ligament release and bearing design contributed [27].

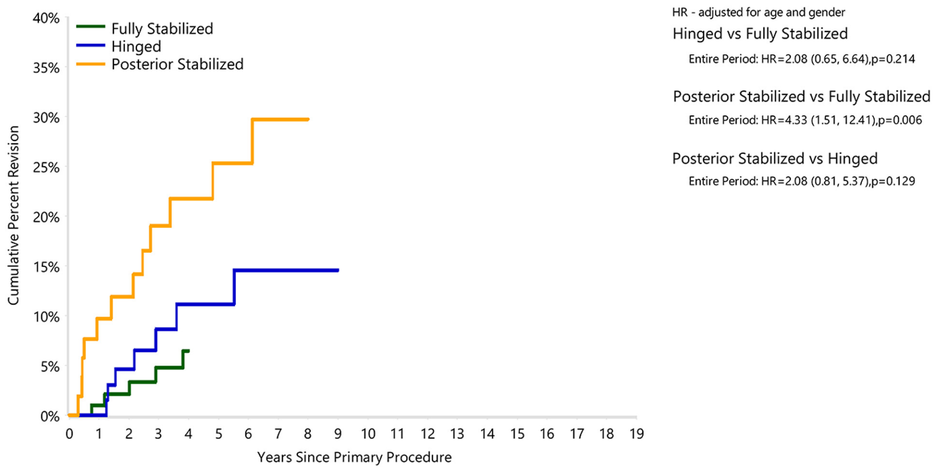
Results of Revision for Instability

After a revision for instability 24% had a second revision by 14 years, with recurrent instability the reason for 32% of reoperations. Reports of second revision rates vary from 8% to 36%, and recurrent instability is frequently reported [5,45].

MS primary prostheses accounted for 67% of the revisions for instability and in over half a simple change in insert was carried out. Although this approach may be appropriate with a symmetrical flexion gap laxity [46], others suggest that modifying the insert thickness alone may not be the preferred option [7,47–49]. Although the change in insert thickness was similar to other studies [46,49], we found that the rate of further revision was independent of the thickness change, or use of a more conforming design.

Major revision of both femoral and tibial components was associated with the lowest rate of further revision. Major revision enables use of a more constrained device. When MS knees were revised there was no difference in the second revision rate if another MS or if a PS design was used, but there was a trend for lower second revision if FS or hinged designs were used in the revision. Conversion of MS components to PS may only correct instability if there is isolated PCL insufficiency [5,7,12,48]. When PS components were revised, we found a lower rate of second revision using an FS device. This finding supports the recommendation to use more constrained devices when revising for instability [45,50], but it may also reflect surgeons' reluctance to offer further revision to those with constrained prostheses.

A strength of this study is the large registry data set used to analyze a reason for revision that would be difficult to investigate otherwise. Case series reports and even systematic reviews of instability are limited in the numbers studied [6]. Due to the infrequency and heterogeneity of instability, it is difficult to design a clinical trial for treatment alternatives. Another advantage is that rare occurrences, such as second revision procedures, can be more completely captured and examined, as data collection is community-based, and not limited to a research group or hospital.



Number at Risk	0 Yr	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs	8 Yrs	9 Yrs
Fully Stabilized	107	91	80	66	51	35	32	23	19	13
Hinged	82	68	55	42	33	32	21	13	11	10
Posterior Stabilized	53	43	39	31	25	20	18	13	9	5

Number at Risk	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs	16 Yrs	17 Yrs	18 Yrs	19 Yrs
Fully Stabilized	10	7	5	2	2	1	1	1	0	0
Hinged	4	1	0	0	0	0	0	0	0	0
Posterior Stabilized	4	2	1	1	1	1	1	0	0	0

Fig. 8. Cumulative percent second revision of posterior-stabilized primary TKA for OA where the first revision was for instability, by prosthesis constraint used in the revision.

There are also some limitations to using registry data. Although the findings of this study may be true where MS components are frequently used for primary TKA, they may not be generalizable to other populations where more PS components are used. Also, registry calculated revision rates for instability may underestimate true instability rates as some with less significant forms of instability may avoid revision surgery. There may also be some patients with symptomatic instability and comorbidities that preclude revision surgery. Patients revised for instability are generally younger, suggesting that the number avoiding revision for age-related comorbidities would most likely be small.

Another limitation is that clinical findings and imaging were not assessed to confirm the diagnosis of instability. Registry-recorded instability is the assessment made by the surgeon at the time of the revision procedure. As the revision diagnosis of instability is specifically listed on the data form, it is expected that this is a true diagnosis and the likelihood of misclassification is small.

A further limitation was considering TKA instability as a unified diagnosis, as there have been different forms of instability described (flexion, extension, hyperextension. and mid-flexion) which may require diverse surgical strategies. The degree of instability may also vary from minor to extreme, and attempts to combine or compare these may not be appropriate. Finally, we analyzed prostheses grouped by constraint, but there may be differences in performance of individual implants within each class.

Conclusion

Instability was one of the most common causes for TKA revision and increased during the study period. Revision for instability was more common in females and in patients less than 65 years of age. It was less frequent with MS prostheses. Using a polyethylene insert thickness of more than 14 mm in the primary was a risk factor, as was a mobile-bearing design. We found variation in revision procedures, which likely reflects the diversity in type and extent of instability. Insert exchange was performed in 55% of revisions for instability, usually increasing the thickness and at times the conformity. Although a patient-specific approach to TKA instability is encouraged, these minor revisions were less successful with respect to further revision than major total revisions, which were often due to more constrained prostheses. After revision for TKA instability 24% had undergone a second revision by 14 years, and recurrent instability was the most common cause for the second revision. Using a fully constrained or hinged device when revising for instability lowered the risk of further revision.

Table 7
Analyses of Procedure and Prosthesis Factors With Regard to Second Revision of Primary TKA for OA Where the First Revision Was for Instability.

	Factor	N at Risk	N Second Revision	Comparator	N at Risk	N Second Revision	Time Period	HR	Confidence Intervals	*P* Value
MS insert thickness change	No increase	52	9	<3-mm increase	333	43	Entire	1.36	0.66-2.79	.403
	3- to 5-mm increase	359	52	<3-mm increase	333	43	Entire	1.09	0.73-1.64	.667
	>5-mm increase	136	27	<3-mm increase	333	43	Entire	1.37	0.84-2.23	.208
PS insert thickness change	No increase	43	12	>5-mm increase	79	12	Entire	2.09	0.93-4.71	.075
	<3-mm increase	168	34	>5-mm increase	79	12	Entire	1.52	0.78-2.94	.219
	3- to 5-mm increase	187	27	>5-mm increase	79	12	Entire	1.02	0.52-2.02	.954
MS revisions by insert conformity	Anterior stabilized	94	14	Deep dish	128	18	Entire	1.13	0.56-2.27	.736
	Anterior stabilized	94	14	Cruciate retaining	623	101	Entire	1.01	0.57-1.76	.985
	Cruciate retaining	623	101	Deep dish	128	18	Entire	1.12	0.68-1.85	.654
Type of revision	Minor	1478	235	Major total	856	96	Entire	1.29	1.02-1.64	**.035**
	Major partial	255	51	Major total	856	96	Entire	1.56	1.11-2.19	**.010**
	Major partial	255	51	Minor	1478	235	Entire	1.21	0.89-1.64	.221
Major revisions	Femoral only	198	34	Femoral and tibial	856	96	Entire	1.35	0.91-1.99	.137
	Tibial only	57	17	Femoral and tibial	856	96	Entire	2.01	1.20-3.39	**.008**
	Tibial only	57	17	Femoral only	198	34	Entire	1.49	0.83-2.68	.177
MS major revisions by constraint of revision	Posterior stabilized	232	45	Minimally stabilized	71	13	Entire	1.08	0.58-2.00	.812
	Fully stabilized	228	24	Minimally stabilized	71	13	Entire	0.72	0.37-1.42	.346
	Hinged	186	14	Minimally stabilized	71	13	Entire	10.56	0.26-1.20	.138
PS major revisions by constraint of revision	Posterior stabilized	53	13	Fully stabilized	107	5	Entire	4.33	1.51-12.41	**.006**
	Hinged	82	7	Fully stabilized	107	5	Entire	2.08	0.65-6.64	.214
	Posterior stabilized	53	13	Hinged	82	7	Entire	2.08	0.81-5.37	.129

TKA, total knee arthroplasty; OA, osteoarthritis; HR, hazard ratio; MS, minimally stabilized; PS, posterior stabilized.
The values in bold indicate that they are significant at the 5% level (ie, $P < .05$).

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