A critical examination of the Australian Orthopaedic Association National Joint Replacement Registry: Improving outcomes of hip and knee replacement.

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Forward

I first became aware of joint replacement registries during my time as a Fellow in Hip and Knee Replacement at the Nuffield Orthopaedic Centre in Oxford in 1993. I was following up patients for a cohort study on what was then an emerging problem, how to treat patients with fractures around the femoral stem of a hip replacement. The study examined the causes and treatment of a series of 35 patients presenting with these periprosthetic fractures and, according to the literature at the time, the study represented the largest number of patients with periprosthetic fractures in the world[1]. I was therefore amazed when I saw a presentation on data from the Swedish Hip Arthroplasty Registry, reporting the outcomes associated with all total hip replacements performed in Sweden, and the very large numbers involved compared to a study form a single institution. Although the publication was in Swedish, there was an English translation in summary form which I kept. Regrettably it disappeared somewhere during my return to Australia two years later.

I was fortunate to become involved with the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) in 2004, firstly as a Victorian State member on the Governance Committee, and then was honoured to be invited as a Deputy Director of the AOANJRR in 2007. I had previously worked under Professor Stephen Graves, the Director of the AOANJRR, who had been the Chairman of Orthopaedics at my hospital. My first publication, based on AOANJRR data, was on a thorough analysis of the ASR Resurfacing and total hip replacement system, detailing the high rate of revision compared to other prostheses (1)[2]. The AOANJRR was the first registry to report these findings and the world wide recall has led to significant changes in the way devices are introduced into the market and monitored. This spurred my interest in undertaking a PhD to investigate the role of the AOANJRR in the change of practice of joint replacement surgery in Australia.

[1] This was eventually updated and published with larger numbers and longer follow up in 2009. Fawzy E, de Steiger R, Gundle R et al, The Management of Periprosthetic Fractures - J Arthroplasty 2009 24 6 909-13

[2] This paper published in Journal of Bone and Joint Surgery, 2011 has been cited 105 times

Abstract

A critical examination of the Australian Orthopaedic Association National Joint Replacement Registry: Improving outcomes of hip and knee replacement.

Introduction

Total Hip Replacement (THR) and Total Knee Replacement (TKR) are effective operations for patients with end stage arthritis who can no longer be adequately treated non-operatively. It is increasingly important that these procedures be closely monitored so that the best results can be achieved for patients and optimum use of health resources achieved.

Joint replacement registries collect, analyse and report data on patients undergoing joint replacement surgery and can monitor numbers and changes over time, evaluate outcomes and identify patient and prostheses factors associated with these outcomes.

The aim of this thesis is to study the impact of the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) on hip and knee replacement in Australia. It will explore whether joint replacement outcomes have improved since the introduction of the Registry and critically assess the role of the Registry in this process. Within this main aim, the thesis addresses 4 specific research questions:

1. How are prostheses that are not performing as well as others in their class identified and what are the consequences of this?
2. How does the AOANJRR monitor the impact of new technology such as computer navigation for TKR and the consequences of this?
3. How does the AOANJRR monitor the introduction and impact of new materials with specific reference to crosslinked polyethylene for both THR and TKR?
4. What role has the AOANJRR played in the change of practice, policies and outcomes of hip and knee Replacement in Australia?

Methodology

The thesis involves a systematic investigation using data from the AOANJRR to address the research questions. The questions were appropriately defined to retrieve information from the Registry for critical examination and analysis. The basic framework is empirical. The processes and analytical methods used to answer specific quantitative research questions are standard and currently in place at the Registry.

The research questions were developed to examine data that could specifically be addressed by the AOANJRR and with minimal information available from other national registries or other sources. These were designed with the aim of determining whether any demonstrated improvements in joint replacement outcomes were likely due to the Registry.

Results

The revision rates for hip and knee joint replacements have improved since the inception of the Registry. The revision burden for total joint replacement is defined as the proportion of all hip and knee replacement procedures that are revisions. In Australia, the revision burden for total hip replacement has declined from 13.1% in 2002/2003 (the first year of full Registry national data) to 9.8% in 2015/2016. For knee replacements the revision burden has declined from 9.3% in 2002/2003 to 7.4% in 2015/2016. This equates to a 25% reduction in the burden of revision for hip replacement and a 20% reduction for knee replacement over the respective periods. The rate of revision for primary THR has declined from 4.8% at 6 years for the time period 2003-2006 to 3.6% at 6 years for THR performed between 2011 -2014. A similar reduction is also seen for TKR over the same period with a decrease in the rate of revision from 5.1% for procedures performed from 2003 -2006 compared to 3.8% for procedures performed from 2011-2014.

The role of the Registry in improving the outcomes of joint replacement is addressed within the context of the research questions. The first paper described the process and the evolution over time of methods the Registry has developed to identify devices with a higher than anticipated rate of revision. As a consequence of reporting these devices, there has been a 67% reduction in THRs and a 76% reduction in the use of TKRs that have been so identified in the following year. The international consequence of this process is followed up later in the thesis.

TKR has a higher rate of revision for younger patients and methods to reduce this rate of revision are important. The use of computer navigation results in an overall reduction in the rate of revision for patients < 65 years of age and a reduction for loosening in patients of all ages.

The introduction of crosslinked polyethylene (XLPE) results in a prosthesis specific reduction in revisions for both TKR and THR compared to the use of the standard conventional non cross-linked polyethylene. For younger patients, <55 years of age, there is a fivefold reduction in the rate of revision for THR at 15 years compared to the use of conventional non cross-linked polyethylene. The Registry was the first to report a reduction in revision with the use of XLPE for hip and knee replacements. This has important implications and may enable younger patients to undergo surgery, confident of a reduced need for revision in the long term.

The penultimate chapter outlines the contribution that the Registry has made to the improved outcomes of joint replacement in Australia by examining the interaction with multiple stakeholders. The chapter illustrates the many ways this has been achieved and uses case examples of feedback with resultant change of practice. The interaction of the Registry with the Australian Government, Regulatory authorities, Industry, and Medical Insurers outlines the importance of involving all stakeholders when striving to improve healthcare outcomes.

Conclusion

There has been a substantial improvement in the outcomes of hip and knee replacement in Australia over the past 14 years. This thesis outlines the ways by which this has been achieved and outlines the critical role of the Registry in achieving these improved outcomes.

Declaration

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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I also give permission for the digital version of my thesis to be made available on the web, via the University's digital research repository, the Library Search and also through web search engines, unless permission has been granted by the University to restrict access for a period of time.

I acknowledge the support I have received for my research through the provision of an Australian Government Research Training Program Scholarship.

Richard Noel de Steiger

Presentations resulting from PhD

International Scientific Meetings Peer Reviewed

1. The Use of Cross-Linked Polyethylene for THA in Younger Patients Results in a Marked Reduction in Revision at 15 Years.
   International Hip Society Conference, London, UK. 6-9 September 2017
2. Orthopaedic Registries Around the World.
   55th Annual Meeting Girdlestone Orthopaedic Society,
   Bergen, Norway. 13-16 June 2017
3. The Use of Cross-linked Polyethylene for THA results in a marked reduction in revision at 16 years.
   6th International Congress of Arthroplasty Registries, San Francisco, USA. 20-22 May 2017
4. Lifetime Risk of Primary THR surgery for OA from 2003-2013: A multinational analysis using national registry data.
   6th International Congress of Arthroplasty Registries, San Francisco, USA. 20-22 May 2017
5. Overview of International signal detection.
   5th International Congress of Arthroplasty Registries (ISAR)
   Manchester, U.K. 28-31 May 2016
6. Learning Curve for Total Hip Arthroplasty with New Prostheses.
   5th International Congress of Arthroplasty Registries (ISAR)
   Manchester, U.K. 28-31 May 2016
7. Computer navigation reduces Total Knee Arthroplasty revision for patients under 65.
   13th Meeting of the Combined Orthopaedic Associations
   Cape Town, South Africa. 11-15 April 2016
8. Identification of Prostheses Outliers and Implications.
   13th Meeting of the Combined Orthopaedic Associations
   Cape Town, South Africa. 11-15 April 2016
9. How does the surgeon influence the results of joint replacement?
   13th Meeting of the Combined Orthopaedic Associations
   Cape Town, South Africa. 11-15 April 2016
10. How Registries Identify Outlier Prostheses.
    3rd International Congress of Arthroplasty Registries (ISAR).
    Boston, USA. 31 May – 2 June 2014

11. Database management.
3rd International Congress of Arthroplasty Registries (ISAR).
Boston, USA. 31 May – 2 June 2014

12. The outcome of computer navigation for primary knee arthroplasty.
European Federation of National Associations of Orthopaedics & Traumatology (EFORT).
London, UK. June 2014

13. The outcome of Cross-Linked and non Cross-Linked Polyethylene in Primary Total Knee Replacement.
European Federation of National Associations of Orthopaedics & Traumatology (EFORT).
London, UK. June 2014

14. The outcome of Cross-Linked and non Cross-Linked Polyethylene in Primary Conventional Total Hip Replacement.
European Federation of National Associations of Orthopaedics & Traumatology (EFORT).
London, UK. June 2014

15. How does the surgeon influence the results of joint replacement?
European Federation of National Associations of Orthopaedics & Traumatology (EFORT).
London, UK. June 2014

16. Identification of Prosthesis Outliers and Implications.
European Federation of National Associations of Orthopaedics & Traumatology (EFORT).
London, UK. June 2014

17. How the Registry Identifies Outliers.
51st Annual Girdlestone Orthopaedic Society Meeting.
Torbay, UK. September 2013

18. Computer Navigation for TKR.
10th Computer Assisted Orthopaedic Surgery (CAOS) Asia Pacific Meeting – Cairns, Australia. July 2013

19. How has CAS changed in the last 15 years?
10th Computer Assisted Orthopaedic Surgery (CAOS) Asia Pacific Meeting – Cairns, Australia. July 2013

20. Computer Navigation for Total Knee Replacement.
International Society of Arthroplasty Registries Conference (ISAR)
Stratford-Upon-Avon, UK. June 2013

21. How the Registry Identifies Outlier Prostheses.
International Society of Arthroplasty Registries Conference (ISAR)
Stratford-Upon-Avon, UK. June 2013

22. The Impact of Surgeon Volume on the Outcome of Hip Replacement.
International Society of Arthroplasty Registries Conference (ISAR) -
Stratford-Upon-Avon, UK. June 2013

23. Registry Access for the Surgeon via the Net.
1st International Congress of Arthroplasty Registries (ISAR) -
Bergen, Norway. May 2012

24. The 10 year outcome of highly cross linked polyethylene bearing surfaces in primary conventional total hip replacements: Analysis of over 84,000 procedures.
European Federation Orthopaedic Trauma (EFORT) Scientific Congress –
Berlin, Germany. May 2012

National and State Scientific Presentations Peer Reviewed

1. The use of cross linked polyethylene for total hip arthroplasty markedly improves outcomes at 15 years in younger patients.
AOA Annual Scientific Meeting, Adelaide, Australia. October 2017

2. Difference in outcomes of a specific computer navigation system for TKR.
AOA Annual Scientific Meeting, Adelaide, Australia. October 2017

3. THA for young patients.
AOA Annual Scientific Meeting, Cairns, Australia. October 2016

4. A Dummies Guide to Interpreting NJRR Data.
AOA Annual Scientific Meeting, Brisbane, Australia. October 2015

5. Changing Reasons for Revision THA.
Australian Orthopaedic Association COE Scientific Program, Sydney, Australia.
May 2015

6. NJRR Update: Learning Curves and New Prostheses.
Arthroplasty Society, Annual Scientific Meeting, Freemantle, Australia. 2014

7. The outcome of computer navigation for primary knee replacement.
Australian Orthopaedic Association, Annual Scientific Meeting, Darwin, Australia. 2013

8. How the Registry Identifies 'Outlier' Prostheses.
   Australian Orthopaedic Association, Annual Scientific Meeting, Sydney, Australia. 2012

9. Surgeon Effect on the Outcomes of Joint Replacement.
   Australian Orthopaedic Association, Annual Scientific Meeting, Sydney, Australia. 2012

10. The Effect of Surgeon Experience on the Outcomes of Hip and Knee Arthroplasty.
    Arthroplasty Society of Australia Annual Scientific Meeting.
    Melbourne, Australia. May-June 2012

11. Registry Access for the Surgeon via the Net.

    Combined AOA & NZOA Scientific Meeting. Rotorua, New Zealand, October 2011

12. Computer Navigation for Total Knee Replacement. Combined AOA & NZOA Scientific Meeting. Rotorua, New Zealand. October 2011

Invited Faculty Presentations

1. Can registries and audits improve patient outcomes?
   Victorian Surgical Consultative Council
   Royal Australasian College of Surgeons (RACS)
   Melbourne, Australia. 21st February 2017

2. Bench to bedside - how to measure the impact of technology using a national registry.
   22nd Annual Australian & New Zealand Orthopaedic Research Society (ANZORS)
   Melbourne, Australia. 14 October 2016

3. The Outcome of Computer Navigation for Primary Total Knee.
   Zimmer Biomet Institute, Medical Education
   Gold Coast, Australia. 2 September 2016

4. The Outcome of Cross-linked & Non Cross-linked Polyethylene in Primary Total Knee Arthroplasty.
   Zimmer Biomet Institute, Medical Education
   Gold Coast, Australia. 2 September 2016

5. The Outcome of Computer Navigation for Primary Total Knee Arthroplasty.
   Brain Lab Users Meeting
   Munich, Germany. 17 June 2016

6. The Role of Consortia like ISAR.
   17th European Federation of National Associations of Orthopaedics and Traumatology (EFORT)
   Geneva. Switzerland. 1-3 June 2016

7. Bearing Surface Options for Total Hip Arthroplasty.
   17th European Federation of National Associations of Orthopaedics and Traumatology (EFORT)
   Geneva, Switzerland. 1-3 June 2016

8. Debate: The Value of Registries. 'Registries have led the way!!'
   5th International Congress of Arthroplasty Registries (ISAR)
   Manchester, UK. 28-31 May 2016

9. What the Registries tell us about revision.
   Arthroplasty Hip Day
   Wrightington, UK. 27 May 2016

10. Top 3 Findings from Australian Orthopaedic Association National Joint Replacement Registry.
    American Academy of Orthopaedic Surgeons. Hip and Knee Speciality Day
    Florida, USA. March 2016

11. The Outcome of Computer Navigation for Primary Knee Arthroplasty.
    British Orthopaedic Association – Annual Congress
    Liverpool, UK. September 2015

12. What the NJRR has taught us about new technologies.
    Zimmer Institute, Medical Education
    Melbourne, Australia. August 2015

13. Joint registry approach for identification of outlier prostheses.
    OrthoDays, International Symposium. Basel, Switzerland. February 2015

14. AOANJRR Overview.
    OrthoDays, International Symposium. Basel, Switzerland. February 2015

15. Highly X-Linked Poly: To the Infinity- What's New & What's the News?
    5th Annual Current Concepts in Knee Joint Replacement.
    Taipei. June 2014

16. The outcome of computer navigation for total knee arthroplasty in 44,000 cases.
    5th Annual Current Concepts in Knee Joint Replacement.
    Taipei. June 2014

17. How Registries Improve Quality of Care.
    Combined ANZCA Annual Scientific Meeting & RACS Annual Scientific Congress
    Singapore. May 2014

18. Registries – How they can change clinical practice. (Plenary Session)
Combined ANZCA Annual Scientific Meeting & RACS Annual Scientific Congress
Singapore. May 2014

19. How Registries Improve Quality of Care.
Centre of Research Excellence in Patient Safety (CREPS). Alfred Hospital, Melbourne, Australia. February 2014

20. Should there be a learning curve for implants?
Mathys – Innovations, Technology and Trends Forum. Sydney, Australia. March 2013

21. Joint Registries: Stifling or promoting good quality research?
Mathys – Innovations, Technology and Trends Forum. Sydney, Australia. March 2013

22. Monitoring safety of orthopaedic devices.
Experience from the Australian Orthopaedic Association – National Joint Replacement Registry.
Centre of Research Excellence in Patient Safety Meeting. Melbourne, Australia. February 2013

23. Improving outcomes of hip and knee replacements with a population based joint replacement registry.
Epworth HealthCare Benefactors Research Update
Melbourne, Australia. June 2012.

24. How can we measure the effect of interventions in OA research in the long term? The role of a joint replacement registry.
Australian Institute for Musculoskeletal Science Inaugural Seminar. Western Health, Sunshine Hospital, Melbourne, Australia. December 2011

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My academic executive assistant, Diana Royce, has been a tower of strength and at times I have wondered how she has put up with me. She has helped me enormously in tracking down difficult to find papers, typing up blocks of badly written text and showing me the finer points of spread sheets and formatting. At the same time, she has kept all the other facets of my academic practice in line, which has been no mean feat. I am indebted to her for her help over the past six years.

Mandy, my wife of thirty years, has always been extremely supportive of my career. When I discussed taking on a PhD she was very encouraging and, at the same time she commenced her own business which meant she was equally as busy as me. The two of us have come full circle, as I was a student when she first met me and I am still a student almost 40 years later! I could not have proceeded with this thesis without her help. My two sons, Nicholas and Justin have also been university students over the same time, and I am delighted that they have both recently graduated with double degrees. Hopefully I have instilled into them a lifelong passion for learning. Watching them play high level sport at the weekends has provided me with a welcome break from my studies.

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Finally to Professor Stephen Graves who was the founder and is the Director of the AOANJRR and the inspiration behind this thesis. I believe that the practice of joint replacement has improved in Australia and this is in no small way due to Stephen's huge contribution and ongoing efforts. I thank you for you mentorship and friendship over the many years we have worked together.

Note on References and Published Papers

This Thesis contains several published papers. All references to the work of others are fully cited and, to lessen the confusion, for the purpose of this thesis I have decided to list in the bibliography all references for the whole body of work. This has necessitated converting the PDFs of the published papers to a Word format to enable the references to be listed in the appropriate order. There are also several footnotes detailing the sources of data and some of these refer directly to Board Reports to the Australian Orthopaedic Association (AOA) and to Commercial in Confidence data. While these cannot be referenced in a publically available document, the Chief Executive Officer of the AOA has stated that the AOA Board supports the use of these documents.

Glossary of Abbreviations

Abbreviation	Name
ACMD	Advisory Committee on Medical Devices
ACSQHC	Australian Commission on Safety and Quality in Health Care
AdvaMed	Advanced Medical Technology Association
AJR	American Joint Registry
ANZORS	Australian & New Zealand Orthopaedic Research Society
AOA	Australian Orthopaedic Association
AOANJRR	Australian Orthopaedic Association National Joint Replacement Registry
ARTG	Australian Registry Therapeutic Goods
ASA	American Society of Anaesthesiologists
ASM	Annual Scientific Meeting
ASR	Articular Surface Replacement
BMI	Body Mass Index
CAOS	Computer Assisted Orthopaedic Surgery
CI	Confidence interval
CPD	Continuous Professional Development
CPE	Conventional polyethylene
CPR	Cumulative Percent Revision
CR	Cruciate Retaining
CREPS	Centre of Research Excellence in Patient Safety
CT	Computerized Tomography
EFORT	European Federation of Orthopaedics and Traumatology
FAR	Finnish Arthroplasty Register
FDA	Food and Drug Administration US
HR	Hazard Ratios
HRQOL	Health related quality of life
HTARR	Higher Than Anticipated Rates of Revision
ICOR	International Consortium of Orthopaedic Registries
IDI	Image Derived Instrumentation
IPL	International Prosthesis Library
ISAR	International Society of Arthroplasty Registries
KP	Kaiser Permanente

Abbreviation	Name
LROI	Dutch Arthroplasty Registry
MARCQI	Michigan Arthroplasty Registry Collaborative Quality Initiative
MHRA	Medicines and Healthcare Products Regulatory Agency
MRI	Magnetic Resonance Imaging
NAR	Norwegian Arthroplasty Register
NARA	Nordic Arthroplasty Register Association
NHMRC	National Health and Medical Research Council
NIS	Nationwide Inpatient Sample
NJR	National Joint Registry - England, Wales, Northern Ireland and the Isle of Man
NJRR	National Joint Replacement Registry
NZJR	New Zealand Joint Registry
NZOA	New Zealand Orthopaedic Association
OA	Osteoarthritis
ODEP	Orthopaedic Device and Evaluation Panel
PCA	Porous Coated Anatomical
PLAC	Prostheses List Advisory Committee
PMN	Premarket Notification
PROMS	Patient Reported Outcome Measures
PTIR	Patients Time Incidence Rate
QI	Quality Improvement
RACS	Royal Australasian College of Surgeons
RCT	Randomised Controlled Trial
SAP	Scottish Arthroplasty Project
SCP	Superior Performance Suffix
SD	Standard deviation
SHAR	Swedish Hip Arthroplasty Register
SKAR	Swedish Knee Arthroplasty Register
TGA	Therapeutic Goods Administration
THA	Total Hip Arthroplasty
THR	Total Hip Replacement
TKA	Total Knee Arthroplasty

Abbreviation	Name
TKR	Total Knee Replacement
UKR	Unicompartmental Knee Replacement
UK	United Kingdom
USA	United States of America
XLPE	Cross linked polyethylene
YLD	Years lived with disability

CHAPTER ONE

Introduction

1.1 - Burden of Hip and Knee Replacement

There is an increasing burden of hip and knee osteoarthritis. The Global Burden of Disease 2010 study was a comprehensive effort to measure epidemiological levels and trends of 291 diseases across 187 countries. The Osteoarthritis (OA) Expert group reported a global prevalence of radiographically confirmed knee OA to be 3.8%, and hip OA 0.85%. The prevalence varied between regions with knee OA higher in the Asia Pacific area and hip OA in North America. Hip and knee OA was ranked as the 11th highest contributor to global disability as measured by years lived with disability (YLD), and had risen from the 15th highest contributor to YLD in 1990(2). While non operative management of OA is recommended for most patients, surgery may be required when conservative treatments are not successful. Total Hip Replacement (THR) and Total Knee Replacement (TKR) are effective operations for those patients with end stage arthritis and numerous studies have demonstrated decreased pain, improved function and better health related quality of life (HRQOL) following joint replacement (3-8). The success of both hip and knee replacement, along with an ageing population, rising rates of obesity (9-11), patient expectations of an active, pain free lifestyle and access to health care have all contributed to increasing numbers of these operations being performed (12-15). The annualised incidence per 100,000 of all THR has increased from 94.5 in 2003 to 149.6 in 2016 and for TKR from 110.2 in 2003 to 215.3 in 2016. It is anticipated that this

rate of increase will continue in the foreseeable future (16). A recent study, using a logistic growth model that assumes an upper limit of THR and TKR incidence, predicts an increase in volume in Australia of 219% for THR and 142% for TKR from 2014 to 2046 (17). Other studies using data from Norway, Sweden, Finland, Denmark and Australia to estimate the risk of undergoing a THR or TKR in an individual's lifetime, have demonstrated a significant increase in the lifetime risk for these procedures in all five countries from 2003 to 2013(18, 19). As both the volume and overall cost of THR and TKR procedures increase, and new technology is introduced into the marketplace, it is increasingly important that these procedures be closely monitored, so that the best results can be achieved for patients and optimum use of health resources achieved (20-22).

Surgeons use multiple sources of information to make decisions about what types of hip and knee replacements to use for their patients. These include personal experience, attendance at scientific meetings, published literature, industry sponsored events, peer discussion and, increasingly, the use of joint registry data.

Traditionally, publications on implant performance have largely been from single centre sites, often from designer surgeons or a developer institution. The special expertise from centres required to design, develop, or perform the trials, means that results may not be applicable to

the wider community (23-25). It is in this context that joint replacement registries provide a valuable means of ongoing information regarding the outcomes of prostheses and a system of continuous quality control (26-28). Sir John Charnley, the pioneer of THR in the 1960s, advocated the need for rigorous follow up and documentation of his low friction arthroplasty patients, and even suggested that consideration should be given to establishing a national register (29).

Sweden pioneered the implementation of joint replacement registries in the 1970s due to concerns from surgeons in their orthopaedic associations about the outcomes of joint replacement surgery. Finland and Norway followed over the next decade. The Australian Orthopaedic Association recognised the need to establish a Joint Replacement Registry in 1993. The Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) commenced initial data collection at a state level in 1999 and full nationwide implementation commenced in January 2003. While it was accepted that there were already quality international registries, it was not clear if the outcomes could be attributable to the Australian population. This was largely due to the range of different prostheses used in Australia not recorded by these registries, differences in methods of fixation of the implants, possible dissimilarities in patients and surgeons, and different methods of healthcare delivery. While the AOA believes that the AOANJRR has become an integral part of orthopaedic practice in

Australia[3], the contribution of the Registry to the practice of joint replacement in Australia has not been formally evaluated. At the commencement of this thesis, the AOANJRR had 10 years of data collection and the final chapters were completed with 16 years of data available for analysis.

1.2 - Aim and Research Questions

The aim of this thesis is to study the impact of the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) on hip and knee replacement in Australia. It will explore whether joint replacement outcomes have improved since the introduction of the Registry and critically assess the role of the Registry in this process.

Within this main aim, the thesis addresses four specific research questions:

1. How are prostheses that are not performing as well as others in their class identified and what are the consequences of this?

[3] Source: Australian Orthopaedic Association Board of Directors, AOANJRR Update, February 2017

2. How does the AOANJRR monitor the impact of new technology such as computer navigation for TKR and the consequences of this?
3. How does the AOANJRR monitor the introduction and impact of new materials with specific reference to crosslinked polyethylene for both THR and TKR?
4. What role has the AOANJRR played in the change of practice, policies and outcomes of Hip and Knee Replacement in Australia?

A major function of all registries is to report the outcome of joint replacements and this is usually performed by the Kaplan-Meier method to estimate survivorship of a prosthesis at a particular time point. The AOANJRR presents the data as the cumulative percent revision (complement of the survivorship estimate). The first research question examines the methods by which prostheses that have a higher cumulative percent revision than comparable prostheses are identified.

Research questions two and three examine some of the technical aspects of joint replacement surgery that the Registry has tracked since its inception. Computer navigation involves linking a preoperative or intraoperative image of the patient's anatomy with rigid bodies attached to the patient's bones, a tracking system to monitor the motion of the limb and surgical tools in 3D space, and a sophisticated computer program that allows accurate measurement of the surgical cuts required to implant the prosthesis. Navigation has been adapted from industry

and initially used for neurosurgery to image the brain and allow more accurate identification and operation of intracranial lesions. It was first used in France to implant a TKR in 1996 and in Australia, by the author, in 2001.

The major long term issue with the longevity of joint replacement has been wear of the polyethylene bearing surface, traditionally used in the joint articulation. Wear particles induce an inflammatory reaction that results in bone loss and eventual loosening of the prosthesis. This may lead to revision surgery, an operation that carries not inconsiderable risk to the patient and cost to the community. This problem of wear has been of major concern to younger patients who may require joint replacement surgery, but have been denied because of concerns about the longer term performance, the inevitable revision surgery and subsequent risks. The Registry was amongst the first in the world to specifically track the introduction of a new modification of polyethylene which involved cross–linking molecules with electron bombardment and heating the polyethylene to toughen the structure. Laboratory studies demonstrated very low wear rates and the initial early clinical studies, using state of the art measurement tools, showed almost no wear when compared to conventional polyethylene. The AOANJRR was the first registry to report on the outcomes of this improved bearing surface.

1.3 - Structure of the Thesis

Chapter Two presents a brief history of registries and outlines how the data from the AOANJRR is utilized to address the research questions in this thesis.

Chapter Three presents a literature review relevant to the aim of the thesis.

Chapter Four, entitled 'Joint Registry approach for identification of outlier prostheses' published in ACTA Orthopaedica (August 2013, Vol. 84, (4) 348-352), addresses the first research question of how prostheses that are not performing as well as others are identified by the Registry.

Chapter Five presents a paper entitled 'Computer navigation for total knee arthroplasty reduces revision rate for patients less than sixty-five years of age' published in the Journal of Bone and Joint Surgery (2015 97(8) 635-642). It addresses the second research question about how the AOANJRR monitors the outcomes of new technology. It is the first study to describe a reduced rate of revision for TKR using computer navigation.

Chapter Six includes a paper entitled 'Lower prosthesis-specific 10 year revision rate with cross-linked than with non cross-linked polyethylene in primary total knee arthroplasty' published in Acta Orthopaedica (2015; 86 (6) 721-7). It addresses research question three on the impact of new materials with regard to improved bearing surfaces with TKR. It is the first published paper to demonstrate reduced rates of revision with specific brands of TKR using new cross-linked polyethylene.

Chapter Seven contains a paper entitled 'The use of Cross Linked Polyethylene for Total Hip Arthroplasty markedly reduces revision surgery at 16 years' (to be published in the Journal of Bone and Joint Surgery, May 2018) and further explores research question three with regard to THR.

Chapter Eight presents a paper entitled 'International overview of joint registries and their role in outlier prosthesis identification' (accepted for publication in Bone and Joint Research) and is an extension of research question one with regard to involving international registries in prosthesis identification and the international influence that the AOANJRR has had following publication of the paper contained in Chapter Four.

Chapter Nine addresses research question four and explores whether outcomes of joint replacement have improved since the introduction of the Registry and critically assesses the role of the Registry in this process. The chapter discusses the interaction of the Registry with multiple stakeholders including surgeons, government and regulatory authorities, industry, hospitals, and patients and outlines the contribution that the Registry has made to these outcomes.

Chapter Ten provides a brief summary of the thesis and outlines areas for further research.

CHAPTER TWO

Background to Registries

2.1 - Brief Overview of Registries

The National Committee on Vital and Health Statistics is the statutory body in the USA which provides information and advice to the Secretary of Health and Human Services on policy related to community and population health. It describes registries as 'an organised system for the collection, storage, retrieval, analysis and dissemination of information on individual persons who have either a particular disease, a condition (e.g. risk factor) that predisposes to the occurrence of a health related event, or prior exposure to substances (or circumstances) known or suspected to cause adverse health effects' (30). By their nature registries use an observational study design, monitor all forms of treatment and have few, if any, exclusions (31). They also evaluate care as is provided irrespective of protocol and are more representative of a "real world practice" (32). This enables a registry to provide data on a broad range of patients thereby making the results more generalizable. This is in contrast to clinical trials where an experiment with an active intervention intended to change an outcome is studied. Generally in clinical trials there are strict inclusion and exclusion criteria and therefore results may not be applicable to a whole population (33, 34) and adverse events may not be reported adequately (35). Just as clinical trials are rated in terms of quality, registries are also subject to quality measurements (36-38). This is to ensure that the design, data collection, analysis and reporting of the registry minimises bias or errors in inference (39, 40). Registries need to have clear outcomes which are defined as an end result of a particular healthcare interaction (41).

These may differ according to the perceptions of different stakeholders, yet all will have the objective of improving patient care.

Registries may be used for many purposes but the important factor for patient based registries is that they are used for evaluating outcomes (31). This is distinct from geographic population registries created for public health incident reporting, or registries that track patients with a particular disease. There are important elements that are common to quality clinical registries and these include:

- Data are collected in a naturalistic manner such that treatment is determined by the caregiver and not by a registry protocol.
- Data are reflective of clinical care routinely used for patient management.
- Data are collected in a uniform manner for every patient, with consistent data elements and definitions.
- Data are purpose driven and this is defined before collecting and analysing the data. This is distinct from administrative data sets designed for other means, but does not exclude the use of such data for linkage.

The intention of individual registries should be designated from the start and can vary according to the type of registry. There can be more than one objective. Registries can define the natural history of a disease, show the outcome of devices and be used for post market surveillance, in particular for monitoring rare events. They can determine effectiveness of interventions and can therefore be used for cost-effectiveness studies. Perhaps the most important function of a registry is to monitor quality of care and how outcomes change over time.

The first registry to be established in the world is generally considered to be the Leprosy Registry of Norway, which was founded in 1856 by royal decree. The intention of the Registry was twofold, in part to quantify the leprosy problem using the Registry as one of the control measures and to clarify the aetiology of leprosy using the Registry material for epidemiological analyses (42). This Registry became an important tool in the public health efforts against leprosy and used a minimum data set and a central system of registration, very similar to what is in use today. The number of new patients contracting leprosy in Norway dropped rapidly with over a tenfold reduction in 30 years. This was thought to be due to the identification and registration of new cases by the Leprosy Registry leading to local isolation of patients in dedicated leprosy hospitals. G. Armauer Hansen was able to work with patients that the Registry had identified to further study the disease and discovered Mycobacterium Leprae in 1874 (43). Leprosy is still known as Hansen's disease. At the first international leprosy

congress in Berlin in 1897 the resolution was adopted that 'the system of compulsory notification, surveillance and isolation, as performed in Norway, is recommended in all nations' (44). This is the first example of how a registry played an important role in a significant public health problem but this was not widely recognised until the registry protocols were found in 1970, just before the centenary of the discovery of the leprosy bacillus. Although the value of the Leprosy Registry was clearly established, there was a distinct gap of over 100 years before the development of any further clinical registries for improvement of patient care. The Medical Birth Registry of Norway commenced in 1967 (45) and the Nordic countries soon recognised the great potential of this type of research.

2.2 - Joint Replacement Registries

The first national joint replacement registry was initiated by the Swedish Orthopaedic Society in 1975 and situated in Lund. The aim was to prospectively monitor knee replacement surgery. In the early 1970s knee replacement was relatively uncommon, with little information published in the literature. Swedish orthopaedic surgeons felt it was appropriate to collect and analyse information to enable surgeons to make the most appropriate choice of implants and operative methods for their patients (46). The Scandinavian countries subsequently have had a

long history of joint registries. The Swedish Hip Arthroplasty register commenced in 1979, the Finnish in 1980, the Norwegian in 1984, and the Danish in 1995.

Joint replacement registries collect, analyse and report data on patients undergoing joint replacement surgery. Information includes, but is not limited to, age, date and side of surgery, surgeon, type of prosthesis inserted, patient diagnosis, methods of implant fixation, and other information associated with the operation. In general, a minimal data set ensures a greater chance of capturing data from a large population. For joint replacement registries the principal outcome measure is time to first revision using Kaplan-Meier estimates of survivorship. A revision procedure reflects a serious problem with the implant itself or method of intervention and is an objective measure that can be readily documented. It implies that both surgeon and patient have agreed that the problem is of sufficient magnitude to undergo revision surgery. Additional information is collected at the time of revision on the type of revision, the reasons for revision and further details of prostheses used. The analytical approaches used by the registry investigate associations with statistical methods to limit the impact of bias.

Joint registries can be used to monitor joint replacement numbers and changes over time, evaluate outcomes and practice variation, identify patient and prostheses factors associated with these, record device utilisation and provide information for comparative effectiveness

studies (47, 48). They are also necessary to evaluate rare outcomes. While a minimal data set ensures the best chance of successfully collecting information (49), expanding the data collection can lead to a more comprehensive assessment. A four level data hierarchy for arthroplasty registries has been proposed and, while there is general agreement on Level 1 data, there are some differences in the elements required in the other three levels (Table 1). All joint registries that are full members of the International Society of Arthroplasty Registries (ISAR) collect Level 1 data but there is variation in the amount of data collected on the other three levels (50).

In 1993, largely as a result of the Scandinavian experience, the Australian Orthopaedic Association recognised the need to establish a Joint Replacement Registry and, after consultation with the Commonwealth Department of Health and Ageing, an agreement was signed to fund the Australian Orthopaedic Association (AOA) to establish a joint registry. Data collection first began on 1st September 1999. Full national data have been available from January 2003. The method of data collection was based on the Scandinavian process and has been refined over time. Data are submitted by hospitals on specific forms which are completed in the operating theatre. These forms are sent to the Registry office and then entered by experienced data entry personnel. Validation of Registry data is by a sequential multi-tiered matching process against State and Territory health department separation record data. Following retrieval of unreported records and further checking of unmatched data the Registry

is able to obtain an almost complete record of hip and knee replacements performed in Australia. A matching program is run monthly to search for all primary and revision arthroplasty procedures recorded in the Registry that involve the same side and joint of the same patient, thus enabling each revision to be linked to the primary procedure. Data are also matched bi-annually with the Department of Health and Ageing National Death Index to obtain information on the date of death. Survivorship is estimated using the Kaplan-Meier method and the survival estimate at each time is accompanied by a 95% confidence interval based on the method of Greenwood. The Registry presents the survival information by the proportion of prostheses revised by a certain time, rather than surviving (not revised). This is termed the cumulative percent revision (CPR) and is the complement of the Kaplan-Meier survivorship. Age and gender adjusted hazard ratios (HR), calculated from Cox proportional hazard models, are used to compare the rate of revision between different groups of interest. The Kaplan-Meier method overestimates the risk of revision in the presence of competing risks and in such circumstances the Registry uses the cumulative incidence function for all competing risks. In this method patients who have already had a revision, or died, are excluded from the set of observations at risk of being revised. Competing risk graphs are most often used by the Registry to demonstrate the different causes of revision for joint replacements.

An Annual Report is published in mid-September and this is based on data analysis from all procedures reported to the Registry up until 31st December the previous year. As a result of the increased amount of data and information to be presented by the Registry, not all of this can be included in the Annual Report. Supplementary Reports on a range of specific topics including state variation, mortality, demographics and the outcome of revision surgery are available on the Australian Orthopaedic Association website. These reports have increased in both number and complexity over the years. In 2017 there were 11 supplementary reports compared to just one in 2012.

2.3 - Assessment of the Quality of AOANJRR

The Australian Commission on Safety and Quality in Healthcare (ACSQHC) was established by the Council of Australian Governments in 2006 to lead and coordinate national improvements in safety and quality in healthcare (51). Guidelines have been developed by the ACSQHC to assist with the quality of clinical registries and these include various criteria relating to the purpose, data capture, identification, security and governance issues (51). It is important that the above criteria are met by the AOANJRR so it is recognised as a Quality Clinical Registry and, for the purposes of this thesis, it is also important, so that it is deemed an appropriate body of data on which to base this research (52). The AOANJRR is designated as a

Federal Quality Assurance Activity under the Commonwealth Health Insurance Act of 1973, amended in 1992 to include Quality Assurance Activity. This ensures that the information is free from subpoena and allows surgeons to contribute data with confidence that it will not be used for purposes other than quality improvement. This has been tested in the Australian Federal Court in June 2016 and upheld (53). Over time the Registry has developed into a quality improvement activity as a result of continuous provision of data and feedback to all the stakeholders involved in joint replacement. This process is outlined in detail in Chapter nine.

2.4 - Strengths and Limitations of the AOANJRR

As well as the general benefits of joint registries there are some specific strengths to the AOANJRR. The Australian Orthopaedic Association is the data custodian, contribution by surgeons is voluntary and almost 100%, and surgeons have a distinct sense of ownership of the data. These factors have played an important role in the development and ongoing running of the Registry. The AOANJRR has a robust governance structure which is subject to regular review. The day to day management working group consists of a Director and three Deputy Directors, all of whom are orthopaedic surgeons and the author is the senior Deputy Director. There is also a Registry Manager, statisticians and a data entry manager who meet with the

directors on a weekly basis. The Registry reports to an AOANJRR Governance Committee, consisting of orthopaedic surgeons representing the Australian state branches and specialist societies, and this in turn reports to the AOA Board. This is in contrast to the U.K. National Registry, which is owned by the government and initially had only two orthopaedic surgeons of a total of twenty on the steering committee. A survey of consultant surgeons' views on the governance of the UK National Registry reported some concerns that the British Orthopaedic Association did not have more control over the data (54). A possible consequence of less stakeholder engagement by surgeons is less engagement with registry findings and potentially less likelihood for improved patient outcomes.

The Registry captures almost all hip and knee replacements performed in Australia and is able to analyse data based on both prosthesis and patient factors (Table 1). The Registry has an *opt out* consent process, and, since commencement of data collection up till December 31st 2017, there have only been 47 patients who have declined participation from a total of 1,353,290 procedures. It is a true population registry and therefore has wide application and relevance and reflects community practice. The Annual Report is widely read and in 2016 there were over 30,000 log-ins to the Report worldwide. As a result of the Report's clarity and the amount

of information presented, tables and figures are frequently used in presentations from leading surgeons throughout the world[4].

By their very nature, successful joint replacement registries collect a minimal data set with the firm end point of revision surgery. However an unrevised prosthesis does not necessarily have a good outcome as measured by clinical or radiological markers or patient reported outcome measures (55, 56). The Swedish, New Zealand and the UK National Registry have all, to a variable extent, recorded Patient Reported Outcome Measures (PROMs) for a subset of registry data (55, 57-59). The AOANJRR, at present, does not include these patient outcome measures. Information that may be pertinent to the outcome of joint replacement, including co-morbidities and imaging, are not collected by the AOANJRR. Recently the Registry has recorded data on the American Society of Anaesthesiologists (ASA) score, which can be used as a surrogate for patient co-morbidity (60), height and weight thereby enabling body mass index (BMI) to be calculated; and the surgical approach to THR. These data may be used to adjust for outcomes in the future. Physicians have previously expressed concerns regarding ownership, usage, and reporting of data and the publication of league tables (54, 61). These potentially may have a detrimental effect by discouraging surgeons from taking on higher risk patients and

[4] Personal Communication: Dan Berry, former president, American Academy of Orthopaedic Surgeons and current Director, American Joint Registry

ranking may not be a true reflection of a surgeon's skill in delivering a satisfactory outcome (62-64). The improvement in outcomes in coronary artery bypass surgery in New York State, and paediatric cardiac surgical mortality in Bristol, are compelling examples of improved clinical performance as a consequence of feedback of results (65, 66). While the AOANJRR is unable to publically disclose information on individual surgeons under the terms of the Federal Quality Assurance Activity it liaises closely with the AOA to provide feedback and advice on how best to manage surgeon performance. This process has been increasingly refined and is discussed in detail in Chapter Nine.

Table 1: Proposed Hierachy of Data Elements for Arthroplasty Registries General Data Elements by Level		Data that the AOANJRR Captures
Level I	Patient identifiers (identifying numbers, name, national register identification, sex, and date of birth)	✓
	Date of Procedure	✓
	Primary diagnoses for the procedure	✓
	Type of procedure	✓
	Medical device information (catalog and lot numbers)	✓
	Surgeon identifier	✓
	Hospital identifier	✓
Level II	Patient comorbidities	✓
	Body mass index	✓
	Patient ethnicity or race	
	General health status of patient at time of surgery	
	Surgical techniques	✓
	Surgical prophylaxis	
	Intraoperative complications	
Level III	Patient-reported outcomes	To commence 2018
	Clinical and/or functional outcome assessments	
	Patient socioeconomic status	
	Costs of surgery	
Level IV	Radiographic assessments	

Table adapted from Understanding Orthopaedic Registry Studies (47)

CHAPTER THREE

Literature Review

The aim of this thesis is to study the impact of the AOANJRR on hip and knee replacement in Australia, exploring whether joint replacement outcomes have improved since the introduction of the Registry and critically assessing the role of the Registry in this process. A literature review was performed interrogating PubMed, Medline, Embase, and Scopus to assess the current state of the international literature around the research questions. The research strategy was applied to PubMed and adapted for the other databases. In addition the most recent publications of all national registry annual reports were reviewed to assess if information was provided within the reports, but not indexed, and to review any relevant publications listed in the reports.

The literature review:

(i) explores whether other joint replacement registries have improved the outcomes of joint replacement in their respective countries or regions and the means by which this has been achieved; and

(ii) examines the literature with respect to the specific research questions.

Examination of the literature with respect to other registries improving outcomes of joint replacement

There are many factors that may lead to registries changing practice and improving outcomes for patients. In order to explore whether registries improve outcomes of joint replacement several years may be required before change is demonstrable, principally as there is a relatively low failure rate of joint replacement surgery. Established national registries with longer follow up are therefore more likely to demonstrate change within their respective countries. However smaller, or regional registries can also influence specific areas of practice and influence local outcomes. The Swedish and Norwegian Joint Registries are the longest running and therefore are best placed to report on change of practice over a period of time.

In a Presidential Guest Speaker address to the American Academy of Orthopaedic Surgeons, Peter Herberts, the founder of Swedish Hip Arthroplasty Register (SHAR), discussed how outcome studies have changed THR in Sweden (67). He stated that the aim of the Register is twofold:

> *'to describe the epidemiology of hip replacement surgery in Sweden, and to identify, by study of revisions, risk factors for poor outcome which are related to the patient, to the implant, and to the surgical technique. The primary goal of the register is to widen knowledge of the surgical techniques and the various types of implants, so as to improve continually the quality of hip replacement surgery.'*

SHAR distributes reports annually or every second year and these are presented at the annual scientific association meetings and institution specific data are distributed to each participating hospital in the country. Reports on aggregate data are also publically available.

Herberts and Malchau (28) evaluated the outcomes of 158,172 THR performed after the introduction of the SHAR in 1979 up till 1997. They demonstrated a successive decline in the cumulative revision incidence for aseptic loosening for patients with osteoarthritis (OA) over several time periods. Patients operated on in 1987 were revised for loosening in 3% of cases after ten years compared to 9% of those operated on in 1979. They also compared two time periods (1979-1986 and 1987-1997) and reported on both cemented and un-cemented implants. They demonstrated a reduction in revision for both types of fixation in the latter cohorts and attributed the changes to improved prostheses and cement technique. The authors specifically stated that the willingness of Swedish surgeons to adopt modern cementing techniques, as a result of feedback, contrasted with the UK where only 25% of surgeons used these methods. There were poorer outcomes when older cementing techniques were used (68).

They also compared variation in hospital performance and there was a marked reduction in inter-hospital differences over several years. They demonstrated that yearly feedback of

outcome data impelled most clinics to use safer and well documented implants, which contributed to the lower revision rate. The authors stated this change was a good example of quality improvement and *'can be ascribed to many years of information provided by the register'*

The world's first joint registry, The Swedish Knee Arthroplasty Register (SKAR) was established in 1975 and was an early adopter of survivorship analyses for evaluating outcomes of arthroplasty (69, 70). The SKAR has identified key areas where it has improved the outcomes of knee surgery in Sweden. These include: providing early warnings regarding major problems with implants and techniques, collaboration with other researchers to link SKAR with specific scientific studies, and provision of information to surgeons and institutions to aid in best practice (71). The information provided by SKAR partly explains why the long term rate of revision after TKR in Sweden is very low when compared internationally (72).

There are several examples of the influence of SKAR. A multicenter study of 3,777 unicompartmental knee replacements compared three types of implants, the PCA, the Marmor and the St Georg. The PCA had a much higher rate of revision and was subsequently withdrawn from the market (73). Another prosthesis, the Oxford unicompartmental knee replacement (UKR), while achieving good results from the developer's institution, did not perform as well in Sweden. This led to the manufacturing company developing an education

program for surgeons prior to implanting their device (74). An early study demonstrating the value of collaboration involved retrievals of polyethylene liners from revision knee replacements which showed a higher risk of deformation and loosening when the polyethylene was ≤ 6mm in thickness (75). This led to a recommendation for thicker polyethylene and the minimum thickness for polyethylene inserts in modern designs is 9mm. The SKAR also was able to show that the use of UKR for patients with rheumatoid arthritis (an intervention commonly performed in the early years of knee replacement) was unsuitable and the use of UKR for this diagnosis stopped. The SKAR provides comparative institutional information in table format demonstrating hospital outcomes in a number of key areas and this information is distributed to the heads of departments at each hospital. The SKAR states that '*it is important to inform colleagues about the report* to *stimulate discussion in order to initiate improvement efforts'* (76). Sweden has the lowest rate of TKR revisions in the world.

The success of these joint registries has led the way for Quality Registries in Sweden. The two oldest are the SKAR (1975), and the SHAR (1979), and, since 1990, there have been an additional 98 registries certified by the Swedish Association of Local Authorities and Regions (77), partly as a result of the improvements demonstrated by the joint registries. They focus on specific disorders, have largely been initiated by physicians, and allow researchers to follow patients for life. As well as the documented improvements in joint replacement outcomes, Swedish Quality Registries have contributed to improved outcomes in multiple medical fields

including improved survival of childhood cancer (78), a reduction in complications from cataract surgery (79), and improving guideline adherence for the treatment of acute myocardial infarction (80).

The Norwegian Arthroplasty Register (NAR) commenced in 1987, a little later than the Swedish Registries, and there have been many publications from the Registry on aspects of joint replacement that have contributed to improved outcomes of surgery. Fevang et al (27) used the data from the Norwegian Arthroplasty Register over a 21 year time period 1987-2007 to demonstrate improved results of total hip replacement. There were 110,882 THR reported to NAR during this time and they divided their analysis of hip replacement into four time periods, according to the year of primary surgery. The earliest time, 1987-1992, was used as the reference period. Adjusted Cox regression analyses were performed to compare the risk of revision at the different time periods compared to the reference. The sex and mean age of patients and proportion of cemented and cementless prostheses remained largely unchanged though there were different types of prostheses introduced. There was a decline in the overall number of revisions for any cause throughout the study period similar to the findings from SHAR. This was largely due to a reduction in revisions for acetabular and femoral aseptic loosening. There was a small increase compared to the initial time period in revision for dislocation, which the authors ascribed to a decrease in head size from 32mm to 28mm. There was also a small increase in the latter time period for revision for infection which the authors

attributed to a number of factors including increased awareness of septic revisions, and patient factors such as increased incidence of obesity and diabetes. Information was provided to all hospitals in Norway performing THR and there was a general improvement during two time periods 1987-1997 and 1998-2007 with the mean survival for the latter period higher than the first.

The authors stated that *'an important cause of the improvement on results seen in our study can be attributed to the increasing use of well documented implants with good results'* and that *'publication of registry studies pointing out inferior implants and cements have played an important role in this development'*. Publications from the NAR that have contributed to the improved survivorship include studies on cement fixation (81-83), studies which have identified certain brands of cementless acetabular and femoral components associated with an increased risk of loosening (84-87), and reports on the use and duration of antibiotic prophylaxis for THR (88, 89).

The NAR has also published on improved results of TKA. In a study by Dyrhovden et al (90), the revision rate of 60,623 primary TKR was evaluated comparing two time periods, 1994 to 2004 and 2005 to 2015. There was a similar median term follow up in both time periods. A reduced rate of revision for the latter time period was demonstrated and this was due to a decline in revisions for aseptic loosening of the femoral component, polyethylene

wear/breakage, patella dislocation, and unexplained pain. Similar to NAR's findings with THR there was an increased incidence of revision for infection but this was just seen in the early post-operative time period. However, unlike the study by Fevang et al above, the authors did not make a direct attribution of the influence of NAR on the reduced rates of revision for TKR.

There are three other Scandinavian joint registries, the Finnish, the Danish Knee and the Danish Hip which commenced in 1980, 1995 and 1997 respectively (91-93). While these Registries publish regular reports and articles on the results of joint replacement, there is no specific information on improved outcomes in their respective countries. With regard to the Finnish Arthroplasty Register (FAR), this has in part been due to changes in the administrative structure of FAR and issues of ownership of data. In 1993 FAR became part of the National Agency for Medicines and, in 2009, the National Institute for Health and Welfare. In 2012 the Finnish Arthroplasty Society determined that there was a need to revise the data collection and reporting of FAR, and a new advisory board was established. More comprehensive annual reports have been published from 2015 and the aim is to report at a hospital level on length of stay, early revisions and re-admissions (94). An analysis of 438,733 THR based on the Nordic Arthroplasty Register Association database demonstrated a lower 15 year prosthesis survival for Finland compared to the other Nordic countries, Sweden, Norway and Denmark (95) A number of reasons for this finding were discussed including a younger age group in Finland, differences in patient diagnoses and prosthesis variation with a higher use of uncemented and

metal on metal bearing surface devices in Finland. The reduced effectiveness of FAR during the study time period, compared to the registries from other Nordic countries may also have had a bearing on the results[5].

The National Joint Registry for England, Wales, Northern Ireland and the Isle of Man is now the world's largest and commenced in April 2003. '*The aim of the NJR is to provide information to all those involved in the management and delivery of joint replacement surgery with regard to surgical and implant performance and clinical best practice.*' There have been multiple publications using data from the UK Registry, with several of these relating to the higher revision rate of prostheses with metal on metal bearing surfaces (96, 97). There has been no specific analyses of the UK Registry and its role in the outcome of joint replacement and this may reflect the relatively short time that the UK registry has existed compared to the Scandinavian registries. However in the 2017 Annual Report (98) there are figures comparing the relative rates of revision for prostheses implanted over different years for both THR and TKR. The trend is for an improvement in survivorship in the latter years (99).

[5] Personal communication Keijo Makela, Chairman of Advisory Board, FAR

The UK Registry also reports on hospital variation using revision surgery from the past five years excluding prostheses with metal on metal bearing surfaces (because they have been withdrawn from the market due to a high failure rate) and to reflect more contemporary use of implants. Hospital variation is examined with the use of funnel plots with a standardised revision ratio plotted against the number of expected revisions. Control limits are set at approximately 2 or 3 standard deviations and hospitals with a revision rate above 3 standard deviations are termed outliers. In the 2017 Annual Report there were twelve hospitals reporting higher than expected rates for knees, and five for hips from a total of 149 National Health Service Trusts and Health Boards (98).

The New Zealand Joint Registry (NZJR) published its 18th Annual Report in 2017 and commenced data collection a few months prior to the AOANJRR in January 1999 (100, 101). There have been no specific studies demonstrating improvements in outcomes as a result of the Registry but the annual report highlights with an asterisk prostheses that have revision rates significantly higher than the overall rate of 0.73 /100 observed component years (see chapter 8). In the latest report the New Zealand Registry makes some recommendations on the best and worst combinations for THR suggesting that an all cemented THR, with a ceramic on cross-linked polyethylene bearing surface and a 32 mm diameter femoral head, performs best and a cementless metal on metal bearing surface with a head diameter ≥ 36 mm has the worst performance.

The NZJR has also collected information on Patient Reported Outcome Measures (PROMS) and was the first registry to establish that a disease specific joint score (the Oxford Hip and Knee) could be predictive of subsequent revision surgery. A statistically significant relationship has been confirmed between worse Oxford scores at six months, five, and ten years post-surgery and joint revision within two years of the Oxford 12 questionnaire collection date (102, 103). The NZJR has also recently linked PROMS to a higher revision rate for first revision joint replacements (100). This information is important as it may help reduce regular follow up of joint replacement patients to those that had the worst Oxford scores, thereby reducing costs and improving access to clinics for new patients.

Kaiser Permanente (KP) is the largest not for profit health care plan in the United States and covers approximately 9 million members with over 90% residing in California. In response to the increase in volume of implantable medical devices and the associated costs and safety issues, KP developed implant registries in 2001 (104). The aim of the registries was to '*enhance patient safety, quality of care and cost-effectiveness for KP's members'*. As well as standardized registry data collection for the specific types of registries the KP registries make use of existing administrative databases, the Electronic Health Record, and electronic screening algorithms to identify complications and to facilitate adjustment for potential confounders (105). The KP

registry can identify variation in its medical centres and has designated physicians to communicate the findings locally. It also has a number of feedback mechanisms to providers including risk–adjusted quarterly reports, reports on outlier devices and centres and individual surgeon reports documenting both descriptive details and complications.

The THR revision burden has decreased within the KP Healthcare group from 15.4% in 2002 to 10.1% in 2010 and this is thought to be due to a number of causes including outlier implant detection and prosthesis variability, identifying and monitoring product recalls, and notification of medical centre variation (48, 106-108).

Regional registries with more comprehensive data collection than the minimal dataset collected by national registries can initiate quality improvement activities by identifying variation in practice of factors associated with joint replacement (109). Using feedback to surgeons in Clinical Quality Assurance meetings, changes in practice can be initiated to improve patient outcomes.

The HealthEast Care System was the first community based joint replacement registry to commence in the USA and, in 1991, began data collection from surgeons in the greater metropolitan area of St Paul, Minnesota (110). The Registry stated that the general goals of a

joint registry were similar regardless of whether it was community based or at a national level and acknowledged that the majority of primary hip replacements in the United States were carried out by low-volume community based surgeons (111).

The HealthEast Joint Registry has been used *'to generate information of practical use to the practicing orthpaedist and can influence surgeon behaviour. Sharing the results of registry studies with the surgeon, as well as furnishing the individual surgeon with information regarding the revision rate of his or her primary operations, should only improve each surgeon's practice in the future'.* Examples of studies that have led to a change in surgeon behavior within the region include a reduction in the use of unicompartmental knee replacement from 23% of all knee replacement surgery in 1992 to 9.8% in 2004 following a study demonstrating a higher revision rate, especially for disease progression (112), and an increase in the use of all cemented TKRs after a study demonstrated improved outcomes compared to cementless TKR (113). This study also demonstrated economic benefits for using an all polyethylene cemented tibia in the older population which could have generated USD 900,000 in savings over the twelve year study period.

The Michigan Arthroplasty Registry Collaborative Quality Initiative (MARCQI) commenced in 2011 with the aim of improving the quality of care for patients undergoing hip and knee

replacement in Michigan (a state in the USA with a similar sized population to Sweden) (114). It is part of a Collaborative Quality Initiative program by the insurance provider and includes several medical disciplines. Quarterly hospital meetings, led by a clinical champion, are a critical part of the model to provide a forum for dissemination and discussion of results. Several quality improvement projects have been initiated by MARCQI. There was substantial variation in blood transfusion amongst hospitals involved in the Registry. Blood transfusion has known risks (115-117) and methods exist to reduce transfusion following joint replacement (118, 119). An education program was introduced to raise awareness of the American Association of Blood Bank's guidelines and a quality improvement (QI) program was instituted initially at two hospitals. Overall the percentage of patients transfused with a postoperative haemoglobin ≥ 8g/dL (the target level) decreased 80% after the educational intervention (109). The QI was expanded across 28 hospitals involved in MARCQI with regular feedback from senior surgeons and data officers in the Registry presenting each hospital's transfusion risk compared to other participating hospitals. This registry based intervention resulted in a decrease in the rate of transfusion and elimination of unnecessary transfusions for patients undergoing both THR and TKR in the time period following identification (120).

It is notable that both these registries contribute data to the American Joint Registry (AJR) (121) which, after many years of planning and regulatory approval, commenced a pilot project in 2011 (122) and released its first Annual Report in 2017 (123). It will soon have the largest

amount of data due to the numbers of joint replacements performed in the USA, but it will be a while before analyses, other than descriptive, will be reported.

Larsson et al, in a study using data from 13 disease registries from five countries concluded that '*by making outcome data transparent to both practitioners and the public, well managed registries enable medical professionals to engage in continuous learning and share best clinical practices. The apparent result: improved health outcomes, often at a lower cost' (124).*

There has been one analysis of the economic benefits of the AOANJRR which was undertaken by Monash University and Health Outcomes Australia on behalf of the Australian Commission on Safety and Quality in Health Care[6]. The study examined five clinical quality registries, including the AOANJRR, and concluded that registries may improve clinical practice at relatively low cost, but that the return on investment varied between the registries, and that full national coverage was desirable. The authors estimated that the net benefit of the AOANJRR was $53 million over 13 years, with a benefit to cost ratio of 5:1. The conclusion stated that the report '*will be used to support the development of a national policy context for clinical quality registries'*.

[6] Economic evaluation of clinical quality registries. Australian Commission on Safety and Quality in Health Care. November 2016. Final Report.

Examination of the literature with respect to the specific research questions.

As well as an overall view of the contribution of the AOANJRR to the practice of joint replacement, I have chosen specific research questions to examine aspects of joint replacement where the AOANJRR has collected, monitored and reported on data before other national or regional registries or, in most cases, before the publication of any scientific studies. This was firstly to demonstrate the detail of the data that the Registry has captured in order to provide more comprehensive analysis of the many factors that may influence joint replacement outcomes, and secondly to explore the effect of the Registry on outcomes separate from other possible influences.

Research Question One: Registry Approach for Identification of Outlier Prostheses

While registries have reported that most prostheses perform well, there are a number of prostheses that have rates of revision that are much higher than other prostheses in their class. Poorly performing prostheses have, in part, led to the development of the NAR and the UK National Registry.

The Norwegian Arthroplasty Registry began in 1987 as an indirect result of problems with the first hemiarthroplasty prosthesis developed in Norway, the Christiansen artificial joint (125). Tor Christiansen (1917-1981) was a Norwegian general and orthopaedic surgeon who initially developed a hemiarthroplasty in the early 1960s for the treatment of fractured neck of femur. In 1970 he introduced a THA made of a stainless steel stem and femoral head and a cemented cup made from polyoxymethylene (trade name Delrin), manufactured by a French company Benoist Girard & Co. This was widely used in Scandinavia and Italy. Although there were early reports of higher revision rates of the Christiansen THA, it was not until a clinical study from the Coastal Hospital in Norway (126), demonstrating inferior results of the Christiansen hip to the Charnley, that production and sales of the Christensen THA ceased. As a result of this experience, at the 1983 annual general meeting, the Norwegian Orthopaedic Association adopted a proposal for the establishment of a national register to be situated in Haukeland

University Hospital in Bergen. The logo of the NAR is a picture of the asymmetric wear of the Christiansen acetabular socket. The NAR publishes on the outcomes of many prostheses but does not have a formal method in the Registry Annual Reports to identify underperforming devices.

A similar situation arose in the United Kingdom, again indirectly leading to the formation of a national joint registry. The Capital Hip (3M) was introduced in 1991 and was based on the well performing Charnley prosthesis but differed in manufacturing and design techniques. Its original purpose was to introduce a cheaper prosthesis into the market place based on previous long term results. The Capital Hip had revision rates of 19-21% at five years which was much higher than expected (127, 128). The failure of the Capital Hip resulted in a message to all Directors of Public Health to ascertain the need for a national register to unite the various databases, audits and research that existed (129). The Trent Regional Registry in the UK noted a higher rate of revision of the Capital Hip compared to the Charnley before its use was discontinued in 1995 (130). The case for a national joint register in the United Kingdom was discussed in a BMJ editorial in 1996 (131) but the National Joint Registry did not commence till 2003.

A major advantage of the observational data that is collected by joint registries is the ability to report on comparative performance of prostheses and this may lead to the use of better performing devices. However actually highlighting within a publically available report those prostheses that do not perform well and detailing the methods by which this is done results in a much stronger statement. At the commencement of this thesis a literature search of all joint registries did not reveal any formal reporting or methods by which registries identified prostheses that were not performing as well as expected. This is discussed in Chapter 4. A repeat literature search at the completion of this thesis demonstrated that two registries, Kaiser Permanente and the MARCQI had both formally adopted the AOANJRR approach and the UK National Joint Registry and the Dutch Registry are currently using a similar process.

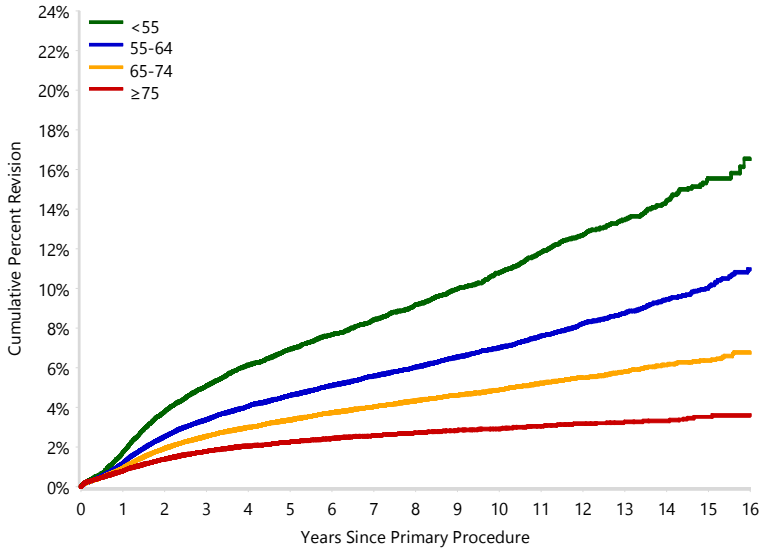
Research Question Two: New Technology and the use of Computer Navigation for TKR.

The number of TKA procedures has increased in Australia by 139.8% from January 2003 till the end of December 2016. This trend is consistent with reports from other registries and administrative datasets and is greater than the increase in the number of THR performed. There are several reasons for this including, initially, an unmet demand, and improved results of more modern prostheses compared to those in the 1970s and 1980s making the procedure more widely accepted. The rising prevalence of obesity amongst western nations is also

strongly correlated with knee arthritis and TKR. Studies from the US, Spain, Norway and Australia, using longitudinal data or linked registry data, demonstrate a temporal association between increased weight gain and the increased numbers of TKR for both males and females (11, 132-134).

The differences with respect to age and the outcome of TKR is markedly dissimilar to that of THR and these findings have consistently been reported by the AOANJRR. The revision rate for TKR increases with time and at 16 years following initial surgery patients < 55 years of age have over an eightfold revision rate compared to patients ≥ 75 years old (135).

Cumulative Percent Revision of Primary Total Knee Replacement performed for OA, by Age



Source: AOANJRR Annual Report 2017 Fig KT10

When examining the effect of age, the Registry often groups patients undergoing TKR into those < 65 years and those ≥ 65 years of age, and this allows sufficient numbers of procedures for analysis. Younger patients ≤ 65 years of age undergoing TKR currently make up 33% of the 547,407 recorded cases in the 2017 Annual Report. As the rate of revision for patients ≥ 65 years is relatively low it is more difficult to demonstrate if an intervention improves outcomes in this age group and easier to detect a difference, if one exists, in the younger age group. Because of the higher revision rate in younger patients it is therefore important to investigate methods by which the rate of revision can be reduced. One such method is the use of computer navigation which has allowed surgeons to more accurately implant the TKR prostheses. The second is the

use of cross-linked polyethylene which has demonstrated lower wear rates *in vitro* than the conventional polyethylene which has been traditionally used in TKR.

Computer navigation for TKR requires a computer with appropriate software and a display screen linked to a tracking unit, most commonly an infrared camera. All navigation systems monitor the patient's limb and the surgical instruments in space, registering these objects to the computer and finally guiding the surgeon to perform the surgery on a virtual plan. Navigation allows the surgeon to obtain accurate mechanical alignment of the prosthesis, to verify the position of the components, and adjust accordingly while in the operating theatre (136, 137).

The majority of studies on the use of computer navigation for TKR have demonstrated that navigation improves alignment compared to conventional instrumentation (138, 139). The alignment of the lower limb following TKR is generally believed to be important for long term success (140-143). Whether this improved alignment leads to a reduction in the long-term rate of revision is yet to be determined. Accurate lower limb alignment, along with the ability of navigation systems to measure and improve the balance of the TKR may be expected to also improve functional patient outcome. The evidence for this is less strong in randomized controlled trials of TKA performed with navigation compared to conventional instruments (144, 145). Most of the early studies investigating the use of computer navigation for knee

arthroplasty have been performed in specialist orthopaedic centres, where the procedures were often done by highly experienced surgeons (146-148). Orthopaedic surgeons tend to be early adopters of new technology, and it is important to determine the outcome of this technology in a broader population.

Previously there has been only one registry study on the use of computer navigation for TKR. The Norwegian Arthroplasty Register reported on the short-term outcome of 1,465 computer navigated TKR from 2005-2008 (149). The registration of TKR in NAR began in 1994 but the use of computer navigation was not captured until 2005. For the study, the authors restricted the population to the three most frequently used navigation systems and the five most frequently used TKR inserted with navigation. There were 1,465 TKR with a mean follow up time of 1.4 years in the navigation group and 8,214 TKR with a mean follow up of 1.8 years in the conventional group. Cox regression analysis was adjusted for age, sex, prosthesis brand, American Society of Anesthesiologists grade (ASA), pre-operative diagnosis, previous knee surgery, and fixation method. There was a higher relative risk of revision in the navigation group than the conventional TKR group (RR=1.7 95% CI 1.1-2.5; p=0.02). The results demonstrated one particular TKR, the mobile bearing LCS Complete (Depuy, Warsaw), had a higher rate of revision for navigation whereas there was no difference for the other four knees. The authors stated that the findings may suggest there are brand specific problems when using navigation. Computer navigation may also have been used by surgeons for more difficult cases

with malalignment or abnormal anatomy (150). While computer navigation has clearly demonstrated improved alignment in TKR, any benefit that this provides would be unlikely to be realized for several years following the initial procedure. This would most likely be in the form of reduced revisions for loosening, or wear related issues, and more likely to be demonstrated in younger, more active patients.

The paper on Computer Navigation in Chapter 5 of this thesis was designed to analyse prospectively collected Australian data from 2003 with a maximum of nine years follow up and to examine the effect of navigation specifically in younger patients <65 years of age undergoing TKR, as this group of patients has the highest rate of revision.

Research Question Three: The introduction and impact of cross-linked polyethylene for TKR and THR

Both TKR and THR have traditionally used conventional polyethylene as the bearing surface for the articulation of the joint. The long term survival of both TKRs and THRs can be affected by particles of polyethylene wear which has been associated with osteolysis and loosening of the prosthesis (151-153). Polyethylene wear is multifactorial and can be influenced by prosthesis design and sterilization, technical issues such as alignment, and patient-related

factors. In order to reduce the effect of wear and subsequent osteolysis, different types of bearing surfaces have been introduced. Cross linked polyethylene (XLPE) is one such new material and was developed in 1999. XLPE is a modified form of polyethylene, manufactured from conventional polyethylene that has been subjected to radiation doses of 50-100 kGy, and either heated above or below its melting point (154-156). The AOANJRR has identified the use of XLPE for THR and TKR since its introduction in Australia in 2000 and 2002 respectively. The definition of XLPE was confirmed with industry and crosschecked with the Australian Prosthesis Advisory List which records XLPE separately from conventional polyethylene. This has enabled a comparison of the two types of polyethylene to be performed.

While laboratory and clinical studies of XLPE have demonstrated less wear in both hip and knee replacements (157-161), studies demonstrating an improvement in clinical outcomes and reduced rates of revision are scarce. There have been no published or registry studies prior to this thesis that had demonstrated a reduced rate of revision for TKR with XLPE. One study from the Kaiser Permanente Registry in the US analysed 62,177 TKR with a median follow up time of only 2.8 years (162). The authors stated that there was no significant reduction in all cause revision and revision for aseptic loosening with the use of XLPE compared to non XLPE.

There are differences in the causes of revision for THR compared to TKR that the use of XLPE may alter. The commonest cause for revision for THR in the first six years is dislocation. After this time period loosening is the most common reason and is related to wear issues similar to TKR (135). One of the major contributing factors to dislocation in THR is the size of the femoral head and it is thought that a larger femoral head to neck ratio allows for increased motion before impingement of the neck on the edge of the socket occurs (163-165). Increasing the femoral head size has its limitations with the use of non XLPE as this increases the volumetric wear leading to increased particle induced osteolysis. The first widely used THR, the Charnley prosthesis, had a femoral head diameter of 22.25mm and, while this was thought to be optimal for lubrication and wear reduction (166) there was a higher dislocation rate with this smaller head size. The use of larger head sizes to reduce dislocation has been associated with increased wear when used with conventional non XLPE polyethylene (167, 168). The use of XLPE for THR might therefore improve survivorship of THR if larger head sizes led to fewer revisions for dislocation without the increased wear problems associated with conventional polyethylene (169).

As with TKR there are numerous publications on reduced wear with THRs using XLPE but there has been little evidence of a reduction in the revision rate as a consequence of its use. The Nordic Arthroplasty Register Association (NARA) reported on design specific differences between XLPE and conventional polyethylene in total hip replacement (170). A study from the

Kaiser Permanente Total Joint Replacement compared 1815 metal on conventional polyethylene THR to 25,008 metal on XLPE and found a higher adjusted all cause rate of revision at 7 years in the conventional polyethylene group (171).

A study using pooled data from six joint replacement registries, including the AOANJRR, did not demonstrate a reduced risk of revision (172). This study was limited to THRs with cementless fixation with a standard 32mm head size, in patients 45 to 64 years of age with a short follow up. The hazard ratio in the adjusted model was in the same direction in favour of XLPE, but did not reach significance. The UK National Joint Registry is not able to distinguish between conventional and XLPE and reports both types as polyethylene.

Chapter Six on the outcome of XLPE for TKR was designed to analyse prospectively collected data from 2003 at 10 years follow up to examine the effect of XLPE on revision rate for TKR compared to patients receiving a TKR with conventional polyethylene. As with computer navigation, there was specific reference to younger patients < 65 years of age who have the highest rate of revision. Chapter Seven on the use of XLPE for THR was designed to analyse prospectively collected data at 16 years to examine the effect of XLPE on both the early and later revision rates and the causes of revision.

This literature review has given a broad overview of the aim of this thesis. In general, the registries that have been established the longest have demonstrated improvements in joint replacement outcomes in a number of ways by publishing regular reports and scientific papers, and by hospital and, to a lesser extent, surgeon feedback. With regards to the specific research questions, there is scarce literature available. There were no studies on methods to detect or report prosthesis outliers. There was only one Registry study on research question two, with small numbers and short follow up, and this did not demonstrate an improvement with the use of computer navigation for TKR. The literature research for question three revealed no improvement for the use of XLPE in TKR and minimal prosthesis specific evidence for lower revision rates with THR. Again, these studies had short term follow up and lower numbers and highlight the need for studies with large numbers and longer term follow up to demonstrate benefits, in the presence of a low revision rate. Research question four was specific to Australia but built on the existing knowledge base from older, established registries.

The strength of the review lies not just with the evaluation of the published literature and international registry reports but also access to grey literature, attendance at scientific meetings and personal communication with international registry scientists to confirm or refute matters. A review of theses published mainly in the Scandinavian registries did not reveal topics specific to National registries and improvement of joint replacement outcomes A limitation of

this review is that there are also numerous smaller national and regional registries (largely in Europe) that do not have publically accessible documents.

CHAPTER FOUR

Joint registry approach for identification of outlier prostheses

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Contribution to the Paper	R N de Steiger helped design the research question, wrote the manuscript and together with co-authors, was responsible for editing and final approval. He submitted the paper and responded to reviewers comments.
Overall percentage (%)	65%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
Signature	Date 16/5/18

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate to include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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Signature	Date 18/5/18

4.1 - Preface

This chapter contains the first of five articles submitted for publication in peer reviewed journals. The article has been published in *Acta Orthopaedica, 2013; 84 (4):348-352*.

This paper specifically addresses the first research question of 'How are prostheses that are not performing as well as others in their class identified, and what are the consequences of this?' Joint replacement registries play a major role in monitoring arthroplasty outcomes by publishing data on survivorship of individual prostheses or combinations of prostheses. These outcomes may vary for a variety of reasons. Identifying prostheses with a higher rate of revision than other prostheses in a similar class is one way of reducing the use of these devices and encouraging best practice. The process must be transparent, accountable and have clinical relevance. This paper outlines how the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) has developed a method to report "outlier" prostheses. It is the first registry to undertake this process.

4.2 - Published Paper

Background and purpose

Joint Replacement Registries play a significant role in monitoring arthroplasty outcomes by publishing data on survivorship of individual prostheses or combinations of prostheses. The difference in outcomes can be device- or non-device-related, and these factors can be analyzed separately. Although registry data indicate that most prostheses have similar outcomes, some have a higher than anticipated rate of revision when compared to all other prostheses in their class. This report outlines how the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) has developed a method to report prostheses with a higher than expected rate of revision.
These are referred to as "outlier" prostheses.

Material and methods

Since 2004, the AOANJRR has developed a standardized process for identifying outliers. This is based on a 3-stage process consisting of an automated algorithm, an extensive analysis of individual prostheses or combinations by registry staff, and finally a meeting involving a panel from the Australian Orthopaedic Association Arthroplasty Society. Outlier prostheses are listed in the Annual Report as identified but no longer used in Australia (2) those that have been re-identified and that are still used, and (3) those that are being identified for the first time.

78 prostheses or prosthesis combinations have been identified as being outliers using this approach (AOANJRR 2011 Annual Report). In addition, 5 conventional hip prostheses were initially identified, but after further analysis no longer met the defined criteria. 1 resurfacing hip prosthesis was initially identified, subsequently removed from the list, and then re-identified the following year when further data were available. All unicompartmental and primary total knee prostheses identified as having a higher than expected rate of revision have continued to be re identified.

Interpretation

It is important that registries use a transparent and accountable process to identify an outlier prosthesis. This paper describes the development, implementation, assessment, and impact of the approach used by the Australian Registry.

Introduction

Many factors influence the outcome of joint replacement surgery. Arthroplasty registries are able to identify differences in outcome based on patient-, surgery-, or prosthesis-specific factors (67, 173-175). The principal measure of primary joint replacement surgery is time to first revision, generally estimated using the Kaplan-Meier survival method (176). This measure is an unambiguous and clear indication of a problem with the primary procedure, where both the patient and surgeon have agreed that it is serious enough to require further surgical intervention (55, 177).

It is known that prostheses have variable outcomes and, while most perform well, some have outcomes well outside what would be regarded as acceptable. This variability in prosthesis performance highlights the need for adequate pre-market assessment and vigilant post-market surveillance. Joint replacement registries play a critical role in providing quality post-market surveillance, as well as helping to understand prosthetic use and improving patient outcomes (27, 28, 34, 178). Registries have also been very effective in identifying prostheses or combinations of prostheses that are outliers with respect to revision rate, when compared to others in the same class (179-181).

It is important that registries use a transparent and accountable process to identify an outlier. The AOANJRR was one of the first registries to develop a standardized process for identification of such prostheses (182). This process attempts to take into account the extent of difference and to determine the possible reasons for that difference. In this paper we describe the development, implementation, and assessment of that approach.

Materials and methods

The AOANJRR began a staged implementation on September 1, 1999 and has collected full national data since 2002. This registry has developed a standardized 3-stage approach to identifying prostheses that have a higher than expected rate of revision. Stage 1 has been present since the Registry commenced, stage 2 was introduced in 2003, and stage 3 in 2007.

Stage 1

The first stage is an initial screening test. It is an automated analysis that identifies prostheses where the revision rate (per 100 component years) exceeds twice that of all other prostheses in

the same class, and the Poisson probability of observing that number of revisions, given the rate of the class, is statistically significant ($p < 0.05$). Additional criteria include that there must be at least 10 primary procedures for that prosthesis, or the proportion revised is at least 75% and there have been at least 2 revisions. In addition, if a particular class contains a prosthesis that represents more than 25% of the group, a second probability analysis is performed in stage 1. This analysis excludes the prosthesis from the overall rate and the probability is re-estimated using only the remaining prostheses. This is to avoid any bias on the revision rate that may occur by including a dominant prosthesis. This initial algorithm is based on a well-established epidemiological model identifying person-time at risk. This represents the observational experience in which disease onsets can be observed (183). Component years are substituted for person-years in the Registry model. Individual prostheses are identified but, specifically with primary hip replacement, a combination of prostheses may be identified. This occurs when a femoral stem and acetabular component are implanted together and the combination has a higher than expected rate of revision. Knee replacements are identified as a specific variant of the same brand if only the variant of the brand has a higher rate of revision, e.g. Genesis II Oxinium (cementless)/MBK.

Stage 2

In stage 2, Registry staff—including 3 orthopedic surgeons— review more detailed information on all prostheses identified in stage 1. An important part of stage 2 is the analysis examining the impact of potential confounders, such as age, primary diagnosis, and reason for revision, which are known to influence implant survival (184). This process seeks to identify patient and surgeon factors as well as device related factors that may have contributed to the observed higher rate of revision. Prostheses may be excluded from further review for a variety of reasons, some of which may include inadequate numbers or use in complex primary situations, or if they have been combined with prostheses already known to have a higher rate of revision. Age and sex-adjusted hazard ratios are calculated using Cox regression models. If the hazard ratio of a particular prosthesis—compared to all other prostheses in the same class combined—is statistically significant, then the prosthesis or prosthesis combination progresses to stage 3. Additionally, all prostheses identified in the previous Annual Report are included in stage 2, regardless of re-identification in stage 1. The reason for this is to ensure that these previously identified prostheses undergo a complete follow-up assessment.

Stage 3

In 2007, a third stage of assessment was added, enabling senior clinicians from the Australian Orthopaedic Association Arthroplasty Society to review the detailed analyses of prostheses and combinations identified in stage 2. The panel meets with staff from the AOANJRR at a 2-day workshop to critically appraise all the information and to determine which prostheses should be identified as outliers in the Annual Report. At this stage, the expert panel may request Registry technical staff to provide further information or additional statistical analyses.
At the conclusion of stage 3, the AOANJRR then lists identified prostheses in 1 of 3 groups: (1) those that are no longer used in Australia, (2) those that have been re-identified and are still used, and (3) those that are being identified for the first time. Summary data for each prosthesis or prosthesis combination are provided in the Annual Report, and a full analysis is available in the supplementary report section on the AOANJRR website https://aoanjrr.dmac.adelaide.edu.au/ annual-reports-2012.

Results

Between 2004 and 2011, the AOANJRR identified 78 prostheses or prosthesis combinations using its 3-stage approach. These included 42 conventional and 6 resurfacing hip prostheses and also 5 unicompartmental and 25 total knee prostheses. In general, once a prosthesis or prosthesis combination has been identified, it continues to be identified as an outlier in subsequent years. There have been 5 primary conventional hip prostheses or combinations that have been used in more than 150 procedures that were initially identified and subsequently after 1 year no longer satisfied the defined criteria. 1 resurfacing hip prosthesis was initially identified, subsequently removed from the list, and then re-identified the following year when further data were available. All unicompartmental and primary total knee prostheses previously identified as having a higher than expected rate of revision have been reidentified (185).

During preparation of the 2011 Annual Report, the AOANJRR identified 217 prostheses or prosthesis combinations in stage 1. Of these, 123 (56.6%) were analyzed in more detail in stage 2. Those that did not show a statistically significant difference in the rate of revision compared to the combination of all other prostheses in the same class were excluded. In stage 3, there were 95 (44%) prostheses or prosthesis combinations reviewed by the independent panel of orthopedic surgeons and 17 were excluded. Reasons for exclusion included identifying non-prostheses-related factors such as major differences in primary diagnosis, or where surgeon specific factors were felt to be contributing to the higher than expected revision rate.

Table 1

Identification of outlier prostheses by stage

Prosthesis type	Identified in stage 1	Analyzed in stage 2	Reviewed in stage 3	Identified overall	Newly identified in 2011
Hips					
Total conventional	150	83	56	42	13
Total resurfacing	7	6	6	5	1
Knees					
Unicompartmental	5	6	6	6	1
Total knee	55	28	27	25	2
Total	217	123	95	78	17

Overall, there were 78 prostheses (36%) or prosthesis combinations identified in 2011, and 17 of these were newly identified (Table). These prostheses comprise 3.5% of all the different primary hip and knee replacements that have been recorded by the Registry. Of the prostheses identified, 37 of 78 (47%) are no longer used on the Australian market, and of those prostheses that were re-identified and were still used, 18 of 24 (75%) had had reduced use compared to the previous year. 14 combinations of acetabular cup and femoral stems have been reported that do not feature as individual prostheses, but when combined they have a higher than expected rate of revision.

Discussion

The approach to identifying "outlier" prostheses varies between arthroplasty registries. The Swedish Hip Arthroplasty Register publishes survivorship curves of prostheses and combinations but makes no specific comparison (186). The Norwegian Register documents the use of prostheses and publishes outcomes in peer-reviewed journals, but does not report specific survivorship curves in its annual report (187). The New Zealand Joint Registry (188) publishes tables of prosthesis outcomes but does not identify outlying prostheses. The National Joint Registry for England and Wales has developed an outlier subcommittee to discuss strategy and methodology for analysis of data on each implant that has been highlighted as needing evaluation, but these have not been published as yet (189).

The Swedish Knee Arthroplasty Register uses a different approach. A specific knee prosthesis is used as a reference to compare the outcome of other prostheses (190). The choice of an index prosthesis requires that the prosthesis is used in numbers large enough to allow adequate

comparison. At one point, the AOANJRR compared all unicompartmental knees to the most frequently implanted prosthesis, the Oxford 3. This was because at that time it was used in a large proportion (35%) of all unicompartmental prostheses (191). Since then, the proportion has diminished each year and it became no longer appropriate to use an approach for unicompartmental knee replacement that was different to that being used for all other classes of prostheses.

The AOANJRR chose to identify outlying prostheses within 2 years of collecting full national data, and this paper describes the development and evolution of the method over time. It is a transparent and accountable process that culminates in an independent review to determine what devices should be identified as outlier prostheses. It is important for surgeons to have current information on prosthesis outcomes, to enable them to select the best-performing devices for their patients. Registries provide an ideal form of post-market surveillance that is readily able to achieve this. Other surveillance measures such as adverse event reporting are known to have limitations (192-194). Most importantly, these are very dependent on what is reported and there is no provision of information on comparative performance. It is also necessary for regulatory authorities and industry to be aware of outlier prostheses as, even with internal monitoring, the real number of revisions may not be apparent (179, 195, 196). Following a health technology assessment review, and in part based on registry data, the Australian government reclassified hip, knee, and shoulder replacements from Class IIB to Class III (high-risk medical devices) (197). Since 2007, the Registry approach to identification has also been incorporated into the regulatory processes in this country. Following the release of the AOANJRR Annual Report, the Therapeutic Goods Administration (TGA), which is the Australian regulatory affairs body for medicines and devices, requests further information from the industry to justify the continued use of products identified as having a higher than expected rate of revision. The response of the industry to the Registry data is then reviewed by another specialist orthopedic TGA committee, which makes recommendations about the ongoing use of the individual prostheses (198).

The Registry analyses the rate of revision separately for acetabular and femoral components, and if there is a higher than anticipated rate, individual components are published in the Annual Report. The Registry also analyses all combinations of acetabular and femoral components. Occasionally, a combination of prostheses—only when used together—has a higher than anticipated rate of revision, and this combination is noted.

A well-performing prosthesis can also be linked to a prosthesis known to have a higher than expected revision rate, so that the combination performs less satisfactorily. The Corail/ ASR

combination was first reported in 2008 as having a revision rate that was more than twice its comparators even though good results had already been reported for the Corail stem (199). This was the first time that the ASR acetabular component, which had previously been reported with resurfacing (200), was associated with an increased rate of revision in conventional hip replacement. In other cases, an individual component is associated with a higher than expected revision rate no matter what prosthesis it is implanted with. If a prosthesis or combination previously identified no longer meets the criteria, it is not re-identified subsequently and this is documented in the Annual Report. Registries continually monitor changing outcomes, and it is important to note that the report reflects that particular time period.

There are both strengths and limitations to the process by which the AOANJRR identifies prostheses with higher than anticipated rates of revision. Stage 1 is effective as a screening test to flag prostheses but it does not account for changes in revision rate over time. This limitation makes it difficult to detect a difference if the higher risk of revision occurs later in the follow-up period (201). The introduction of stage 2 enabled further analysis to be performed on a number of variables, both device- and non-device-related. Stage 3 has proven to be valuable because it broadens the clinical perspective available to the AOANJRR. With the large number of prostheses reported to the Registry, it is difficult for the Registry surgeons to have a working knowledge of all the devices. The addition of members of the Arthroplasty Society broadens the clinical perspective. Surgeons involved in stage 3 have experience of many of the devices and add valuable input to the Registry findings. This improves the transparency and accountability of the Annual Report by ensuring peer review by the peak arthroplasty body in the country.

The Registry compares prostheses to all remaining components in their class, and therefore under-reports prostheses with a higher than expected revision rate compared to the situation where the Registry only used the better-performing prostheses as the comparator. When a prosthesis with a higher than expected revision rate has been identified, it usually continues to be identified in subsequent reports. . After identification of the device, the usage usually declines—which may have a significant effect on its subsequent outcome, for a variety of reasons. Identification may bring the prosthesis to the attention of surgeons not performing large enough numbers to be aware that it has a higher rate of revision. They may then change their choice of prosthesis. It may also highlight patient selection issues such as resurfacing hip arthroplasty having a higher rate of revision in women, patients with smaller-diameter femoral heads, and older patients (202). This may result in a change of indication for prosthesis use, which has been shown in the Registry (185)

The Registry is most effective at identifying the performance of recently introduced prostheses, but those prostheses with delayed onset of a higher rate of revision are not identified as readily. It has become evident that the approach to identification may be too broad, and it is important to perform a careful range analysis of prostheses to identify which particular type is responsible for the higher than expected rate of revision within that particular group. An early example of this process was the Preservation Unicompartmental Knee, which was first identified in 2004 (182). In 2006, it became apparent that only the mobile bearing component had an increased rate of revision (191). More recent examples of prostheses that were not identified on routine screening but that required specific sub-analysis include the LCS/Duofix knee and size issues associated with the Spectron femoral stem. The Registry will continue to develop further strategies to identify specific prostheses within a broader group, keeping in mind that reducing the numbers available for analysis may reduce statistical precision.

The Registry is aware that a single surgeon may be responsible for a prosthesis combination that has a higher rate of revision. This situation has occurred twice, and on both occasions subsequent use of the combination ceased following publication of the Annual Report.

Identification by registries of prostheses with a higher than expected rate of revision is a process that will continue to evolve and develop. This will be enhanced by international collaboration between registries, which includes the possibility of using other registries to verify or confirm outlier prostheses. In addition, systems could be established to enable data pooling, which would allow enhanced analysis to better understand the role of device-related and non-device-related factors that may contribute to the higher revision rate identified.

Conclusion

Many approaches for systematic reduction of the rate of revision have been described. Identification of prostheses with a higher than expected rate of revision is far less widely reported. Arthroplasty registries are effective in identifying outliers, and they can determine multiple factors that affect outcome—including device- and non-device-related issues. The Australian Registry has been successful in doing this and, as a result, many outlier prostheses are no longer on the market. Registries and international collaboration between registries will continue to play a major role.

RdS, SG and DD designed the research question. RdS wrote the manuscript. LM performed data extraction and, together with PR, did the statistical analysis. All the authors were responsible for editing and final approval of the paper.

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No competing interests declared.

4.3 - Additional Discussion

The Registry has continued to refine and update the process by which implants with a higher rate of revision are identified. The publication of these data has become an important method by which information on these prostheses is distributed to a national and international audience, and the impact of this has been monitored.

The Registry has carefully tracked the use and the ongoing outcome of all prostheses and prostheses combinations that have been identified as having a higher than anticipated rate of revision (HTARR) in the Annual Reports since this first commenced in 2004. These devices are compared to prostheses within their own joint class and these include Unipolar Modular, Bipolar, Total Conventional THR, Resurfacing Hip Replacement Patella/Trochlear, Unicompartmental Knee Replacement and Total Knee Replacement. The Registry has also kept data on the number of implants that have been used in the year before identification and again the number in the year after identification. This allows the Registry to determine the influence of the identification of prostheses in the Annual Report, as this information can be directly attributable to the Registry analysis and reporting. For the examination of the effect of the HTARR, process data were used from 2004, (the commencement of identification) up till Dec 31st 2016. Only primary conventional THR and TKR were studied, as these comprise over 95%

and 88% of all primary hip replacements and knee replacement procedures respectively. There have been a total of 64 types of THR prosthesis and 39 types of TKR prosthesis identified with an HTARR since 2004. The Registry has recorded a total number of 47,699 THR and 37,033 TKR using a prosthesis or combination with a HTARR from a total of 930,530 hip and knee procedures in the database. Over this period 84,702 procedures (9.1%) had one component or the combination that had been identified. This does not imply that all these procedures are revised but as a group they have at least twice the rate of revision of all other THR and TKR.

An important metric of the result of the HTARR process is the use of devices after listing in the Annual Report as having a higher rate of revision. In the year after identification, 67% of all THR prostheses identified had a reduced use, with 23% having no recorded usage. A similar effect was seen with TKR with 76% of those identified having a reduced use, with 29% of these components having less than four recorded procedures. The Registry has been the first body to document these outcomes and this has led to a marked reduction in the number of patients exposed to devices with a higher than anticipated rate of revision. Surgeons still have a wide choice of devices that they can use for their patients. The Registry also continues to analyse all prostheses that we have identified and circumstances may change such that the prosthesis no longer fits the category and therefore is no longer identified. Over the past 11 years, there have been 34 prostheses which, following initial identification with an HTARR, are no longer identified in subsequent years. There are reasons why this may occur. There may be initial

problems with some devices but with larger numbers implanted, longer follow up, and fewer, later revisions, these devices no longer meet the criteria for HTARR. Surgeons also may become more experienced using these prostheses, leading to improved performance over time. It could be argued that a higher revision rate in this situation is not necessarily device related but there are ample prostheses available that are technically straightforward to implant. Therefore the 'usability' or ease of implantation of a device is an important feature. When prostheses no longer meet the HTARR criteria a paragraph within the Annual Report is devoted to discussing their changed status.

The Registry has developed further methods to identify specific prostheses subsets within a family of devices, and clinical experience and feedback have been of benefit. An example of this was briefly discussed in Chapter 4 and is now outlined in more detail. The process by which the Registry became aware of this outlier highlights how important surgeon feedback is to the Registry. The problem with this specific TKR (the LCS/DuoFix TKR, Depuy, Warsaw, In) was due to a manufacturing change by the company. In 2006, following the successful modification of the tibial base plate, a layer of hydroxyapatite was added to the porous beaded surface of the femoral LCS component. In 2009, a high failure rate of the LCS DuoFix femoral component led to a worldwide recall. It was hypothesised that the implant failure was related to retained particles used during the manufacturing process which then produced excessive metal abrasion and the resulting debris was associated with pain and loosening (203, 204). This

prosthesis had not been picked up by the AOANJRR's usual surveillance methods and was first brought to the Registry's attention by an experienced surgeon who noted complications with his patients. A thorough analysis of this particular type of TKR subset revealed a HTARR and the LCS/Duofix was identified in the HTARR section in the 2012 Annual Report. The rate of revision at 4 years was over fourfold higher than all other TKR but, because this particular LCS subset was included in a large number of otherwise well performing LCS components, the Registry did not initially flag this in the Stage 1 automated algorithm.

Our identification process now includes a careful analysis by more detailed prosthesis identification including catalogue number, and lot numbers if required, and also the methods by which implants are fixed to bone. For example, there are TKRs that only have a higher rate of revision when they are performed without cement or with a posterior stabilized version. These prostheses are then identified with the appropriate characteristics separate from other knees with the same family name.

The clinical input of surgeons at the weekend workshop where the final decision about HTARR is made has become increasingly valuable. The addition of members of the Arthroplasty Society broadens the clinical perspective for the Registry Directors and, with time, surgeons have become more confident in interpreting the data presented at the workshop. This has been

reflected over time by fewer questions to the statisticians about methodology, more questions regarding possible confounders and a far shorter time frame devoted to the HTARR discussion at the weekend workshop. Devices that are flagged in Stage 2 but not listed as HTARR are followed carefully in subsequent years and discussed, to enable an ongoing educational process. This is also the case with those devices that are no longer identified in Stage 2.

The Registry has refined the process by which prostheses are initially flagged. Hazard ratios (HR) are now run on all prostheses or combinations in the Registry with over four recorded revisions and those with a significant HR compared to other devices in the same class are then more comprehensively analysed.

This paper has been cited 16 times (refer 4.4 Citations). Studies have cited this paper with respect to the method of reporting on metal on metal bearing surfaces or other outlier prostheses (205-208). Three papers have cited the study with regards to introducing the same concept for identification in their own registries (209-211).

As outlined in Chapter 8, a few registries have followed the AOANJRR's initiative, though most fall short of actually identifying these devices in publically available reports, though they may be identified internally. There are reasons for this including the inability to risk adjust

before notification and potentially the legal consequence of doing so. However, patient safety should take priority and the Registry has been robust in its defense of the process and continues to report these devices in the Annual Report. The HTARR identification reinforces the benefit of having the AOANJRR rather than relying on international registries to provide data on devices. To date, no section of the orthopaedic industry has seriously challenged this process, particularly in light of the ASR debacle.

One of the results of this paper has been the formation of a sub-committee of the International Society of Arthroplasty Registers (ISAR) to investigate the pooling of data to enable early signal detection of prostheses. This will enable a better understanding of the role of device-related and non-device-related factors that may contribute to the higher revision rate identified. It will also allow registries that may have concerns with a device, but insufficient numbers, to contribute data to an international analysis. The sub-committee consists of statisticians and clinicians and is investigating new methods for identifying prostheses with potentially higher revision rates. A machine learning algorithm has been developed using data from an international registry (Kaiser Permanente, California, USA) to address the confounding effect of individual device components. This program was then compared to data from the AOANJRR to validate the outcome. As a result of this collaboration a paper has been prepared for submission entitled *Active Post-Market Surveillance of Orthopaedic Devices in an International*

Multi-Registry Study, Authors G Cafri, S Graves, A Sedrakyan, J Fan, P Calhoun, R de Steiger, A Cuthbert, M Lorimer, and E Paxton.

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CHAPTER FIVE

Computer Navigation for Total Knee Arthroplasty Reduces Revision Rate for Patients Less Than Sixty-five Years of Age

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Name of Principal Author (Candidate)	Richard N de Steiger
Contribution to the Paper	R N de Steiger designed the research question, wrote the manuscript and together with co-authors, was responsible for the interpretation of data and for editing and final approval of the paper.
Overall percentage (%)	80%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of

Signature Date 19/5/18

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate to include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	Yen-Liang Liu
Contribution to the Paper	YL Liu performed data extraction and performed the statistical analysis. Together with all the authors he was responsible for editing and final approval of the paper

Signature Date 14/5/18

Name of Co-Author	Stephen E Graves
Contribution to the Paper	S E Graves was responsible for the interpretation of data, editing and final approval of the paper

Signature Date 18/5/18

Please cut and paste additional co-author panels here as required.

5.1 - Preface

This chapter contains the second of five articles submitted for publication in peer reviewed journals. The article has been published in *the Journal of Bone and Joint Surgery 2015 Volume 97A (10):635-644*, the most widely read orthopaedic journal. It addresses the second research question of this thesis on how the AOANJRR monitors the impact of new technology with reference to computer navigation for TKR.

The higher rate of revision in younger patients having a TKR is reported in numerous registries and clinical trials. Methods to address this problem generally focus on new implant modifications and these data are recorded by all registries. The recording and reporting on a novel method of inserting a TKR to improve the position of implants has had limited attention from registries. Computer navigation for TKR has improved limb alignment compared to conventional, non-navigated TKR and this has been demonstrated in multiple RCTs. This study analysed data from the Australian Orthopaedic Association National Joint Replacement Registry to examine the effect of computer navigation on the rate of revision of primary TKR to determine if it improved outcomes, particularly for younger patients at most risk of revision.

The Additional Discussion reports on extended follow up of the use of navigation in Australia, confirming the reduced rate of revision and compares the data to other countries who record the use of the technology. It also outlines how the Registry's experience with the use of recording navigation has enabled expanded data collection of new technologies as they come into the marketplace.

5.2 - Published Paper

Background

Computer navigation for total knee arthroplasty has improved alignment compared with that resulting from non-navigated total knee arthroplasty. This study analyzed data from the Australian Orthopaedic Association National Joint Replacement Registry to examine the effect of computer navigation on the rate of revision of primary total knee arthroplasty.

Methods

The cumulative percent revision following all non-navigated and navigated primary total knee arthroplasties performed in Australia from January 1, 2003, to December 31, 2012, was assessed. In addition, the type of and reason for revision as well as the effect of age, surgeon volume, and use of cement for the prosthesis were examined. Kaplan-Meier estimates of survivorship were used to describe the time to first revision. Hazard ratios (HRs) from Cox proportional hazards models, with adjustment for age and sex, were used to compare revision rates.

Results

Computer navigation was used in 44,573 (14.1% of all) primary total knee arthroplasties, and the rate of its use increased from 2.4% in 2003 to 22.8% in 2012. Overall, the cumulative percent revision following non-navigated total knee arthroplasty at nine years was 5.2% (95% confidence interval [CI] = 5.1 to 5.4) compared with 4.6% (95% CI = 4.2 to 5.1) for computer-navigated total knee arthroplasty (HR = 1.05 [95% CI = 0.98 to 1.12], p = 0.15). There was a significant difference in the rate of revision following non-navigated total knee arthroplasty compared with that following navigated total knee arthroplasty for younger patients (HR = 1.13 [95% CI = 1.03 to 1.25], p = 0.011). Patients less than sixty-five years of age who had undergone non-navigated total knee arthroplasty had a cumulative percent revision of 7.8% (95% CI = 7.5 to 8.2) at nine years compared with 6.3% (95% CI = 5.5 to 7.3) for those who had undergone navigated total knee arthroplasty. Computer navigation led to a significant reduction in the rate of revision due to loosening/lysis (HR = 1.38 [95% CI = 1.13 to 1.67], p = 0.001), which is the most common reason for revision of total knee arthroplasty.

Conclusions

Computer navigation reduced the overall rate of revision and the rate revision for loosening/lysis following total knee arthroplasty in patients less than sixty-five years of age.

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

Peer Review: *This article was reviewed by the Editor-in-Chief and one Deputy Editor, and it underwent blinded review by two or more outside experts. It was also reviewed by an expert in methodology and statistics. The Deputy Editor reviewed each revision of the article, and it underwent a final review by the Editor-in-Chief prior to publication. Final corrections and clarifications occurred during one or more exchanges between the author(s) and copyeditors.*

Disclosure: *None of the authors received payments or services, either directly or indirectly (i.e., via his or her institution), from a third party in support of any aspect of this work. None of the authors, or their institution (s), have had any financial relationship, in the thirty-six months prior to submission of this work, with any entity in the biomedical arena that could be perceived to influence or have the potential to influence what is written in this work. One or more of the authors has had another relationship, or has engaged in another activity, that could be perceived to influence or have the potential to influence what is written in this work. The complete Disclosures of Potential Conflicts of Interest submitted by authors are always provided with the online version of the article.*

Introduction

Total knee arthroplasty is a successful operation for patients with severe arthritis for whom non-operative treatment has failed. Many studies have shown good long-term implant survivorship (212, 213) although there are age-related differences (214). Prosthetic design, surgical technique, surgeon experience, and overall alignment can all have a bearing on the success of the procedure. Computer navigation for total knee arthroplasty was first introduced in Europe in the 1990s, and there has been a widespread increase in its use throughout the world in the last decade. The proposed benefits of computer navigation for total knee arthroplasty include improved accuracy of both tibial and femoral component positioning and overall mechanical alignment. Most studies comparing computer navigation with standard total knee arthroplasty have demonstrated a greater number of patients with coronal mechanical axis alignment within 3 degrees of neutral in the navigation group (215-220). Whether this improved alignment leads to a reduction in the long-term rate of revision is yet to be determined.

Most of the early studies investigating the use of computer navigation for knee arthroplasty have been performed in specialist orthopaedic centers, where the procedures were often done by highly experienced surgeons (136, 147, 148). Orthopaedic surgeons tend to be early adopters of new technology, and it is important to determine the outcome of this technology in a broader population. Joint replacement registries collect and report data on patients who have undergone joint arthroplasty, and analyses can be performed on device and non-device-related characteristics13. Joint replacement registries also provide the ideal platform for monitoring the introduction of new technology at a population level. Computer navigation was introduced into Australia in 2001, and the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) began collecting data on its use for knee arthroplasty in 2003. The aim of this study was to determine if there was a difference in the rate of revision after navigated total knee arthroplasty compared with that after non-navigated total knee arthroplasty.

Materials and Methods

This prospective study was designed to evaluate the rate of revision of computer-navigated total knee arthroplasty with use of registry data on the Australian population of patients who underwent total knee arthroplasty. The AOANJRR began data collection on September 1, 1999, and includes data on almost 100% of the arthroplasty procedures performed in Australia since 2002.

Registry data are validated against patient-level data provided by each of the state and territory health departments in Australia with use of a sequential, multilevel matching process. A

matching program is run monthly to search for all primary and revision arthroplasty procedures recorded in the Registry that involved the same side and joint of the same patient, thus enabling each revision to be linked to the primary procedure. Data are also matched biannually with the Department of Health and Aging's National Death Index to obtain information on the date of death. In 2003, an addition to the form for total hip and total knee arthroplasty marked "computer assisted" was included, and this enabled information to be collected on the use and type of navigation. Data were analyzed for all procedures recorded from January 1, 2003, to December 31, 2012. The Registry records the reason for and type of revision of total knee arthroplasty and categorizes revision surgery as major or minor. A major revision involves the revision of either the tibial or the femoral component, or both. Minor revisions are all other revisions—usually patellar resurfacing and tibial insert changes.

The cumulative percent revision was compared between the non-navigated and navigated total knee arthroplasties over the same time period, and the impacts of age, sex, reason for revision, type of revision, and brand of navigation were assessed. Data were also analyzed according to the number of computer-navigated knee arthroplasties performed by the surgeons (ten or fewer, eleven to twenty-five, twenty-six to seventy, or more than seventy) to adjust for the influence of surgical volume on the rate of revision. The revision rates of prostheses of the same type were also compared between the no-navigation and navigation groups to adjust for the influence of known prosthesis-dependent revision rates after total knee arthroplasty.

Statistical Analysis

The AOANJRR uses Kaplan-Meier estimates of survivorship to describe the time to the first revision of an arthroplasty, with censoring at the time of death or closure of the database at the time of analysis. The unadjusted cumulative percent revision at the end of the first nine years after the primary arthroplasty, with an accompanying 95% confidence interval (CI), was calculated with use of unadjusted pointwise Greenwood estimates. The unadjusted cumulative incidence functions of the reasons for revision of navigated and non-navigated total knee arthroplasties were also calculated at the end of the first nine years. The hazard ratio (HR) was calculated with use of Cox proportional hazards models, adjusted for age and sex, and was used to make statistical comparisons of the revision rates between the groups. The assumption of proportional hazards was checked analytically for each model; if the interaction between the predictor and the log of the postoperative time was significant in the standard Cox model, then a time-varying model was used. For this study, the reported HRs pertain to the entire follow-up period. All tests were two-tailed at the 5% level of significance. Statistical analysis was performed with use of SAS software (version 9.3; SAS Institute, Cary, North Carolina).

Source of Funding

The AOANJRR is entirely funded by the Commonwealth of Australia's Department of Health and Aging.

Results

Computer navigation was used for 44,573 (14.1% of all) primary total knee arthroplasties recorded by the AOANJRR, and 270,545 (85.9%) were recorded as having been performed without computer navigation. The use of computer navigation for primary total knee arthroplasty increased from 2.4% of all procedures in 2003 to 22.8% in 2012 (Table I). Computer navigation was used in 239 of 304 hospitals performing total knee arthroplasty throughout the country. The Registry recorded the use of ten different navigation systems, with six systems used in more than 100 cases each and the majority of the arthroplasties performed with the aid of a Stryker (48.6%) or Brainlab (31.8%) system. The specific system was not recorded for 757 (1.7%) of the total knee arthroplasties for which navigation was used.

TABLE I Primary Total Knee Arthroplasties Performed with and without Navigation by Year of Procedure

	Computer-Navigated		Non-Navigated		Total	
Procedure Year	No.	%*	No.	%*	No.	%*
Patients of all ages						
2003	526	2.4	21,205	97.6	21,731	100.0
2004	727	3.1	22,875	96.9	23,602	100.0
2005	1291	4.9	25,038	95.1	26,329	100.0
2006	2201	8.0	25,182	92.0	27,383	100.0
2007	2960	10.1	26,323	89.9	29,283	100.0
2008	4099	12.6	28,512	87.4	32,611	100.0
2009	6156	17.9	28,142	82.1	34,298	100.0
2010	7906	20.9	29,994	79.1	37,900	100.0
2011	9176	22.8	30,995	77.2	40,171	100.0
2012	9531	22.8	32,279	77.2	41,810	100.0
Total	44,573	14.1	270,545	85.9	315,118	100.0
Patients <65 yr old						
2003	150	2.3	6247	97.7	6397	100.0
2004	255	3.6	6760	96.4	7015	100.0
2005	407	5.1	7543	94.9	7950	100.0
2006	755	8.9	7758	91.1	8513	100.0
2007	1009	10.7	8417	89.3	9426	100.0
2008	1482	13.4	9582	86.6	11,064	100.0
2009	2240	19.0	9531	81.0	11,771	100.0
2010	2862	21.6	10,386	78.4	13,248	100.0
2011	3463	24.2	10,863	75.8	14,326	100.0
2012	3397	23.8	10,897	76.2	14,294	100.0
Total	16,020	15.4	87,984	84.6	104,004	100.0

*Percent of primary total knee arthroplasties performed in the specific year.

The cumulative percent revision at nine years after non- navigated total knee arthroplasty was 5.2% (95% CI = 5.1 to 5.4) compared with 4.6% (95% CI = 4.2 to 5.1) after computer navigated total knee arthroplasty (HR = 1.05 [95% CI = 0.98 to 1.12], p = 0.15) (Table II, Fig. 1). There was an interaction effect on the rate of revision between the use of navigation and the patient's age (p = 0.0282). There was a significant difference in the rates of revision of non-navigated and navigated total knee arthroplasties for patients less than sixty-five years of age. In that group, the cumulative percent revision at nine years following non-navigated total knee arthroplasty was 7.8% (95% CI = 7.5 to 8.2) compared with 6.3% (95% CI = 5.5 to 7.3) after navigated total knee arthroplasty (HR = 1.13 [95% CI = 1.03 to 1.25], p = 0.011). There was no significant difference between the rates of revision of non-navigated and navigated total knee arthroplasties for patients at least sixty-five years of age (Fig. 2).

TABLE II Yearly Cumulative Percent Revision of Primary Total Knee Arthroplasty According to Whether Navigation Was Used and Age

	Cumulative Percent Revision (95% CI)				
Navigation	1 Yr	3 Yr	5 Yr	7 Yr	9 Yr
Patients of all ages					
Computer-navigated	1.0 (0.9, 1.1)	2.8 (2.6, 3.0)	3.7 (3.5, 4.0)	4.4 (4.0, 4.7)	4.6 (4.2, 5.1)
Non-navigated	1.0 (1.0, 1.1)	2.8 (2.8, 2.9)	3.8 (3.7, 3.9)	4.5 (4.4, 4.6)	5.2 (5.1, 5.4)
Computer-navigated					
<65 yr old	1.1 (1.0, 1.3)	3.6 (3.3, 4.0)	5.0 (4.5, 5.5)	5.9 (5.2, 6.6)	6.3 (5.5, 7.3)
≥65 yr old	0.9 (0.8, 1.0)	2.4 (2.2, 2.6)	3.0 (2.7, 3.3)	3.6 (3.2, 4.0)	3.7 (3.2, 4.2)
Non-navigated					
<65 yr old	1.4 (1.3, 1.4)	4.0 (3.8, 4.1)	5.5 (5.3, 5.6)	6.5 (6.3, 6.8)	7.8 (7.5, 8.2)
≥65 yr old	0.9 (0.8, 0.9)	2.3 (2.2, 2.4)	3.0 (2.9, 3.1)	3.5 (3.4, 3.6)	4.0 (3.8, 4.1)

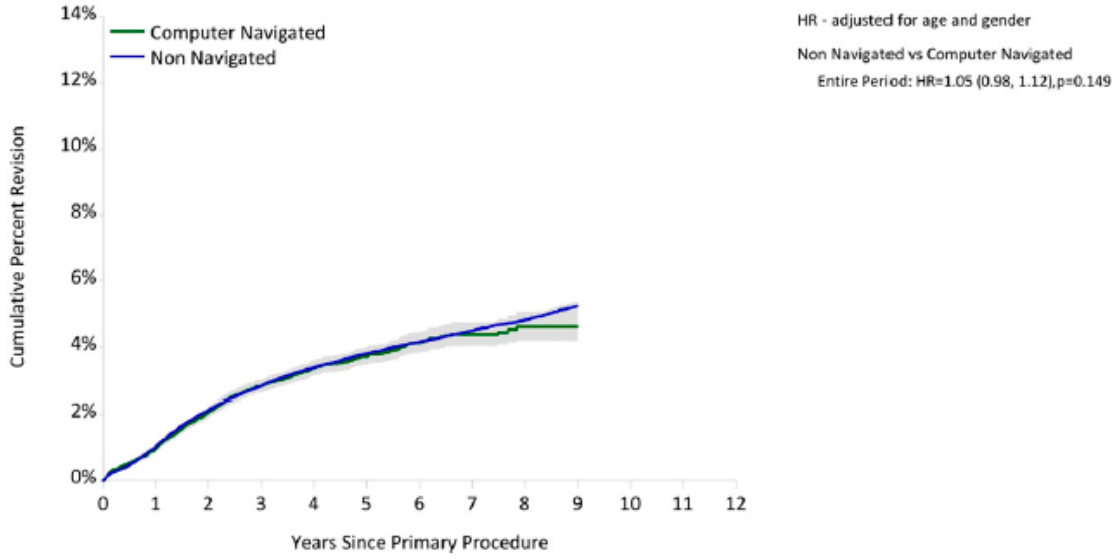

Fig. 1

Cumulative percent revision of primary total knee arthroplasty, according to whether computer navigation had been used. The shaded area represents the 95% CIs for the two sets of data.

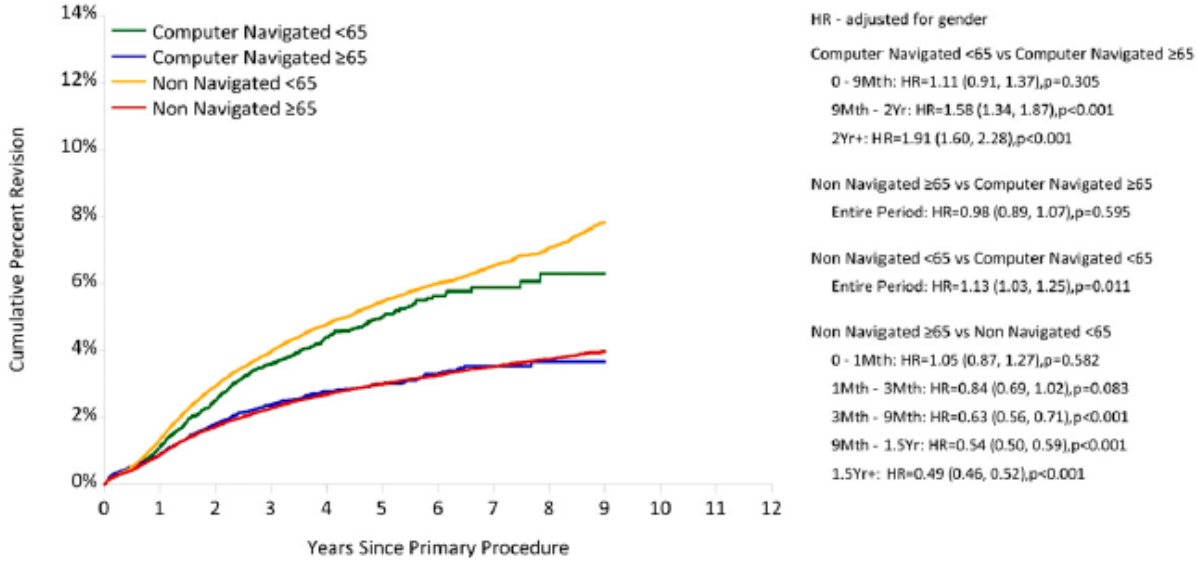

Fig. 2

Cumulative percent revision of primary total knee arthroplasty, according to whether computer navigation had been used and by age.

In patients less than sixty-five years of age, computer navigation led to a significant reduction in the rate of revision due to loosening (the most common reason for revision) (Table III), with a cumulative percent revision of 1.6% (95% CI = 1.3 to 2.1) at nine years compared with 2.6%

(95% CI = 2.4 to 2.8) for those with non-navigated arthroplasty (HR = 1.38 [95% CI = 1.13 to 1.67], p = 0.001) (Fig. 3). There was no difference between the navigated and non-navigated groups with regard to the percentage of knees revised because of infection or fracture.

TABLE III Reasons for Revision of Primary Total Knee Arthroplasty According to Whether Navigation Was Used, in Patients Less Than Sixty-five Years of Age

	Computer-Navigated		Non-Navigated	
Revision Diagnosis	No.	%*	No.	%*
Loosening/lysis	118	0.7	1293	1.5
Infection	99	0.6	782	0.9
Patellofemoral pain	47	0.3	515	0.6
Pain	49	0.3	324	0.4
Instability	37	0.2	263	0.3
Arthrofibrosis	26	0.2	172	0.2
Patellar erosion	15	0.1	110	0.1
Malalignment	11	0.1	92	0.1
Metal sensitivity	17	0.1	81	0.1
Incorrect sizing	11	0.1	67	0.1
Fracture	6	0.0	60	0.1
Other	38	0.2	251	0.3
No. of revisions	474	3.0	4010	4.6
No. of primary total knee arthroplasties	16,020		87,984	

*Percent of primary total knee arthroplasties.

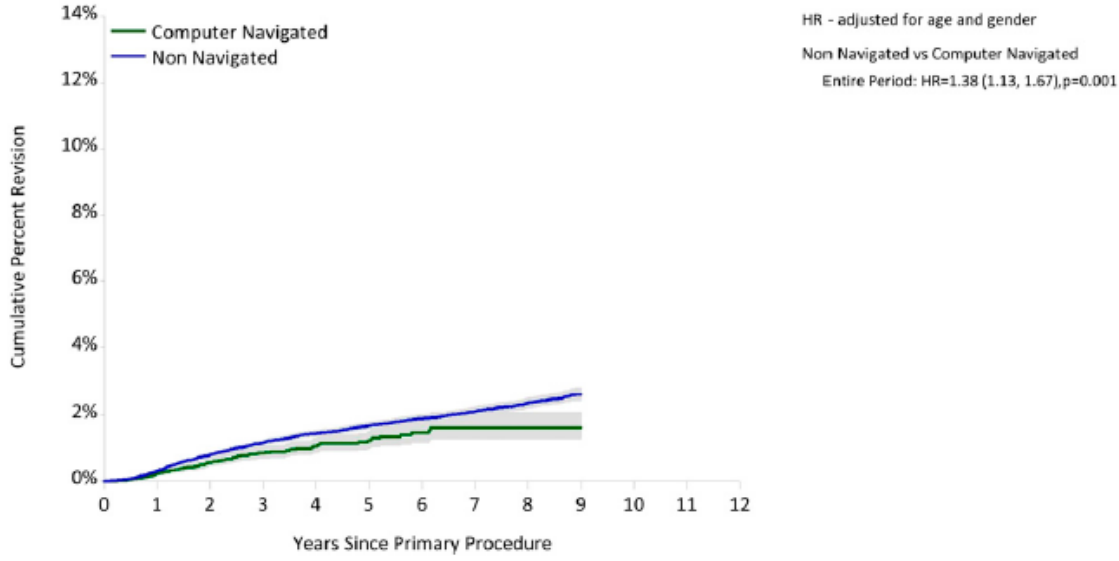

Fig. 3

Cumulative percent revision due to loosening, according to whether computer navigation had been used, in patients less than sixty-five years of age. The shaded area represents the 95% CIs for the two sets of data.

The cumulative percent major revision of non-navigated primary total knee arthroplasty at nine years was 2.7% (95% CI = 2.6 to 2.8) compared with 2.1% (95% CI = 1.8 to 2.4) for navigated total knee arthroplasty (HR = 1.18 [95% CI = 1.07 to 1.31], $p < 0.001$) (Fig. 4). There was no difference in the rates of minor revision between the arthroplasty groups. There was also no difference in the rate of revision between the non-navigated and navigated total knee arthroplasties when the rates were compared in each of the four surgeon-volume groups. Analysis of prosthetic fixation in patients less than sixty-five years of age showed the benefit of navigation to be more apparent in patients who had undergone all-cemented fixation than in those who had cementless or hybrid fixation (HR = 1.2 [95% CI = 1.05 to 1.38], $p = 0.007$).

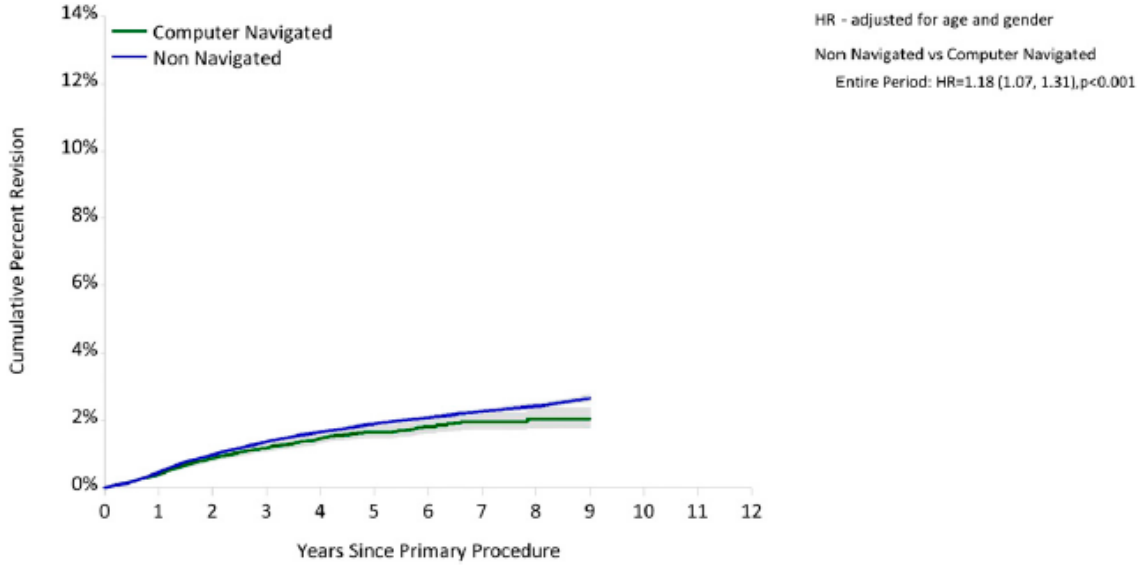

Fig. 4

Cumulative percent major revision, according to whether computer navigation had been used. The shaded area represents the 95% CIs for the two sets of data.

Discussion

We believe that this is the first study to demonstrate that the use of computer navigation reduced the rate of revision of total knee arthroplasty in younger patients in a population-based registry. Computer navigation for total knee arthroplasty has widespread acceptance in Australia and was used in >22% of all cases in 2012. This study demonstrates that a joint registry can be used to monitor the introduction of new technology within an entire population. A registry is the ideal vehicle for assessing the performance of new technology as it identifies problems and benefits in the "real world." There were early concerns that the introduction of navigation would increase operating times and the use of pin fixation would increase the rates of revisions due to infection and fracture. This study showed no difference in the percentage of knees revised for those diagnoses between navigated and non-navigated total knee arthroplasties, highlighting the Registry's role and importance in postmarket surveillance. While registries can often identify early problems with new technology (221), demonstrating a benefit of navigation is more complex, particularly if the benefit is a reduced rate of revision. Modern knee prostheses have a low rate of revision. It is therefore likely that, if there is a benefit, identifying it requires long-term follow-up and a large sample size. The revision rates following total knee arthroplasty vary significantly with age, with younger age groups having a higher revision rate (214). Therefore, if navigation has an effect on revision, it will more likely be detected in the younger age groups. The majority of total knee arthroplasties are performed in older age groups, in which the rate of revision is low and it would be more difficult to

demonstrate that navigation reduces the rate of knee revisions, especially those due to wear-related issues such as loosening or lysis.

It is well established that navigation improves coronal mechanical alignment and reduces outliers from what is regarded as acceptable alignment. A systematic review of thirteen randomized controlled trials (139) showed a significant odds ratio of 2.32 (95% CI = 1.77 to 3.04, $p < 0.00001$) in favor of computer navigation obtaining satisfactory postoperative alignment—i.e., a neutral mechanical axis (±3).

Alignment of the total knee prosthesis is believed to be important for long-term success (213, 222, 223). However, Parratte et al. (224), in a study of 398 patients followed for fifteen years after undergoing a total knee arthroplasty, did not show that mechanically well-aligned knees had better survivorship than those in which the axis was not within 3 degrees of neutral. Bonner et al. (225) found only a weak tendency toward improved survival with restoration of a neutral mechanical axis. Despite these studies, it is important not to infer that alignment is not important after total knee arthroplasty. However, most studies of computer navigation for total knee arthroplasty have not shown the improvement in alignment to have any clinical advantage such as superior physical function, range of motion, patient-assessed outcomes, or rates of revision (226-234). Three studies have shown improved patient outcomes associated with alignment. Choong et al. (235), in a randomized controlled trial comparing conventional and navigated total knee arthroplasties, and Huang et al. (144), in a follow-up study of the same group, demonstrated that patients with a mechanical axis within 3 degrees of neutral had a significantly higher Knee Society score at one and five years. There was also improvement in the physical and mental components of the Short Form-12 health score at five years. Hoffart et al. (236) also showed an improvement in functional outcomes, with better Knee Society scores at five years, for navigated total knee arthroplasty compared with conventional total knee arthroplasty.

The strengths of our study include the number of patients involved, the use of population-based data including all surgeons performing total knee arthroplasty in Australia, and the longer-term follow-up. More than 44,000 total knee arthroplasties performed with the aid of computer navigation were analyzed, making this the largest study of navigated total knee arthroplasties reported, to our knowledge. These type of data can be obtained only from a national registry. Most reported trials on the use of computer navigation were from specialized centers at which high volumes of knee arthroplasties were performed. It could be argued that navigation is best suited for surgeons or centers performing lower volumes of procedures, as experienced surgeons may have a limited number of alignment outliers (237, 238). While our study showed that surgeons who performed twenty-five or fewer procedures per year had a lower rate of revision when they had used navigation, this decrease was not significant.

The introduction of registry data collection to capture data on computer navigation for total knee arthroplasty coincided with its more widespread use in Australia. Before 2003, only a few specialized centers were performing computer navigation, whereas now it has widespread community acceptance. Our data include all total knee arthroplasties performed with and without navigation and thus include surgeons undertaking their first cases, those who had performed a small number of procedures, as well as those who had performed many hundreds of navigated total knee arthroplasties. Therefore, this study has strong external validity. There is evidence that surgeons can achieve good alignment with the first few navigated total knee arthroplasties that they perform (239, 240). While the AOANJRR does not contain information on overall alignment, it showed significantly fewer revisions due to loosening/lysis following computer-navigated total knee arthroplasties. It may be expected that the effect of improved alignment would not be apparent until longer-term follow-up had been completed, when wear and loosening may become more important causes of revision. This would likely result in fewer major revisions with better alignment, which was shown in our study. Schnurr et al. (241) examined the results of 1121 consecutive primary total knee arthroplasties, including the last 342 conventional procedures and the first 779 navigated procedures done at their clinic. After a duration of follow-up of one to six years, the navigated technique was associated with a significantly lower revision rate, which was largely due to a reduced rate of aseptic implant loosening. That observation concurs with our findings and with our belief that longer-term follow-up is necessary to show the benefits of navigation. In the only other registry study on navigation for total knee arthroplasty, which was from Norway (242) and which included 1465 navigated total knee arthroplasties, the follow-up was short-term (a mean of less than two years) and it showed an increased rate of revision following computer-navigated total knee arthroplasty but the increase was significant for only one prosthesis. The authors suggested that longer-term follow-up in randomized controlled trials and registry studies was important. Although our results showed no difference in the rate of revision between navigated and non-navigated knee arthroplasties in the population as a whole, there was a significant difference in the younger age group (less than sixty-five years of age). This group of patients has been consistently shown to have a higher rate of revision than older patients, and it may be important to consider the use of navigation in this select group. As has been demonstrated in multiple studies, improved alignment may well reduce the rate of revision due to loosening and lysis.

There are costs associated with the use of computer navigation, including those for the computer, camera, software support, and disposable items. All new technology comes at a price, and it is important to demonstrate cost-effectiveness. Gøthesen et al. (243), using data from the Norwegian registry, employed a Markov model to compare the cost-effectiveness of computer-navigated total knee arthroplasty with that of conventional total knee arthroplasty.

Sensitivity analysis demonstrated that, for sixty-year-old patients, the ten-year implant survival rate needed to rise from 89.8% to 90.6% for institutions performing twenty-five arthroplasties per year and from 89.8% to 89.9% for those performing 250 per year for computer navigated surgery to be considered cost-effective. Our study supported the cost-effectiveness of navigation for patients less than sixty-five years of age, who had a nine-year implant survivorship of 93.7% compared with 92.2% for those who underwent non-navigated total knee arthroplasty. Cost-effectiveness studies, however, may differ from country to country, depending on multiple factors, and would need to be carefully evaluated further.

There are some limitations to this study. Although the AOANJRR is confident that all procedures that were reported as navigated were navigated, it is possible that a small number of cases were navigated and not recorded as such. This would mean that some total knee arthroplasties in the non-navigated group could have been actually implanted with navigation. However, with more than 270,000 non-navigated knee arthroplasties in the Registry it is unlikely that this would make any difference in the rate of revision. Also, it is possible that navigation was abandoned during the procedure but recorded by the Registry as having been performed. As the study was based on intention to treat, this does not change the analysis. Some of the potential complications of using computer navigation surgery may not be reported to the Registry. These include pin track infections and fractures associated with pin insertion. Anecdotal reports in the literature have highlighted such concerns (244-246), but clinical studies on navigation have not shown them to be major issues (139). Our results demonstrated no difference between the percentages of navigated and non-navigated total knee arthroplasties revised for infection or fracture.

We also sought to analyze the different systems available for navigation, which were dominated in the Australian market by Stryker and Brainlab. The Stryker system was used essentially with Stryker implants, whereas Brainlab is a cross-platform design and has been used for large numbers for prostheses from several different companies (DePuy, Smith & Nephew, and Zimmer). The confounding variables of different knee systems and different navigation systems made it difficult to draw any firm conclusions about the benefits of any one particular navigation system.

This study showed that the use of computer navigation for total knee arthroplasty reduced the overall rate of revision as well as the rate of revision for loosening/lysis in patients less than sixty-five years of age and also reduced the rate of major revisions in the entire study population. Thus, we concluded that the use of navigation for total knee arthroplasty improves implant survivorship in younger patients treated with total knee arthroplasty and may be cost-effective in the long term.

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5.3 - Additional Discussion

Computer Navigation for Total Knee Arthroplasty Reduces Revision Rate for Patients Less Than Sixty-five Years of Age

One of the novel features of the data captured by the AOANJRR has been the inclusion of the methods used to implant devices, as distinct from the standard instrumentation conventionally employed.

Computer navigation for Total Knee Replacement (TKR) was first performed in Australia in 2001 by the thesis candidate. This followed extensive laboratory and cadaver research. The aim of the initial introduction of navigation was to compare its accuracy to the standard of care, which was the use of standard instruments to insert a TKR. There were rapid developments in this field, and, over 18 months, navigation progressed from needing pre-operative patient CT scans to what is termed 'image free navigation', which entailed the registration of the patient to the computer system by acquiring a number of anatomical markings on the patient's bone (137). The initial studies of computer navigation for TKR demonstrated improved alignment with the use of navigation compared to conventional technique, but there was no evidence of improved outcomes. For reasons similar to those behind the commencement of the world's

first joint registry (Swedish Knee Arthroplasty Registry) it was felt the best way of looking at longer term outcomes was to record all patients who had a TKR with computer navigation in the Registry. The AOANJRR was the first registry in the world to record and report such data and, with the preceding paper, the first to demonstrate a reduced rate of revision in younger patients having TKR with computer navigation compared to conventional instrumentation. The Registry has continued to report annually on the outcomes of computer navigation for TKR.

There continues to be an increased use of computer navigation for TKR throughout Australia. Initially 2.4% of all procedures in 2003 used computer navigation and this has increased to 30.8% in 2016 (*Fig 5*). There are now 96,730 primary TKR procedures performed with navigation recorded by the Registry, an increase of 117% over the past four years. This is due to a number of reasons including the use of navigation by younger surgeons who have "grown up" with this technology; and the widespread availability in most hospitals, as opposed to academic and larger centres when it was initially introduced. The Registry has continued to demonstrate that patients aged less than 65 years have a lower rate of revision when computer navigation is used (HR=0.85 (95%CI 0.80,0.91) p<0.001). For all age groups there is now a reduction in the rate of revision for navigated knee replacement compared to conventional knee replacement for diagnosis of loosening, which is the most common overall reason for revision for TKR (HR=0.73 (95%CI 0.64, 0.83) p<0.001). The experience of the AOANJRR is in

contrast to other registries. Only two registries record the use of computer navigation for TKR, the Norwegian Registry and the National Joint Registry of the United Kingdom. The Norwegian Registry commenced data collection in 2005. In the first year of navigation 7% of all TKA used navigation. By 2008 21% of TKA were performed with the use of navigation but this has slowly declined over time. In 2016 only 10% of TKA were performed with navigation. This is in distinct contrast to the use of navigation in Australia where there has been a steady increase over time as documented. The Norwegian Registry has recorded 37,126 TKA performed without navigation and 5,591 performed with navigation. They have not reported any difference in the rate of revision with the use of navigation and this may in part explain why navigation has not enjoyed a more wide spread use. In Norway the cumulative percent survival of TKA at ten years without navigation is 94.1% (95% CI 93.9%-94.3%) and for TKA with navigation the cumulative survival is 94.8% (95% CI 93.8%-95.8%). There is a much smaller number of navigated TKA in Norwegian Register compared to the AOANJRR and there is no breakdown by the two specific age groups. This may partly explain why there is no observed difference in rates of revision[7].

In the U.K. Registry only 2.3% of TKR have been used with navigation and outcomes are not reported. The USA has a low use of navigation for TKR. Using the American College of

[7] Personal communication and data from Oysten Gotheson, Norwegian Arthroplasty Registry, *29/8/2017*

Surgeons National Surgical Quality Improvement Program database, Gholson et al (247) identified 108,277 patients undergoing primary TKA between 2010 and 2014, of which 3573 cases (3.30%) were navigated. Rates of adoption of navigated TKA were determined and navigation utilization decreased from 4.96% in 2010 to 3.06% in 2014. There were no significant differences in short-term complications, readmission rate, or length of stay between navigated and traditional TKA but there was no information on rates of revision from this study. The lack of available data on comparative revision rates in the US and UK may influence the uptake of this technology. It also may demonstrate that surgeons, for whatever reason, may not believe that the Australian data are applicable to their respective countries.

Continued reporting in the AOANJRR of improved outcomes for navigation, particularly in the younger age group has potentially contributed to the more widespread use of navigation within the Australian community. As proportionally more TKR are performed with navigation this may be a factor contributing to the reduced rate of revision overall as demonstrated by the 15% reduction for patients under 65 yrs.

The experience with recording data for computer navigation has set a precedent for the collection of other techniques that have been introduced into the worldwide market place that seek to improve outcomes of arthroplasty. Patient specific or image derived instrumentation is

one such technique. This relies on pre-operative planning with the use of either a Computerized Tomography (CT) or Magnetic Resonance Imaging (MRI) to record details of the patient's anatomy. These data are then used to construct accurate jigs which are then used in place of conventional instrumentation to perform the bony cuts required to insert a TKR or THR. The cutting guides take into account anatomical deformities and bony osteophytes and the pre-operative planning for bone resection uses a predetermined implant size and position based on the images.

The theoretical benefits of the technology are improved alignment of the knee for TKR, better positioning of the acetabular component for THR, a reduction in surgical time, a reduction in the numbers of conventional instruments required to insert the prosthesis and potentially a reduction in costs due to savings in sterilization of instruments. The drawbacks of these techniques include the use of imaging not normally required for standard TKR and the cost of 3D printing associated with the cutting blocks. There have been reported technical errors at the time of use of the blocks. Though the techniques have been widely marketed there has been little evidence of the benefits compared to conventional TKR or THR. (248-250)

The Registry commenced data collection in 2009 on these specific 3D printed tools for use with TKR and coined the term 'Image Derived Instrumentation' (IDI) to cover the range of

proprietary names that orthopaedic manufacturers have used for their technology. The Registry has recorded 20,931 primary TKR procedures undertaken using IDI on 2009 up till 31st December 2016. In 2016 IDI was used in 10.4% of all primary TKR (135). There is a lower rate of revision in the first three months when IDI is used compared to no IDI. From three months to 1.5 years this is reversed and there is a higher rate of revision. After 1.5 years there is no difference in the rate of revision for primary TKR performed with or without IDI. The difference is age dependent and there is no difference in patents aged less than 65 years. However, there is an increased rate of revision for patients aged 65 years or older which is evident after three months. The reason for increased rate of revision in the older population is not clear but may be related to poorer fixation of the custom jigs in more osteoporotic bone. As with the use of navigation, a longer time maybe required before the appropriate place, if any, is found for IDI.

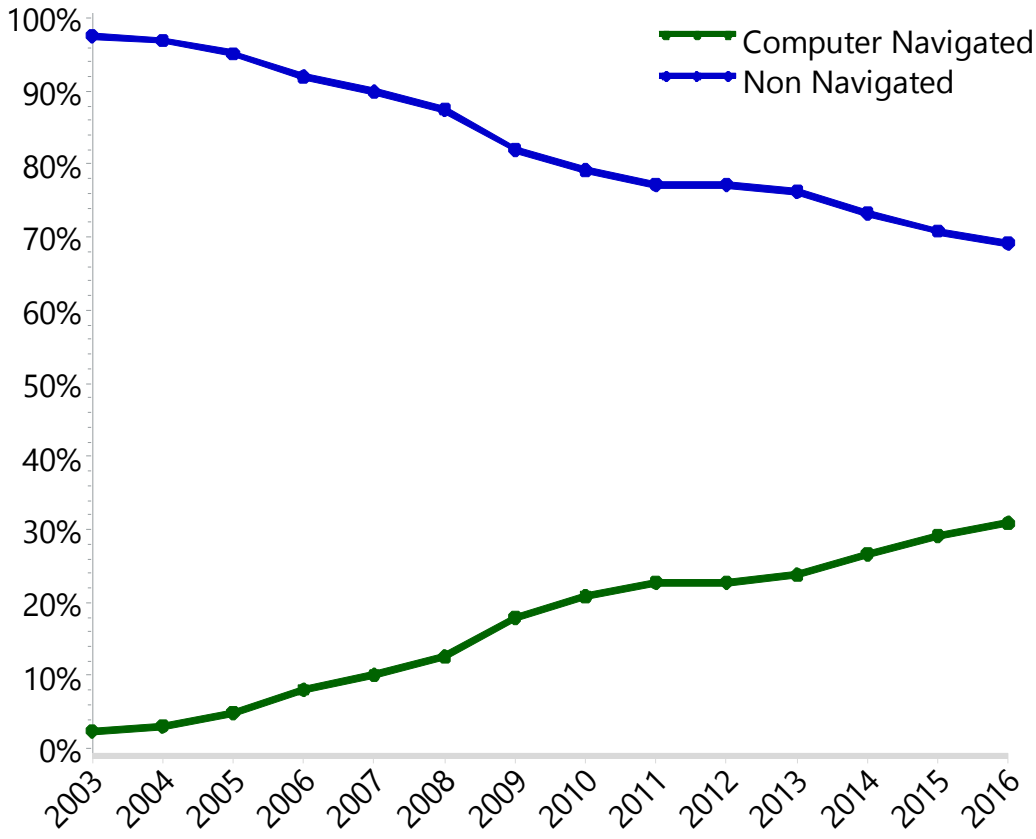
Industry regularly introduces technology, separate from implants, into the marketplace (251, 252) and the success of the Registry tracking these new technologies has led to closer co-operation with the manufacturers. Simple modifications on the Registry data form, along with device specific industry labels have contributed to the ability of the Registry to monitor the impact of new patient technology. Robotic surgery for both hip and knee replacement is a prime example of how industry values the importance of the Registry. Robotic surgery for TKR was introduced into Australia by the manufacturing industry leader Stryker in late 2016, and

the author was approached by the company to facilitate the collection of data from all surgeons who performed robotic surgery. The Registry now collects data on the two types of robotic surgery performed in Australia and the implants that they are used with. The first abstract on the early results of robotic knee replacement surgery has been accepted at international meetings in 2018.

Future research using these data, especially for navigation, will continue to monitor not only whether it is effective, but also if the use of new and more expensive technology is cost-effective. There has been only a limited analysis of the cost-effectiveness of computer navigation at a population level. The study from the Norwegian Arthroplasty Registry suggested that the ten-year implant survival rate needed to rise from 89.8% to 90.6% for institutions performing twenty-five arthroplasties per year and from 89.8%to 89.9% for those performing 250 per year for computer navigated surgery to be considered cost-effective compared to the standard of care. In Australia, for patients <65 of age, the survival rate for navigated TKR at ten years is 92.9% compared to 92.1% for non- navigated TKR.(135). As a result of this work a project with the Centre for Health Policy, Melbourne University School of Population and Global Health, on the cost-effectiveness of computer navigation has commenced.

Paper Five currently has 54 citations (refer 5.4 Citations), the majority acknowledging the study as the first investigation to demonstrate the clinical outcome of a reduced revision rate for patients undergoing TKR.

Fig 5 The increased use of navigation with primary TKR over time



5.4 - Citations of paper Chapter Five

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CHAPTER SIX

Lower prosthesis-specific 10-year revision rate with crosslinked than with non-crosslinked polyethylene in primary total knee arthroplasty

386,104 procedures from the Australian Orthopaedic Association National Joint Replacement Registry

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Contribution to the Paper	R N de Steiger designed the research question and wrote the manuscript. Together with all the co-authors he was responsible for the interpretation of data and for editing and final approval of paper.
Overall percentage (%)	80%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
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By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

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6.1 - Preface

This chapter contains the third of five articles submitted for publication in peer reviewed journals. The article has been published in *Acta Orthopaedica 2015; 86 (6):721-727*. It is one of two papers that address the third research question of this thesis on the introduction and impact of a new bearing material, cross- linked polyethylene (XLPE). It continues the theme of Research Question Two on methods to improve the rate of revision for younger patients and documents the introduction of a new material that is used with different types of TKR from different manufacturers. The following paper in Chapter Seven examines the impact of this material in THR.

While highly crosslinked polyethylene has shown reduced *in vitro* and *in vivo* wear, there have been few long-term clinical studies on its use in TKR and no studies demonstrating a reduced rate of revision compared to conventional polyethylene. This study compared the rate of revision of non-crosslinked polyethylene to that of crosslinked polyethylene in patients who underwent TKA for osteoarthritis**.**

The Additional Discussion updates the data, which continues to demonstrate reduced rates of revision for specific TKR implants, and suggests ongoing analysis and reporting of XLPE for TKR by the Registry may identify which types of XLPE are performing better.

6.2 - Published Paper

Background and purpose

While highly crosslinked polyethylene has shown reduced in vivo wear and lower rates of revision for total hip arthroplasty, there have been few long-term studies on its use in total knee arthroplasty (TKA). We compared the rate of revision of non-crosslinked polyethylene to that of crosslinked polyethylene in patients who underwent TKA for osteoarthritis.

Patients and methods

We examined data from the Australian Orthopaedic Association National Joint Replacement Registry on 302,214 primary TKA procedures with non-crosslinked polyethylene and 83,890 procedures with crosslinked polyethylene, all of which were performed for osteoarthritis. The survivorship of the different polyethylenes was estimated using the Kaplan-Meier method and was compared using proportional hazard models.

Results

The 10-year cumulative revision rate for non-crosslinked polyethylene was 5.8% (95% CI: 5.7–6.0) and for crosslinked polyethylene it was 3.5% (95% CI: 3.2–3.8) (> 6.5-year HR = 2.2 (1.5–3.1); $p < 0.001$). There was no effect of surgical volume or method of prosthesis fixation on outcome. There were 4 different TKA designs that had a minimum of 2,500 procedures in at least 1 of the polyethylene groups and a follow-up of ≥ 5 years. 2 of these, the NexGen and the Natural Knee II, had a lower rate of revision for crosslinked polyethylene. The Scorpio NRG/Series 7000 and the Triathlon Knee did not show a lower rate of revision for crosslinked polyethylene.

Interpretation

There is a lower rate of revision for crosslinked polyethylene in TKA, and this appears to be prosthesis specific and when it occurs is most evident in patients < 65 years of age. The difference in revision rates was mainly due to revisions because of lysis and loosening.

Introduction

Crosslinked polyethylene has shown reduced in vivo wear rates and lower revision rates in clinical studies when used for conventional primary total hip arthroplasty (253-257). However, it is uncertain whether the same benefit occurs with total knee arthroplasty (TKA). Polyethylene wear is multifactorial and can be influenced by prosthesis design, technical issues such as alignment, and patient-related factors. The biomechanical environment differs in the knee, with polyethylene being subject to deformation, delamination, and potential crack propagation. This has led to concerns with the use of crosslinked polyethylene in TKA because of reduced strength and fatigue resistance. In vitro studies have shown a decrease in wear with increasing radiation dose from 50 to 100k Gy, but toughness decreased with the higher radiation dose (157, 258). Knee simulator models of wear have shown less wear for crosslinked polyethylene than for standard compression-moulded polyethylene in both aged and unaged forms of the material. Reduced wear was also found in crosslinked polyethylene when subjected to diverse wear models with a scratched femoral component or an unbalanced knee (159, 161, 259). There have, however, only been a few reports of the clinical results of highly crosslinked polyethylene in TKA (260-262). While these studies have shown no difference in clinical or radiographic outcomes when comparing crosslinked polyethylene with non-crosslinked polyethylene, the longest follow-up was 7 years. Longer-term information is lacking.

We compared the rates of revision of non-crosslinked polyethylene and crosslinked polyethylene for all patients who underwent TKA for osteoarthritis as reported to the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR).

Methods

The AOANJRR began data collection on September 1, 1999, and it includes data on over 98% of the arthroplasty procedures performed in Australia since 2002. Registry data are validated against patient-level data provided by each of the state and territory health departments in Australia using a sequential, multilevel matching process. A matching program is run on a monthly basis to search for all primary and revision arthroplasty procedures recorded in the registry that involve the same side and joint of the same patient, thus enabling each revision to be linked to the primary procedure. Data are also matched biannually with the National Death Index of the Department of Health and Ageing to obtain information on the date of death. The registry records the reasons for revision and the type of revision of TKA, and categorizes revision surgery as major or minor. A major revision involves revision of either the tibial or the femoral component, or both. Minor revisions are all other revisions usually including patellar resurfacing and tibial insert changes.

Crosslinked polyethylene was defined in the registry database as ultra-high-molecular-weight polyethylene that has been irradiated with high-dose (≥ 50 kGy) gamma or electron beam radiation, regardless of remelting or annealing. The definition of polyethylene was confirmed with industry and crosschecked with the Australian Prosthesis Advisory List, which records crosslinked polyethylene separately from conventional polyethylene. Vit E crosslinked polyethylene has been recorded separately but included in the crosslinked polyethylene in this study, due to short-term follow-up and its use with 1 type of prosthesis. The study population was all patients with primary TKAs undergone for osteoarthritis (OA). The registry first recorded the use of crosslinked polyethylene in 2001. During the study period, there were 302,214 primary TKA procedures performed for OA reported to the registry that used non-crosslinked polyethylene and there were 83,890 that used crosslinked polyethylene. There was an increase in the use of crosslinked polyethylene, with over 40% of all primary TKA procedures performed in 2013 using crosslinked polyethylene (Figure 1). Outcomes were determined for all procedures, comparing TKA performed with non-crosslinked polyethylene and crosslinked polyethylene and including the effect of age, sex, and reason for revision. The types of revision were also analyzed.

In order to account for possible confounders, we also performed a number of sub analyses. These included method of fixation, type of tibial bearing, the impact of surgical volume, and brand of prosthesis. The effect of the method of fixation (cemented, hybrid, and cementless) and tibial bearing surface (fixed-bearing, mobile, and rotating) with crosslinked and non-crosslinked polyethylene in TKA was examined. Data on the number of TKAs performed were analyzed. Surgeons were divided into 4 groups based on the average number of procedures per year: ≤ 10, 11–25, 26–70, and > 70 TKAs per year.

A separate analysis was performed on specific prostheses that have both crosslinked and non-crosslinked polyethylene options. The criteria for inclusion were a minimum of 2,500 procedures in at least 1 of the polyethylene groups and a follow-up time of 5 or more years.

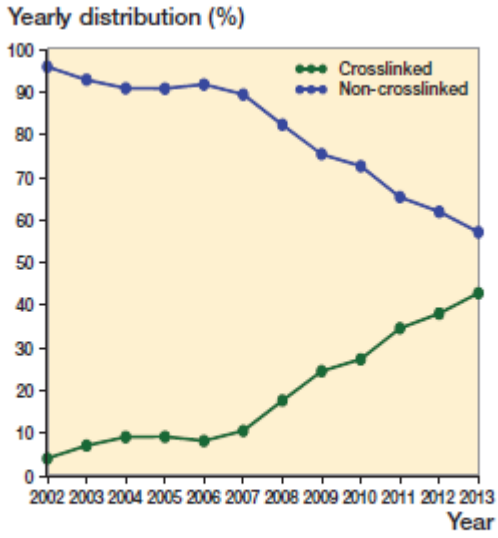


Figure 1. Relative proportions of primary total knee replacements according to type of polyethylene bearing surface (all diagnoses).

Statistics

The registry uses Kaplan-Meier estimates of survivorship to describe the time to the first revision of an arthroplasty, with censoring at the time of death or closure of the database at the time of analysis. The unadjusted cumulative percentage revision (CPR) after the primary arthroplasty, with an accompanying 95% confidence interval (CI), was calculated using unadjusted pointwise Greenwood estimates. Hazard ratios were calculated using Cox proportional-hazards models, adjusting for age and sex, and were used to make statistical comparisons of the revision rates between groups.

The assumption of proportional hazards was checked analytically for each model; if the interaction between the predictor and the log of the postoperative time was significant in the standard Cox model, then a time-varying model was used. Time points were iteratively chosen until the assumption of proportionality was met, and the hazard ratios were calculated for each selected time period. All tests were 2-tailed at the 5% level of significance. Statistical analysis was performed using SAS software version 9.3.

Ethics

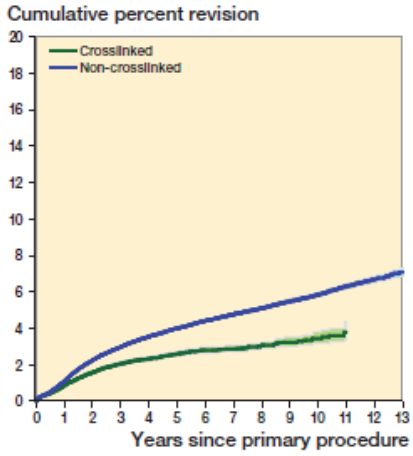
The study was approved by the Commonwealth of Australia as a Declaration of Quality Assurance Activity under section 124X of the Health Insurance Act, 1973. All investigations were conducted in accordance with ethical principles of research (the Helsinki Declaration II).

Results

The 10-year CPR for non-crosslinked polyethylene was 5.8% (CI: 5.7–6.0) and for crosslinked polyethylene it was 3.5% (CI: 3.2–3.8) (HR after 6.5 years = 2.2 (1.5–3.1); $p < 0.001$) (Figure 2). The main reason for the difference in revision rate was a reduction in the rate of revision for the wear-related problems of loosening and lysis. The 10-year CPR for loosening/lysis for non-crosslinked polyethylene was 1.9% (CI: 1.9–2.0) and for crosslinked polyethylene it was 0.9% (CI: 0.7–1.0) (HR = 1.8 (1.6–2.0); $p < 0.001$) (Figure 3). The reasons for revision of TKA for both crosslinked polyethylene non-crosslinked polyethylene are listed in Table 1.

The effect of crosslinked polyethylene was more pronounced in the younger age groups. For patients less than 65 years of age, the 10-year CPR for non-crosslinked polyethylene was 8.8% (CI: 8.5–9.1) and it was 4.9% (CI 4.3–5.5) for crosslinked polyethylene (HR after 2.5 years = 1.95 (1.7–2.3); $p < 0.001$) (Figure 4).

The type of fixation had no effect on the outcomes when comparing non-crosslinked polyethylene and crosslinked polyethylene. For all cemented TKAs, cementless TKAs and hybrid TKAs, the rate of revision was always lower for cross-linked polyethylene. The type of tibial bearing was examined, but there was only 1 type of knee prosthesis that had sufficient numbers of fixed and mobile bearing surfaces with the 2 types of polyethylene for analysis. This was the NexGen Posterior Stabilized TKA, and at 5 years there was no significant difference in the rate of revision between the fixed-bearing knee and the rotating mobile knee regarding the type of polyethylene. The use of crosslinked polyethylene and non-crosslinked polyethylene was evenly spread over all 4 surgical volume groups. For the surgical volume groups 11–25, 26–70, and > 70, there was a significant reduction in the rate of revision and for crosslinked polyethylene ($p < 0.001$). There was no difference in the rate of revision in the low-volume (≤ 10) group, although this was probably due to the smaller numbers of procedures available for analysis.



Legend to Figure 2. HR adjusted for age and sex. Non-crosslinked versus crosslinked

Period	HR (95%CI)	p-value
0–6 months	1.2 (1.1–1.3)	0.005
6–9 months	1.6 (1.3–1.9)	< 0.001
9–12 months	1.3 (1.1–1.6)	0.001
1–2.5 years	1.6 (1.5–1.8)	< 0.001
2.5–6 years	1.9 (1.7–2.2)	< 0.001
6–6.5 years	8.6 (2.2–35)	0.002
> 6.5 years	2.2 (1.5–3.1)	< 0.001

Figure 2. Cumulative percentage revision of primary total knee replacements according to type of polyethylene bearing surface (with OA as primary diagnosis).

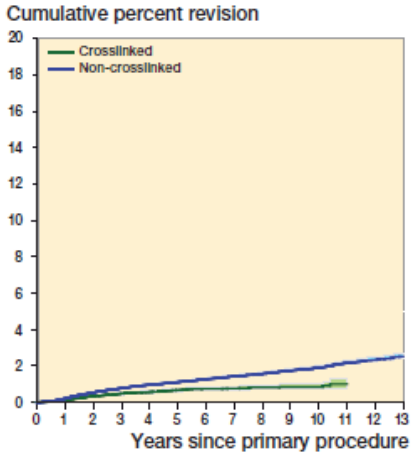
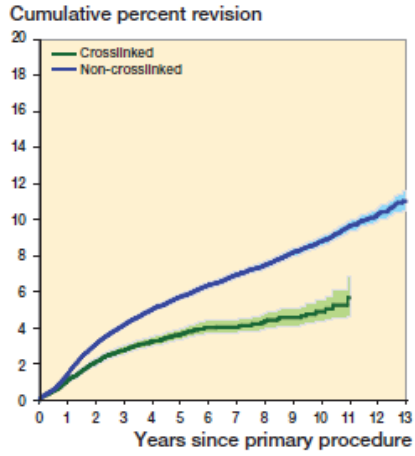


Figure 3. Cumulative percentage revision of primary total knee replacements according to type of polyethylene bearing surface (revision for loosening/lysis, with OA as primary diagnosis). Non crosslinked vs crosslinked (entire period): HR = 1.80 (1.61–2.02), p < 0.001 (HR adjusted for age and sex).



Legend to Figure 4. HR adjusted for sex. Non-crosslinked < 65 versus crosslinked < 65

Period	HR (95%CI)	p-value
0–1 year	1.3 (1.1–1.5)	< 0.001
1–1.5 years	1.9 (1.6–2.4)	< 0.001
1.5–2.5 years	1.4 (1.2–1.7)	< 0.001
> 2.5 years	1.9 (1.7–2.3)	< 0.001

Figure 4. Cumulative percentage revision of primary total knee replacements in patients aged < 65 years, according to type of polyethylene bearing surface (with OA as primary diagnosis).

Table 1. Revision diagnosis of primary total knee replacement according to type of polyethylene bearing surface (with OA as primary diagnosis)

Revision diagnosis	Crosslinked Number	Crosslinked % Revision	Crosslinked % Primary	Non-crosslinked Number	Non-crosslinked % Revision	Non-crosslinked % Primary
Loosening/Lysis	341	23.5	0.4	3,545	30.0	1.2
Infection	461	31.8	0.5	2,463	20.8	0.8
Patellofemoral pain	140	9.7	0.2	1,467	12.4	0.5
Pain	117	8.1	0.1	1,119	9.5	0.4
Instability	86	5.9	0.1	720	6.1	0.2
Arthrofibrosis	56	3.9	0.1	425	3.6	0.1
Patellar erosion	51	3.5	0.1	368	3.1	0.1
Fracture	37	2.6	0.0	292	2.5	0.1
Malalignment	34	2.3	0.0	266	2.3	0.1
Metal-related pathology	3	0.2	0.0	236	2.0	0.1
Tibial wear	16	1.1	0.0	198	1.7	0.1
Other	108	7.4	0.1	723	6.1	0.2
Total number of revisions	1,450	100	1.7	11,822	100	3.9
primaries	83,890			302,214		

Table 2. Cumulative percentage revision (95% confidence intervals) of primary total knee replacements according to type of polyethylene bearing surface and age, for specific prostheses (with OA as primary diagnosis)

Model Polyethylene/ Age	Revised n	Total n	Cumulative percentage revision 1 year	3 years	5 years	7 years	10 years	13 years
Natural Knee II/Natural Knee II								
crosslinked	93	3,312	1.0 (0.7–1.4)	2.1 (1.6–2.7)	2.8 (2.2–3.5)	3.1 (2.5–3.8)	3.8 (3.0–4.7)	
non-crosslinked	190	2,860	0.8 (0.5–1.2)	2.0 (1.5–2.5)	3.0 (2.4–3.7)	4.3 (3.6–5.2)	7.4 (6.3–8.5)	9.9 (8.5–11.6)
Triathlon CR/Triathlon								
crosslinked	369	25,839	0.7 (0.6–0.9)	2.0 (1.8–2.2)	2.7 (2.3–3.1)			
non-crosslinked	182	8,060	0.8 (0.6–1.0)	1.9 (1.6–2.3)	2.6 (2.2–3.0)	3.0 (2.6–3.5)		
Triathlon PS/Triathlon								
crosslinked	72	3,149	1.8 (1.4–2.4)	2.8 (2.2–3.5)	3.2 (2.5–4.1)			
non-crosslinked	126	3,182	1.8 (1.4–2.3)	3.7 (3.0–4.4)	4.6 (3.8–5.5)	5.2 (4.3–6.3)		
Nexgen CR/Nexgen								
crosslinked	437	27,193	0.7 (0.6–0.8)	1.6 (1.4–1.8)	2.0 (1.8–2.2)	2.2 (2.0–2.5)	2.8 (2.5–3.2)	
age < 65	216	9,000	1.0 (0.8–1.3)	2.4 (2.1–2.8)	3.1 (2.7–3.6)	3.4 (2.9–3.9)	4.3 (3.6–5.1)	
age ≥ 65	221	18,193	0.6 (0.5–0.7)	1.2 (1.0–1.4)	1.5 (1.3–1.7)	1.7 (1.4–1.9)	2.1 (1.7–2.5)	
non-crosslinked	224	8,735	0.5 (0.3–0.6)	1.6 (1.3–1.9)	2.1 (1.8–2.4)	2.5 (2.1–2.9)	3.2 (2.7–3.7)	5.2 (4.2–6.5)
age < 65	99	1,968	0.6 (0.4–1.1)	2.4 (1.7–3.2)	3.7 (2.9–4.7)	4.6 (3.6–5.7)	5.8 (4.6–7.1)	10 (7.7–14)
age ≥ 65	125	6,767	0.4 (0.3–0.6)	1.4 (1.1–1.7)	1.6 (1.3–2.0)	1.8 (1.5–2.2)	2.4 (2.0–2.9)	3.3 (2.4–4.5)
total	661	35,928	0.7 (0.6–0.8)	1.6 (1.5–1.7)	2.0 (1.9–2.2)	2.3 (2.1–2.5)	2.9 (2.7–3.2)	4.9 (4.0–6.1)
Nexgen PS/Nexgen								
crosslinked	184	8,364	1.0 (0.8–1.2)	2.5 (2.1–2.9)	3.2 (2.7–3.8)	3.9 (3.2–4.7)		
non-crosslinked	681	1,9281	0.9 (0.8–1.0)	2.3 (2.1–2.6)	3.3 (3.0–3.5)	4.1 (3.8–4.5)	5.2 (4.8–5.7)	6.1 (5.4–7.0)
Scorpio NRG CR/Series 7000								
crosslinked	35	2,454	0.7 (0.4–1.1)	1.6 (1.1–2.3)	2.0 (1.4–2.8)			
non-crosslinked	13	406	0.2 (0.0–1.7)	1.2 (0.5–3.0)	2.1 (1.0–4.2)			
Scorpio NRG PS/Series 7000								
crosslinked	92	2,910	0.9 (0.6–1.3)	3.6 (2.9–4.5)	4.5 (3.6–5.6)			
non-crosslinked	15	504	0.6 (0.2–1.8)	1.6 (0.8–3.2)	3.1 (1.9–5.1)			

Prosthesis-specific analysis

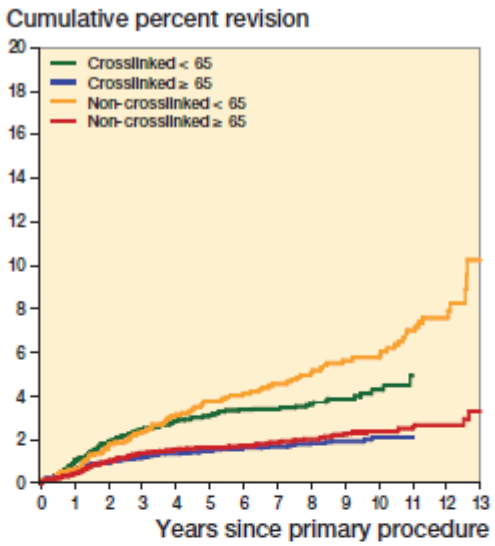
4 different TKA designs fulfilled the criteria of a minimum of 2,500 procedures in at least 1 of the polyethylene groups and a follow-up of 5 or more years. These were the Natural Knee II, the Triathlon, the NexGen, and the Scorpio (Table 2).

The Natural Knee II only includes minimally stabilized prostheses, as the posterior-stabilized option has seldom been used. The registry has 10-year follow-up for both types of polyethylene. Crosslinked polyethylene was used in 54% of the procedures, and had a lower rate of revision after 3.5 years. The 10-year CPR for non-crosslinked polyethylene was 7.4% (CI: 6.3–8.5) as compared to 3.8% (CI: 3.0–4.7) for crosslinked (HR after 3.5 years = 3.2 (2.1–5.0); $p < 0.001$). This difference was evident regardless of age; however, the difference was greater for those who were less than 65 years old.

The Triathlon knee had a minimum 5-year follow-up for both types of polyethylene, and crosslinked polyethylene was used in 72% of the procedures. There was no difference in the rates of revision for both minimally and posterior-stabilized Triathlon prostheses when comparing non-crosslinked and crosslinked polyethylene (HR = 1.0 (0.9–1.2); $p = 0.9$; and HR = 1.3 (0.95–1.7); $p = 0.1$).

The NexGen knee had 10-year follow-up for both crosslinked and non-crosslinked polyethylene for the minimally stabilized prosthesis, and 7-year follow-up for the posterior stabilized prosthesis. Crosslinked polyethylene was used in 76% of minimally stabilized NexGen CR and CR Flex knees, and had a lower rate of revision after 2.5 years. This difference, however, was only evident in those aged less than 65 years. The 10-year CPR for patients aged < 65 with non-crosslinked polyethylene was 5.8% (4.6–7.1), as compared to 4.3% (3.6–5.1) for crosslinked polyethylene (HR after 1 year = 1.6 (1.2–2.1); $p = 0.001$) (Figure 5). Crosslinked polyethylene was used in 30% of posterior-stabilized NexGen LPS and LPS Flex knees. The rates of revision were similar when comparing non-crosslinked and crosslinked polyethylene in the posterior-stabilized group.

The Scorpio NRG/Series 7000 knee had 5-year follow-up for non-crosslinked and crosslinked polyethylene, and the latter was used in 86% of procedures. There was no difference in the rates of revision with minimally and posterior-stabilized Scorpio NRG/Series 7000 prostheses when comparing non-crosslinked and crosslinked polyethylene (HR = 1.3 (0.7–2.6); $p = 0.4$; and HR = 0.61 (0.34–1.1); $p = 0.08$).



Legend to Figure 5. HR adjusted for gender

Period	HR (95%CI)	p-value
Crosslinked < 65 vs crosslinked ≥ 65		
0–6 months	1.3 (0.88–2.0)	0.2
6–9 months	2.2 (1.2–4.0)	0.007
9–12 months	3.5 (2.1–5.8)	< 0.001
12–18 months	1.4 (0.88–2.2)	0.2
> 18 months	2.4 (1.8–3.1)	< 0.001
Non crosslinked ≥ 65 vs crosslinked ≥ 65		
Entire	1.1 (0.89–1.4)	0.4
Non crosslinked < 65 vs crosslinked < 65		
0–12 months	0.8 (0.48–1.2)	1
> 12 months	1.6 (1.2–2.1)	0.001
Non crosslinked < 65 vs noncrosslinked ≥ 65		
0–18 months	2.0 (1.3–2.9)	< 0.001
> 18 months	3.0 (2.2–4.0)	< 0.001

Figure 5. Cumulative percentage revision of minimally stabilized Nexgen primary total knee replacements according to type of polyethylene bearing surface and age (with OA as primary diagnosis).

Discussion

This is the first study to demonstrate a reduced rate of revision for crosslinked polyethylene in TKA in a population-based registry. When a new device or material has been introduced, post-market surveillance is important and registries are ideally suited to determine outcomes—and especially to show whether there are any early problems associated with new prostheses. Concerns regarding the mechanical properties of crosslinked polyethylene in TKA have not been identified in the results reported from the registry. Polyethylene fracture as a reason for revision has only been recorded in 2 cases, suggesting that concerns regarding crosslinked polyethylene toughness are presently unfounded.

While there is a lower rate of revision for crosslinked polyethylene than for non-crosslinked polyethylene, this reduction is not evident for all prostheses. While crosslinked polyethylene is used frequently in hip arthroplasty, the uptake of crosslinked polyethylene for TKA has not been as great, although it accounts for 43% of all tibial polyethylene in 2013. At 10 years, there was a reduction in loosening/lysis as a reason for revision in the crosslinked polyethylene TKA group.

While TKA has a low rate of revision, there is considerable variation with age—with patients younger than 65 having a higher rate of revision (257)). It therefore becomes important to examine factors that may reduce this higher rate of revision. This study has demonstrated that while there is an overall reduction in the rate of revision for all ages when crosslinked polyethylene is used, this is more apparent in the younger age group (< 65). This may become more pronounced as revision for wear-related issues, such as loosening and lysis, increases over time.

In primary TKA, crosslinked polyethylene was used less frequently than non-crosslinked polyethylene and there was considerable prostheses difference in its use. While the registry has shown a lower rate of revision overall for crosslinked polyethylene, the analysis of crosslinked polyethylene may be confounded by well-performing prostheses with a higher use of crosslinked polyethylene. Consequently, any observed difference in revision rate may be confounded by prosthesis type. This study has demonstrated prosthesis variation in the effect that crosslinked polyethylene has on the rate of revision following TKA. A lower rate of revision was identified when crosslinked polyethylene was used in conjunction with the 2 minimally stabilized TKAs with 10-year follow-up (the Natural Knee II and NexGen) in comparison to the use of non-crosslinked polyethylene. This difference was most evident in younger patients. No significant difference in revision rate was identified for either the minimally stabilized or posterior stabilized Triathlon and Scorpio NRG/Series 7000 TKAs.

One possible explanation for the variation in CPR differential between non-crosslinked and crosslinked polyethylene with different designs may be related to the type of crosslinked polyethylene used. The crosslinked polyethylene used in Natural Knee II is manufactured by electron beam irradiation of the polyethylene at an elevated temperature, to 95 kGy, followed by melting. In NexGen knees, the crosslinked polyethylene is made by electron beam irradiation at elevated temperature, to 65 kGy, followed by melting. In Triathlon and Scorpio knees, the crosslinked polyethylene is made by irradiating the polyethylene to 33 kGy in 3 consecutive steps, with annealing (heating to below the melting point) after each irradiation cycle. All 3 types of crosslinked polyethylene knees are packaged in air-permeable pouches and are gas sterilized. Thus, during shelf storage they are exposed to air until implantation. Radiation generates trapped free radicals, which are known to cause oxidation; thus, either melting or annealing is used after irradiation to eliminate or reduce the trapped free radicals. Independent reports have shown that the annealing results in detectable trapping of free radicals, increasing the potential for oxidation during shelf storage and use in vivo. There have also been reports showing increased rates of failure due to damage to the polyethylene component, mainly caused by oxidation. It is therefore possible that radiation-crosslinked and annealed polyethylene components may not necessarily perform as well as radiation-crosslinked and melted polyethylene components in patients, in comparison to their non-crosslinked polyethylene counterparts, as found in the current study.

The first clinical study of crosslinked polyethylene was published by Hodrick et al. (2008), and they reported a consecutive series of 200 Natural Knee II systems (Zimmer), comparing the first 100 cases to receive crosslinked polyethylene with the previous 100 cases using non-crosslinked polyethylene. The crosslinked polyethylene group had an average age of 67, and was followed for a minimum of 69 months, as compared to an average age of 70 and a minimum follow-up of 82 months for the non-crosslinked group. In the crosslinked polyethylene group, there were no revisions for tibial wear but 2 patients had evidence of radiolucencies. In the non-crosslinked group, there were 20 patients who showed radiolucencies and 3 patients had revisions for tibial loosening and wear. The authors commented on some limitations of their study, which included 35 patients who had been lost to follow-up and lack of retrieval analysis. Our study reports on over 3,000 Natural Knee II TKA using crosslinked polyethylene with a 10-year CPR of 3.8%.

2 other clinical studies have reported on the outcomes of crosslinked polyethylene using the NexGen TKA (Zimmer) with Prolong crosslinked polyethylene, which is electron beam-irradiated to 65 kGy at an elevated temperature and subsequently melted. Minoda

et al. (2009) reported on a consecutive series of 113 CR TKAs with non-crosslinked polyethylene, and compared them to 89 CR TKAs using Prolong. At 2 years of follow-up, the clinical outcome was similar between the 2 groups—with no revisions and no evidence of osteolysis or polyethylene failure. Long et al. (2012) reported on a consecutive series of 120 TKAs using the NexGen high flex posterior-stabilized knee. There were 97 patients who had a full clinical and radiographic evaluation at an average of 52 months. There were no cases of radiographic loosening or progressive radiolucent lines. Our study involved 35,557 NexGen TKAs with crosslinked polyethylene, and at 10 years the CPR was 2.8% for the NexGen CR TKA with crosslinked polyethylene. With a shorter follow-up of 7 years, we found no difference in the rates of revision of the NexGen PS knee for the 2 types of polyethylene.

This study has a number of strengths, including the large number of procedures, the use of population-based data, and the longer-term follow-up. Over 83,000 TKAs performed for osteoarthritis with the use of crosslinked polyethylene have been analyzed, making this the largest study to report on the outcomes of crosslinked polyethylene use in TKA. Crosslinked polyethylene is more expensive than conventional polyethylene, so it is important to demonstrate some benefit. The reduction in the rate of revision was seen in both low volume and high-volume surgeons, and is therefore probably due to the crosslinked polyethylene and less likely to be due to surgeon-related factors.

A potential weakness of this study is that when crosslinked polyethylene was introduced, for each implant studied the tibial trays were new. This may have led to bias, as no crosslinked polyethylene tibial trays may have been kept for a longer time period, leading to an extended shelf life before implantation. This could lead to a higher rate of revision. We therefore examined the rate of revision of non-crosslinked polyethylene before and after the introduction of crosslinked polyethylene for the NexGen and Triathlon TKA systems. There was no difference in the rates of revision for non-crosslinked polyethylene before and after the introduction of crosslinked polyethylene for these 2 knee systems.

Conclusion

A lower rate of revision has been shown for crosslinked polyethylene in TKA, and this appears to be prosthesis-specific and confined to minimally stabilized options. When it occurs, the lower rate of revision is most evident in patients who are less than 65 years of age and there is a reduction in revision for loosening/lysis.

RdS designed the research question and wrote the manuscript. AC and ML performed the statistical analyses. SG and OM performed critical revision of the manuscript. All the authors were responsible for the interpretation of data and for editing and final approval of the paper.

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No competing interests declared.

6.3 - Additional Discussion

The Registry first reported on the effect of XLPE for TKR in 2012. The overall lower rate of revision for XLPE for TKR compared to conventional non XPLE continues to be demonstrated by the AOANJRR. The 2017 Annual Report has information on 163,042 TKRs with XLPE and the cumulative percent revision at ten years is 5.7% for non XLPE compared to 3.7% for XLPE. The major reason for the difference is the reduced revisions for loosening and bone lysis, which occurs as a consequence of wear. As has been previously outlined in the Literature Review there is a higher rate of revision in younger patients and the effect of XLPE is more evident in younger patients. The cumulative percent revision at ten years for patients < 65 years of age with a TKR and non XLPE is 8.4% compared to 5.2% for XLPE, (Hazard Ratio from 6.5 years onwards=2.3, $p< 0.001$). There has been an increased use of XLPE since the original paper and, in 2016 for the first time, XLPE was used more frequently (57% of all cases) than non XLPE.

Not all types of XLPE are performing better than conventional non XLPE and this may be due to different manufacturing processes. Since publication of this chapter there have been two further registry based studies which have shown no differences in the overall revision rates between XLPE and non XLPE for TKR (263, 264). Possible reasons for the different findings from these studies and the AOANJRR include a shorter follow up time,

variation in prosthesis selection and much smaller numbers available for analysis. Importantly these studies confirmed the safety profile of XLPE with no observed failures from XLPE component breakage.

The ongoing reporting of a lower overall rate of revision with XLPE in TKR in the AOANJRR Annual Report has contributed to the ongoing use of this material by Australian surgeons and there is a greater proportion of patients <65 years of age who have XLPE with a TKR. The UK National Joint Registry does not distinguish between the types of polyethylene and cannot report on comparative performance. The Swedish Knee Arthroplasty Registry and New Zealand Registry do not report on XLPE and other registries such as the Norwegian, Dutch, and Finnish only have small numbers of TKRs with XLPE. Continued analysis and reporting of XLPE for TKR by the Registry may identify which types of XLPE are performing better and pooling of data with other registries will be beneficial.

As a consequence of Paper 6 an international project has been developed to examine data from 5 registries that identify XLPE to assess the effect of XLPE in specific TKR groups. This will be presented at the Annual Meeting of the International Society of Arthroplasty Registries in June 2018. Chapter 6 has been cited five times (Appendix 3).

6.4 - Citations of paper Chapter Six

MacDonald, D.W., Higgs, G.B., Chen, A.F., Malkani, A.L., Mont, M.A., Kurtz, S.M.
Oxidation, Damage Mechanisms, and Reasons for Revision of Sequentially Annealed Highly Crosslinked Polyethylene in Total Knee Arthroplasty
(2018) *Journal of Arthroplasty*, 33(4),pp.1235-1241.

Brockett, C.L., Carbone, S., Fisher, J., Jennings, L.M.
Influence of conformity on the wear of total knee replacement: An experimental study
(2018) *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine*, 232(2), pp.127-134.

Phan, D.L., Schwarzkopf, R.
Aseptic synovitis
(2017) *Revision Total Knee Arthroplasty*, pp.367-379.

Massin, P., Achour, S.
Wear products of total hip arthroplasty: The case of polyethylene [Produits d'usure des arthroplasties totales de hanche: le cas du polyéthylène]
(2017) *Morphologie*, 101(332), pp.1-8.

Vertullo, C.J., Lewis, P.L., Graves, S., Kelly, L., Lorimer, M., Myers, P.
Twelve-year outcomes of an oxinium total knee replacement compared with the same cobalt-chromium design: An analysis of 17,577 prostheses from the Australian Orthopaedic Association National Joint Replacement Registry
(2017) J*ournal of Bone and Joint Surgery - American Volume*, 99(4),pp.275-283.

CHAPTER SEVEN

The use of Cross Linked Polyethylene for Total Hip Arthroplasty markedly reduces revision surgery at 16 years

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Hip

Statement of Authorship

Title of Paper	The use of Cross Linked Polyethylene for Total Hip Arthroplasty markedly reduces revision surgery at 16 years
Publication Status	☐ Published ☑ Accepted for Publication ☐ Submitted for Publication ☐ Unpublished and Unsubmitted work written in manuscript style
Publication Details	R.N. de Steiger, M. Lorimer, S.E. Graves The use of Cross Linked Polyethylene for Total Hip Arthroplasty markedly reduces revision surgery at 16 years The Journal of Bone and Joint Surgery (A). *Accepted for Publication March 2018*

Principal Author

Name of Principal Author (Candidate)	Richard N. de Steiger
Contribution to the Paper	R N de Steiger designed the research question and wrote the manuscript. Together with all the co-authors he was responsible for the interpretation of data and for editing and final approval of paper.
Overall percentage (%)	80%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is ~~not~~ subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
Signature	Date 17/5/18

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate to include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	Michelle Lorimer
Contribution to the Paper	M Lorimer performed data extraction and the statistical analyses. Together with all the authors she was responsible for editing and final approval of paper.
Signature	Date 15/5/18

Name of Co-Author	Stephen E Graves
Contribution to the Paper	S E Graves designed the research question and performed critical revision of the manuscript. Together with all the authors he was responsible for the interpretation of data and for editing and final approval of paper.
Signature	Date 18/5/18

7.1 - Preface

This chapter contains the fourth of five articles submitted for publication in peer reviewed journals. The article has been published by *The Journal of Bone and Joint Surgery 2018 Volume 100-A, (15),1281-1288*. It is the second paper to address the third research question of this thesis on the introduction and impact of a new bearing material, cross- linked polyethylene (XLPE) and was selected as the highlight article of the month.

The long term success of THR is limited by wear of the polyethylene bearing surface. Cross-linking conventional polyethylene has demonstrated lower wear rates and a reduction in bone lysis in both laboratory and clinical studies. The aim of this study was to compare the rate of revision at 16 years in patients who had a THR for osteoarthritis, and received either cross-linked (XLPE) or conventional non crosslinked polyethylene (CPE). As discussed previously, Chapters Five and Six have outlined methods of reducing the rate of revision in younger patients with TKR. While the age related revision rates are not as apparent with THR the greatest reduction in revision with XLPE compared to CPE is in patients younger than 55 years of age.

7.2 - Accepted Publication

Background:

Total hip arthroplasty (THA) is an effective operation for the management of end-stage hip osteoarthritis, but long-term success can be limited by wear of the polyethylene bearing surface. Cross-linking conventional polyethylene has resulted in lower wear rates and a reduction in bone lysis in both laboratory and clinical studies. The aim of this study was to compare the rates of revision between cross-linked polyethylene (XLPE) and conventional non-cross-linked polyethylene (CPE) at 16 years after THAs performed for the treatment of osteoarthritis.

Methods:

We performed an observational study of data, from a national registry, on all patients who underwent THA for osteoarthritis in Australia from 1999 through December 31, 2016. The outcomes of THAs performed with CPE were compared with those of THAs performed with XLPE, along with an analysis of the effect of age, sex, femoral head size, the method of acetabular and femoral component fixation, and the reason for revision. The principal outcome measure was the time to the first revision, determined using Kaplan-Meier estimates of survivorship.

Results:

CPE was used in 41,171 procedures, and XLPE was used in 199,131. The mean ages of the men and women treated with CPE were 70.0 years (standard deviation [SD] = 9.9 years) and 72.5 years (SD = 9.7 years), respectively, whereas the men and women who received XLPE were slightly younger (mean age, 68.6 years [SD = 10.3 years] and 70.7 years [SD = 9.9 years], respectively. XLPE was associated with a lower rate of revision than CPE at 6 months, and this difference became more apparent with time. The 16-year cumulative percentage of revisions of the primary THAs was 11.7% (95% confidence [CI] = 11.1% to 12.3%]) in the CPE group and 6.2% (95% CI = 5.7% to 6.7%) in the XLPE group. The hazard ratio at 9 years was 3.02 (p = 0.001).

Conclusions:

The use of XLPE has resulted in a significant reduction in the rate of revision at 16 years following THA for osteoarthritis. This evidence suggests that the longevity of THA is

likely to be improved, which may enable younger patients to undergo surgery, confident of a reduced need for revision in the long term.

Level of Evidence:

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

Introduction

Total hip arthroplasty (THA) is one of the most effective surgical procedures and very successful for the management of end-stage hip osteoarthritis. The number of THA procedures has been increasing, and this is expected to continue (16, 19, 265-267). The most common bearing surface for THA has been conventional non-cross-linked ultra-high molecular weight polyethylene (CPE), which has been in use for >50 years. However, the biggest problem limiting the life span of THA has been long-term wear, leading to osteolysis and aseptic loosening (268). As limiting wear of the bearing surface is critical to long-term success, particularly for younger patients, research has led to the development of polyethylene with improved wear characteristics. Methods for manufacturing cross-linked polyethylene (XLPE) differ, but all include radiation doses of 50 to 100 kGy with different radiation techniques and thermal treatments. Initial laboratory hip simulator trials showed less wear of XLPE compared with CPE (154, 269, 270). A phased clinical introduction of this material then commenced with randomized controlled trials (RCTs) using radiostereometric analysis, the early results of which demonstrated reduced wear with XLPE (271, 272).

Clinical studies of XLPE from different manufacturers have all shown reduced wear compared with CPE, confirming the initial laboratory findings (273-276). Examination of liners retrieved during surgery for reasons other than wear-related issues has also demonstrated reduced wear in vivo (277, 278). A meta-analysis of RCTs comparing XLPE with CPE for THA showed a reduction in volumetric and total linear wear of XLPE liners along with a reduction in radiographic evidence of osteolysis (279). However, the follow-up was not long enough to show a difference in the rates of revision surgery, which ultimately is most important for the patient.

The aim of this study was to use data from a national joint replacement registry to compare the rate of revision at 16 years after THA for osteoarthritis between patients who had received XLPE and those treated with CPE.

Materials and Methods

The Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) began data collection on September 1, 1999, and participation is voluntary. The Registry includes data on almost all of the arthroplasty procedures performed in Australia since 2002, and data are validated against patient-level data provided by each of the state and territory health departments in Australia with use of a sequential, multilevel matching process. Data are also matched biannually with the Department of Health and Ageing National Death Index to obtain information on the date of death.

XLPE was defined in the Registry database as ultra-high molecular weight polyethylene that had been irradiated with high-dose (≥50-kGy) gamma or electron beam radiation, regardless of remelting or annealing. This definition was confirmed with industry sources and cross-checked with the Australian Prosthesis Advisory List, which records XLPE separately from CPE. The Registry first recorded the use of XLPE in 2000. The study population consisted of primary THAs undertaken for osteoarthritis and performed with either CPE or XLPE. All other bearing surfaces were excluded.

Outcomes were compared between THAs performed with CPE and those done with XLPE, and the effect of age, sex, femoral head size, the method of acetabular and femoral component fixation and reasons and types of revision were also analyzed.

In order to account for possible confounders in this observational data, we also performed a number of subanalyses. These included the type of femoral head material, femoral head size, and methods of acetabular and femoral component fixation. We also performed an analysis of specific prostheses in order to account for known prosthesis-related outcome variation. This analysis was performed on prostheses that had both CPE and XLPE options, had been used in a minimum of 800 procedures in both polyethylene groups, and had been followed for ≥8 years.

As polyethylene wear is more likely to have an effect in the longer term in younger patients, we performed a separate analysis on patients who underwent THA for osteoarthritis when they were <55 years of age.

Statistical Analysis

The Registry uses Kaplan-Meier estimates of survivorship to describe the time to the first revision of an arthroplasty, with censoring at the time of death or closure of the database at the time of analysis (December 31, 2016). The analytical approach involves high-level statistical methodologies to investigate associations to limit the impact of bias. A full description of the statistical methods that are used is provided in the Appendix.

Results

The Registry recorded the use of CPE for 41,171 procedures and XLPE for 199,131. These procedures accounted for 74% of all THAs performed for osteoarthritis. There were 23,813 women (57.8%) in the CPE group and 110,162 (55.3%) in the XLPE group. The mean age in the CPE group was 70.0 years (standard deviation [SD] = 9.9 years) for men and 72.5 years (SD = 9.7 years) for women. The patients who received XLPE were slightly younger, with a

mean age of 68.6 years (SD = 10.3 years) for men and 70.7 years (SD = 9.9 years) for women. The median follow-up was 9.2 years after the THAs with CPE compared with 4.2 years after those with XLPE. The use of XLPE increased over the study period: from 9.2% of all primary THAs with polyethylene in 2000 to 97.1% in 2016 (Fig. 1). The use of XLPE was also associated with the use of larger femoral heads, with a head size of ≥32 mm used in 12% of all THAs done with CPE compared with 75.9% of those done with XLPE.

The rate of revision at 6 months was lower for the patients treated with XLPE than for those who received CPE. This difference became more apparent with time, with the 16-year cumulative percent of revision being 11.7% (95% confidence interval [CI] = 11.1% to 12.3%) in the CPE group compared with 6.2% (95% CI = 5.7% to 6.7%) in the XLPE group. The hazard ratio [HR] at 9 years was 3.02 (p = 0.001) (Fig. 2). The main reason for the difference in the revision rate was a reduction in the rate of revisions due to loosening, lysis, and dislocation (Fig. 3). The most common reasons for revision of THA in both the CPE and the XLPE group are listed in Table I. A revision that could be directly attributable to polyethylene wear-related issues (wear of the acetabular insert or lysis) was recorded after 332 (0.81%) of the 41,171 THAs with CPE compared with only 102 (0.05%) of the 199,131 procedures with XLPE.

The CPE and XLPE were combined with 3 different femoral head bearing surfaces—ceramic, metal, and ceramicized metal—and XLPE was associated with a lower rate of revision compared with CPE in all 3 of these subgroups. XLPE was also associated with a lower revision rate in the subgroups defined according to the 3 common head sizes (<32, 32, and >32 mm; Table II) and 3 types of THA fixation (cemented, cementless, and hybrid [femur cemented]).

Six brands of acetabular prosthesis were available with both XLPE and CPE bearing options, were used in ≥800 procedures each, and were followed for ≥8 years. Five were associated with a reduced rate of revision at various time points when XLPE had been used, whereas the rate of revision of 1 prosthesis (Vitalock; Stryker) during the entire follow-up period did not differ significantly according to type of polyethylene used (Tables III and IV). Table V lists revision rates for the 10 most commonly used cementless prostheses with XLPE with a minimum 7-year follow-up (maximum, 15 years for 2 models).

According to the Registry, 17,689 primary THAs using either CPE or XLPE had been performed for osteoarthritis in younger patients (<55 years of age), and the 15-year cumulative percent of revisions in this group was 17.4% (95% CI = 15.5% to 19.5%) for those treated with CPE and 6.6% (95% CI = 5.5% to 7.8%) for those who received XLPE. At

7 years, there was a 5-fold increase in the rate of revisions of procedures done with CPE (HR = 5.32, $p < 0.001$) compared with procedures performed with XLPE. (Fig. 4).

Discussion

To our knowledge, this study of the outcomes of the use of XLPE in THA for patients with osteoarthritis represents the longest follow-up of the largest number of procedures reported. The use of XLPE makes THA—already one of the most effective operations—even better. The data confirm the early promise shown by XLPE in RCTs, that is, when compared with CPE, an XLPE bearing surface in THA results in a mid-term to longer-term reduction in all-cause revision. This is due to a reduced rate of revision due to loosening, lysis, and dislocation. The difference is seen both early (due to a reduced rate of revision for dislocation) and in the longer term (as a consequence of the reduction in wear-related problems).

A major strength of this study is the evaluation of the experience with XLPE in an entire national population and therefore has high external validity. Unlike the introduction of large-head metal-on-metal bearings, there was a phased introduction of XLPE, with initial laboratory testing followed by RCTs and then wider clinical use. This study completes the loop of introduction of new technology by reporting the use of XLPE recorded in a national registry with long-term follow-up. As a result, patients, surgeons, hospitals, and other health-care stakeholders can be confident that the use of XLPE will reduce the rate of revision surgery following THA.

Although our data demonstrated a significant reduction in revision overall with the use of XLPE, a study using pooled data from 6 registries, including the AOANJRR, did not demonstrate a reduced risk of revision (172). That study was limited to cementless fixation with a standard 32-mm head in patients 45 to 64 years of age who had a shorter follow-up than the patients in our study. The inclusion criteria used in the previous study (172) may explain the difference between its results and the data in our study, which included all patients in a national registry. The hazard ratio in the adjusted model in the previous study was in the same direction as ours, in favor of XLPE, but it did not reach significance. The rate of revision of THAs with XLPE in our study (4.4%) was higher than that in a recently published RCT by Devane et al. (280) (1.9%) during an equivalent time period (10 years). However, in the RCT, the THAs were performed by experienced hip surgeons who used strict inclusion criteria, whereas our data involved all surgeons in Australia rather than just experienced hip surgeons. We therefore believe that our study has strong external validity and represents a “real world” revision rate.

We were able to adjust for sex, age, method of fixation, and femoral head size, all of which have been demonstrated to affect rates of revision of THA. The Registry data showed that XLPE was associated with a lower rate of revision overall, but the observed difference could have been confounded by prosthesis type, with XLPE being used more often in well-performing prostheses. To account for known differences in prosthesis-specific revision rates, we performed a separate analysis of 6 prostheses that were available with both CPE and XLPE options for the same acetabular implant, and this analysis demonstrated lower rates of revision in association with XLPE in 5 of these models. As for the 6th model, the process for manufacturing the XLPE differs from that used by other companies, and this may account for the lack of observable difference between the XLPE and CPE. This has been previously noted with regard to the XLPE used by this manufacturer for total knee arthroplasty (281).

The Nordic Arthroplasty Register Association (NARA) reported on design-specific differences between XLPE and CPE in THA (170). With regard to cemented designs, XLPE versions of the ZCA (Zimmer) and Reflection (Smith & Nephew) all-polyethylene cups were found to have better survival than the CPE versions. This correlated with our analysis of the Reflection cup, but there were not enough XLPE ZCA cups for us to compare them with the CPE ZCA cups. With regard to all-cementless cup designs, the XLPE shells in the NARA study had better overall survival (with all-cause revisions as the end point) than the CPE shells. Only 1 cementless cup, Trilogy (Zimmer), fulfilled the inclusion criteria for both types of polyethylene in the NARA study, and the revision rates did not differ between the XLPE and CPE versions of that cup. We could not analyze the Trilogy cup because there were not enough of them in the CPE group. The NARA database confirmed design-specific differences in polyethylene and suggested that their results should be confirmed in larger studies with longer follow-up.

There was a reduction in the rate of revision for THA with XLPE after 6 months. This early benefit is not directly due to the better wear-related characteristics of XLPE, but it is an indirect consequence of them. The reason for this is that the use of larger femoral heads reduces the risk of revision due to dislocation, which is one of the most common reasons for early revision (282). While the use of a larger femoral head with a CPE cup is known to increase the risk of long-term wear, this risk is not evident with XLPE. Thus, the introduction of XLPE enabled surgeons to selectively use larger femoral heads, thereby reducing revision for dislocation while avoiding the long-term wear problems associated with CPE.

The most common reason for long-term failure of THA requiring revision is loosening and osteolysis, and periprosthetic osteolysis is largely due to an inflammatory process caused by polyethylene wear (283, 284). While it has been suggested that particle-induced

osteolysis is not a problem with XLPE (285), there remains some concern about wear-related issues in the longer term, especially with the use of larger femoral heads. However, there have been few reports of osteolysis with the use of XLPE (286-288). A systematic review demonstrated an 87% lower risk of osteolysis with XPLE than with CPE (160). In our study, only 80 THAs (0.01%) with XLPE were revised because of lysis and 22 (0.004%) were revised because of wear of the acetabular insert, suggesting that these are not common medium to longer-term clinical problems with XLPE. There was also no evidence of increased mechanical failure with XLPE liners, with only 9 revisions for breakage of the acetabular insert.

Wear-related and implant-longevity issues are particularly important in younger patients, who are generally more active and have a longer expected life span than their older counterparts. There are now some longer-term reports of the clinical results of THA with XLPE in younger patients (289-291), and these studies demonstrated no revisions for polyethylene wear or osteolysis. In light of these findings and our own analysis of 15,502 THAs with XLPE in younger patients, we believe that the evidence of reduced long-term wear with XLPE is now so strong that, when a polyethylene bearing surface is used in THA, it should be XLPE, particularly in younger patients.

There are some limitations with this analysis of Registry data. The utilization of XLPE and CPE has changed over time. There is the potential for surgeon indication bias, but we believe that this would favor XLPE in younger patients. When the analysis was adjusted for age, particularly <55 years, the effect of XLPE was more marked. We do not believe that trends in surgical techniques, perioperative care, or rehabilitation protocols were significant confounding variables in either group. We also do not believe that newer implant design changes over this time period would have favored either group (20).

While we adjusted for known risk factors that may have influenced the rate of wear-related revision of THA, there may be other such factors. We did not have information on body mass index (BMI) from the commencement of data collection, although the Registry now collects those data. However, there is no evidence that BMI would have a more or less detrimental effect on the outcome of THA with XLPE or CPE. We also did not have information on activity levels, which have been shown to influence polyethylene wear rates (292). Age is often regarded as a surrogate for activity, and we demonstrated the most reduction in revision rates in patients who were <55 years old. Evidence from this study shows that the XLPE is better than CPE in younger patients and those most likely to return to more active pursuits.

The use of XLPE has improved the outcomes of THA at 16 years with no observed untoward effects. The benefit is evident both early and late, with a reduced rate of

revisions due to dislocation (because XLPE allows the increased use of larger femoral heads) and to wear-related issues. The evidence from our study suggests that longevity of THA is likely to be improved beyond 16 years and may enable younger patients to undergo THA confident of a reduced need for revision in the long term.

Appendix

Details of the statistical analysis are available with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/XXXXXXX).

Note:
The authors thank the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) and the hospitals, orthopaedic surgeons, and patients whose data made this work possible. The Australian Government funds the AOANJRR through the Department of Health and Ageing.

Fig. 1

The percentages of primary THAs for osteoarthritis (primary diagnosis) done with the different types of polyethylene over the 16-year period.

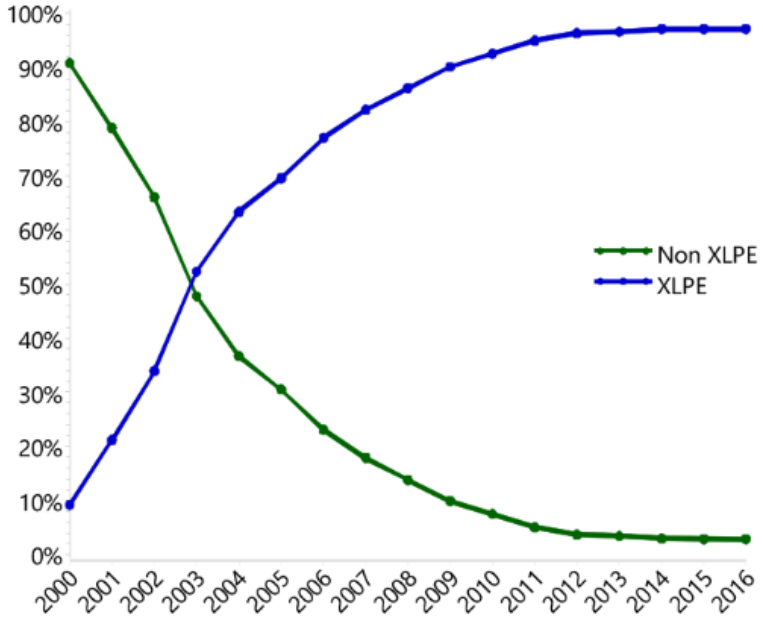
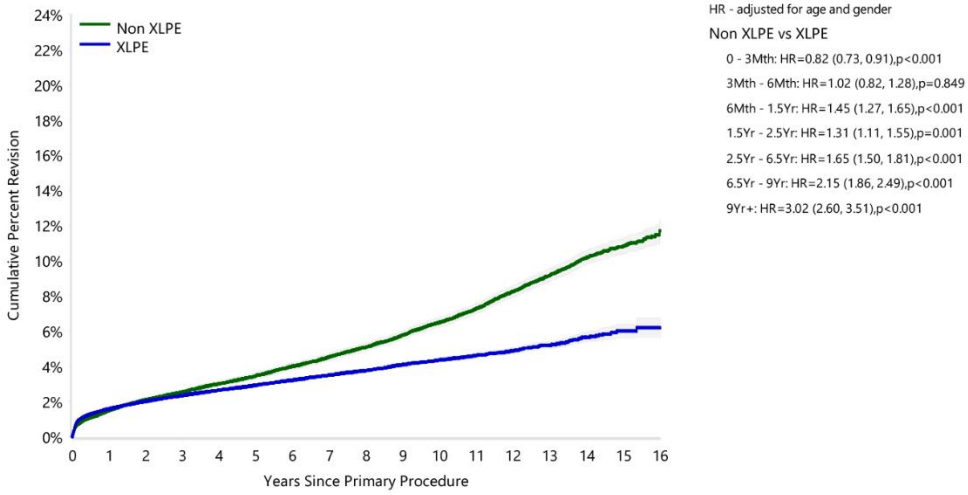


Fig. 2

Cumulative percentages of revisions of primary THAs for osteoarthritis (primary diagnosis) by polyethylene type, adjusted for age, sex, fixation, and femoral head size. The HR for non-XLPE versus XLPE was 0.84 (95% CI = 0.74, 0.94; p = 0.004) at 0 to 3 months, 1.14 (95% CI = 0.96, 1.35; p = 0.13) at 3 to 9 months, 1.47 (95% CI = 1.32, 1.65; p < 0.0001) at 9 months to 3 years, 1.65 (95% CI = 1.43, 1.90; p < 0.0001) at 3 to 5 years, 2.04 (95% CI = 1.82, 2.28; p < 0.0001) at 5 to 9 years, and 3.10 (95% CI = 2.66, 3.60; p < 0.0001) at >9 years.



Number at Risk	0 Yr	1 Yr	5 Yrs	7 Yrs	10 Yrs	15 Yrs	16 Yrs
Non XLPE	41171	39158	32170	27756	19988	3875	1208
XLPE	199131	170003	84803	53785	23727	858	103

Fig. 3

Cumulative percentages of revisions, for different reasons, of primary THAs for osteoarthritis (primary diagnosis) by polyethylene type.

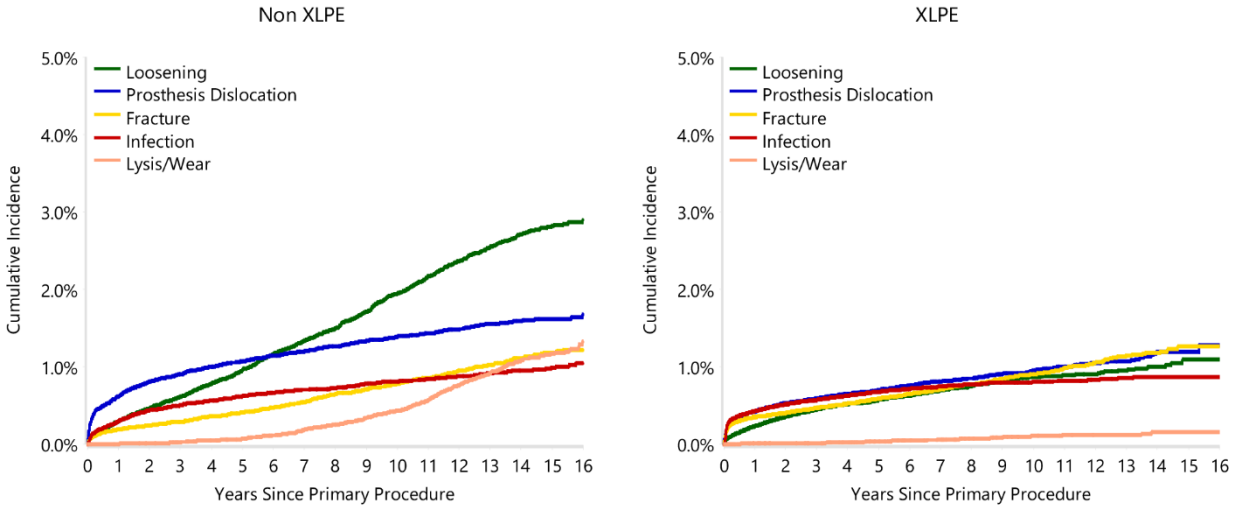
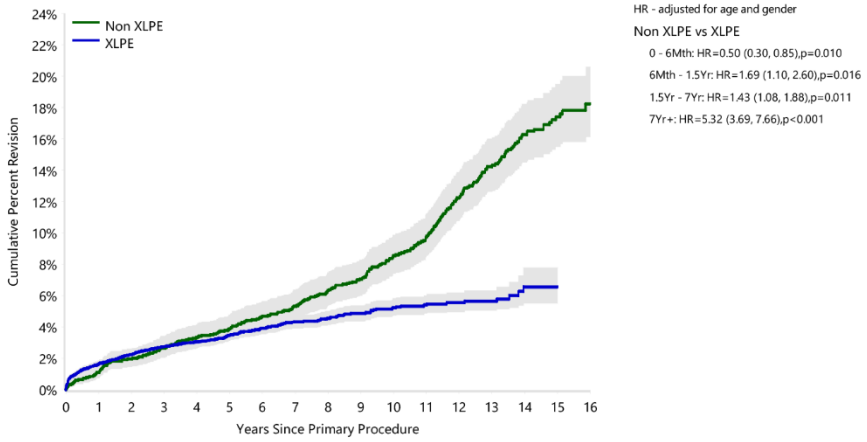


Fig. 4

Cumulative percentages of revisions of primary THAs for osteoarthritis (primary diagnosis) by polyethylene type in patients <55 years of age.



Number at Risk	0 Yr	1 Yr	5 Yrs	7 Yrs	10 Yrs	15 Yrs	16 Yrs
Non XLPE	2367	2265	1916	1790	1484	439	163
XLPE	15502	13069	6222	3915	1981	87	10

TABLE I Reasons for Revisions of Primary THAs for Osteoarthritis (Primary Diagnosis) by Polyethylene Type

	Revisions					
	CPE			XLPE		
Reason for Revision	No.	% of Primary THAs (N = 41,171)	% of All Revisions	No.	% of Primary THAs (N = 199,131)	% of All Revisions
Prosthesis dislocation	601	1.46	21.66	1,404	0.71	24.63
Infection	360	0.87	12.97	1,275	0.64	22.36
Fracture	387	0.94	13.95	1,248	0.63	21.89
Loosening	936	2.27	33.73	1,129	0.57	19.80
Lysis/wear	332	0.81	11.96	102	0.05	1.79
Limb length discrepancy	13	0.03	0.47	86	0.04	1.51
Pain	26	0.06	0.94	86	0.04	1.51
Other	120	0.29	4.32	371	0.19	6.51
Total	2,775	6.74	100.00	5,701	2.86	100.00

TABLE II Cumulative Percentages of Revisions of Primary THAs for Osteoarthritis (Primary Diagnosis) by Polyethylene Type and Femoral Head Size

	No.		Cumulative % (95% CI)				
Polyethylene Type/ Head Size	Revisions	Primary THAs	1 Yr	5 Yr	8 Yr	14 Yr	16 Yr
CPE							11.7 (11.1, 12.3)
<32 mm	2,538	36,230	1.4 (1.3, 1.6)	3.4 (3.2, 3.6)	5.0 (4.8, 5.3)	10.1 (9.7, 10.5)	11.6 (11.1, 12.3)
32 mm	213	4,642	1.6 (1.3, 2.0)	3.8 (3.2, 4.4)	5.5 (4.7, 6.3)	9.8 (7.6, 12.8)	
>32 mm	24	299	3.7 (2.1, 6.6)	8.6 (5.7, 12.8)	9.9 (6.6, 14.6)		
XLPE							6.2 (5.7, 6.7)
<32 mm	1,817	48,001	1.5 (1.4, 1.7)	3.0 (2.8, 3.2)	3.8 (3.7, 4.0)	5.7 (5.4, 6.1)	6.2 (5.7, 6.8)
32 mm	2,089	84,157	1.5 (1.4, 1.6)	2.7 (2.6, 2.8)	3.5 (3.3, 3.7)	4.6 (4.2, 5.1)	
>32 mm	1,795	66,973	1.7 (1.6, 1.8)	3.1 (3.0, 3.3)	4.0 (3.8, 4.2)	8.5 (6.0, 11.9)	
Total	8,476	240,302					

TABLE III Cumulative Percentages of Revisions of Primary THAs for Osteoarthritis (Primary Diagnosis) by Prosthesis and Polyethylene Type

	No.		Cumulative % (95% CI)					
Acetabular Component/ Polyethylene Type	Revisions	Primary THAs	5 Yr	8 Yr	12 Yr	13 Yr	14 Yr	15 Yr
Allofit								
CPE	61	848	3.3 (2.3, 4.7)	5.1 (3.8, 6.9)	8.0 (6.2, 10.4)	8.3 (6.4, 10.7)	9.6 (7.3, 12.5)	11.3 (8.2, 15.5)
XLPE	239	7,845	2.5 (2.2, 2.9)	3.7 (3.2, 4.2)	5.0 (4.2, 5.9)	5.7 (4.7, 7.0)	7.2 (5.1, 10.2)	
Duraloc								
CPE	339	2,994	4.1 (3.4, 4.8)	6.3 (5.5, 7.3)	12.0 (10.7, 13.4)	13.4 (12.0, 14.8)	14.5 (13.0, 16.1)	15.5 (13.9, 17.3)
XLPE	79	1,716	3.0 (2.2, 3.9)	4.3 (3.4, 5.5)	5.5 (4.3, 6.9)	6.5 (5.0, 8.5)	7.1 (5.3, 9.6)	
Mallory-Head								
CPE	246	4,084	2.7 (2.3, 3.3)	4.0 (3.4, 4.6)	6.2 (5.5, 7.2)	7.1 (6.2, 8.1)	8.2 (7.1, 9.4)	9.5 (8.2, 11.0)
XLPE	61	2,946	2.3 (1.8, 3.0)	2.4 (1.9, 3.2)				
Reflection (cup)								
CPE	142	1,079	3.3 (2.3, 4.6)	7.5 (6.0, 9.5)	15.4 (12.9, 18.3)	18.1 (15.3, 21.4)	21.8 (18.4, 25.7)	22.7 (19.1, 26.9)
XLPE	27	1,165	2.3 (1.5, 3.4)	2.4 (1.6, 3.6)	2.7 (1.8, 4.2)			
Reflection (shell)								
CPE	270	2,322	4.3 (3.5, 5.2)	6.8 (5.8, 8.0)	12.6 (11.1, 14.3)	14.3 (12.7, 16.1)	15.6 (13.9, 17.6)	16.7 (14.8, 18.8)
XLPE	331	1,919	2.0 (1.8, 2.3)	2.7 (2.4, 3.1)	3.6 (3.2, 4.1)	3.8 (3.3, 4.3)	4.5 (3.7, 5.5)	6.3 (4.0, 9.8)
Vitalock								
CPE	209	3,569	2.6 (2.1, 3.1)	3.6 (3.0, 4.2)	5.5 (4.8, 6.4)	6.0 (5.2, 6.9)	6.9 (6.0, 7.9)	7.5 (6.5, 8.6)
XLPE	41	1,050	2.4 (1.6, 3.5)	3.3 (2.3, 4.6)	4.7 (3.5, 6.5)	4.7 (3.5, 6.5)		
Total	2,045	31,537						

TABLE IV Hazard Ratios for Revisions of Primary THAs for Osteoarthritis (Primary Diagnosis) by Polyethylene Type (XLPE Vs. CPE) and Acetabular Component

Acetabular Component	HR (95% CI)	P Value
Allofit: entire period	0.68 (0.51, 0.68)	0.012
Duraloc		
0-5 yr	0.75 (0.54, 1.04)	0.089
5-9 yr	0.49 (0.31, 0.79)	0.003
9-9.5 yr	0.18 (0.02, 1.35)	0.096
>9.5 yr	0.28 (0.14, 0.58)	<0.001
Mallory-Head		
0-1 mo	1.22 (0.69, 2.17)	0.497
1-3 mo	0.61 (0.25, 1.49)	0.280
3 mo-1.5 yr	1.15 (0.64, 2.04)	0.640
>1.5 yr	0.42 (0.23, 0.77)	0.005
Reflection (cup)		
0-1 yr	1.92 (0.72, 5.26)	0.187
>1 yr	0.20 (0.11, 0.34)	<0.001
Reflection (shell)		
0-1 yr	0.71 (0.50, 1.02)	0.065
1-5 yr	0.31 (0.22, 0.43)	<0.001
5-10 yr	0.23 (0.17, 0.30)	<0.001
>10 yr	0.15 (0.09, 0.25)	<0.001
Vitalock: entire period	0.82 (0.58, 1.15)	0.249

TABLE V Cumulative Percentages of Revisions of the 10 Most Commonly Used Cementless THAs with XLPE

	No.		Cumulative % (95% CI)					
Model	Revisions	Total	7 Yr	9 Yr	10 Yr	13 Yr	14 Yr	15 Yr
Accolade I/Trident (shell)	280	5,773	4.7 (4.2, 5.4)	5.7 (5.0, 6.4)	6.3 (5.5, 7.2)	7.3 (6.2, 8.5)		
Alloclassic/Allofit	104	3,211	3.2 (2.6, 3.9)	4.1 (3.4, 5.1)	4.1 (3.4, 5.1)	5.3 (3.9, 7.2)		
Anthology/R3	75	3,888	2.3 (1.8, 3.0)					
Corail/Pinnacle	695	24,589	4.0 (3.7, 4.4)	5.1 (4.5, 5.7)	5.4 (4.7, 6.2)	5.6 (4.9, 6.5)		
Polarstem/R3	103	4,381	3.1 (2.5, 3.8)					
Quadra-H/Versafitcup CC	104	3,341	4.1 (3.2, 5.1)					
Secur-Fit/Trident (shell)	210	5,628	4.4 (3.8, 5.0)	4.7 (4.0, 5.5)	4.8 (4.1, 5.6)	6.0 (4.8, 7.5)	6.0 (4.8, 7.5)	6.0 (4.8, 7.5)
Synergy/R3	61	2,713	2.6 (2.0, 3.4)					
Synergy/Reflection (shell)	148	4,827	2.7 (2.2, 3.2)	3.0 (2.6, 3.6)	3.1 (2.7, 3.7)	3.9 (3.2, 4.7)	3.9 (3.2, 4.7)	
VerSys/Trilogy	168	3,474	4.5 (3.9, 5.3)	4.8 (4.1, 5.6)	5.0 (4.3, 5.8)	5.5 (4.7, 6.4)	5.7 (4.9, 6.7)	5.7 (4.9, 6.7)

CHAPTER EIGHT

International Overview of Joint Registries and Their Role in Outlier Prosthesis Identification

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Name of Principal Author (Candidate)	Richard N de Steiger
Contribution to the Paper	R N de Steiger designed the research question, wrote the manuscript and together with all the co-authors he was responsible for the interpretation of data and for editing and final approval of the paper.
Overall percentage (%)	80%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
Signature	Date 19/5/18

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate to include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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Contribution to the Paper	S E Graves helped with the research design and together with all the authors he was responsible for the interpretation, manuscript evaluation and final approval of the paper.
Signature	Date 18/5/18

8.1 - Preface

This chapter contains the fifth and last article submitted for publication in peer reviewed journals. The article was first submitted in January 2018 and resubmitted after response to reviews in April to *Bone and Joint Research Journal*. The first published paper in this thesis, 'How are prostheses that are not performing as well as others in their class identified, and what are the consequences of this?' resulted in widespread discussions within the international registry community. The paper in Chapter Eight follows on from the first research question and describes an overview of how international registries identify outliers and suggests solutions to improve post market surveillance of prostheses. At least four other large registries have now adopted the method outlined by the AOANJRR discussed in Chapter Four.

8.2 – Submitted Publication

Introduction

Total hip and knee replacement are effective operations for the management of end stage arthritis. There are increasing numbers of these operations being performed and the rate of increase is anticipated to continue into the future (13, 265, 267). There is also a substantial rise in the lifetime risk of a person receiving a total hip or knee replacement and this has been shown in several countries (18, 19, 293, 294). There are a large number of joint replacement prostheses on the market available for use and not all perform the same. Many have no published outcomes. Joint replacement registries provide an appropriate way to monitor the outcomes of these procedures and can provide comparative data on the rates of revision for specific prostheses. There are many factors that affect revision rates. Non device related issues may include patient factors, surgical technique, surgeon experience and volume of cases. Device related factors may contribute to the variation in rates of revision with individual prostheses.

Prosthesis outcomes have received closer attention following the high rate of revision and subsequent recall of the ASR Hip Resurfacing System and ASR^{XL} Acetabular System. Over 93,000 patients were implanted with these prostheses and the outcome of these was shown to be device related, independent of multiple other possible causes of a higher rate of revision (1). Concerns regarding the outcomes of the ASR Resurfacing System were first identified by the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) in 2007 (200) and the ASR^{XL} Acetabular System in 2008 (199). These prostheses were withdrawn from Australia in 2009 and worldwide in 2010, following confirmation by the National Registry of England and Wales (295). This resulted in tighter regulations regarding the introduction and monitoring of new implants (296), demonstrating the critical role of registries in post market total joint replacement surveillance.

While many joint replacement registries report comparative revision rates of prostheses it is much less common for registries to publicly highlight specific prostheses or prostheses combinations that are performing outside of the expected norm. The purpose of this review is to determine if joint replacement registries identify prostheses that have a higher than expected rate of revision, to describe the current outlier methodologies, discuss the consequences of this and recommend ways in which the international registry community may co-operate to enhance future surveillance opportunities.

Methods

A detailed search was performed of all Joint Replacement Registries listed on the official Websites of the International Society of Arthroplasty Registries (ISAR) (297) and Arthroplasty Watch (298). In addition, all links from those registries were also evaluated to include smaller regional registries. Available online reports were reviewed to determine if individual registries specifically identified prostheses with a higher than expected rate of revision and, if so, the method by which this was performed. Those Registries that did not have an accessible on line document were contacted to obtain a hard copy version or, if not available, personal communication was made to the relevant registry contact to determine if they identified prostheses but the information was not publically available. The registries that were accessed are listed in *Appendix 1.*

Results

A total of 47 Registries with websites were identified of which 9 did not have publically accessible documents but were contacted by the author. Of those that did there were four, the AOANJRR, the New Zealand National Joint Registry, the Swedish Knee Arthroplasty Registry, and the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man that identified prostheses in their report and the methods by which this was performed. There were two Registries that identified prostheses internally without the information being publically available. These were the Kaiser Permanente National Total Joint Replacement Registry, and the Dutch Arthroplasty Register. The Scottish Arthroplasty Project monitors surgeon outliers and, by association, implants. None of the other Registries had a formal method for prosthesis identification.

The Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) has previously reported on a method for identifying prostheses with a higher than expected rate of revision (221). This involves a three stage process commencing with an automated screening test to identify prostheses that have twice the rate of revision per 100 observed component years of all other prostheses in the same class. The second stage involves a more detailed analysis of the identified prostheses by the AOANJRR Registry staff. Age and gender-adjusted hazard ratios are calculated using Cox regression models. If the hazard ratio of a prosthesis, compared to all others in the same class combined, is statistically significant, then the prosthesis progresses to stage 3. In this stage a panel of independent orthopaedic specialists from the Australian Orthopaedic Association Arthroplasty Society analyse all the data and determine which prostheses will be identified in the Annual Report (16). Prostheses or prosthetic combinations are then listed as 'Identified and not used', 'Identified and still used' and 'Newly Identified'. Since the introduction of the identification process in 2004 the Registry has identified 156 prostheses or combinations

using this approach and this represents 4.3% of the number of prostheses or combinations recorded by the Registry.

The New Zealand Joint Registry lists prostheses combinations that have a minimum of 50 registered primary arthroplasties and they are sorted in order of descending revisions per 100 observed component years. In the 2016 Report (299) there were 24 hip prostheses combinations that have a significantly higher rate of revision than the overall rate of 0.73 per 100 observed component years. These are marked with an asterisk in the report. A similar table is presented for individual knee prostheses sorted by descending revisions per 100 observed component years and there were five prostheses listed as having a significantly higher rate of revision than the overall rate of 0.49 per 100 observed component years.

The Swedish Knee Arthroplasty Registry (SKAR) reports on factors that influence the revision rate of knee replacements. When the implant model is the factor, the Cox regression analysis adjusts for differences in gender, age, and diagnosis, and uses the latest 10 year period for the analysis. The SKAR for many years used the AGC as the reference model with a risk of one to which other implants were compared. In the 2014 Report the reference model was changed to the PFC Sigma-MBT. In the 2016 report (76) there were four implants which were recorded as having a significantly higher rate of revision for TKA when performed for osteoarthritis and three knees which had a lower risk ratio. There was one unicompartmental knee with a higher risk of revision when compared to the reference implant.

The National Joint Registry of England, Wales, Northern Ireland and Isle of Man (300) has an Implant Performances Sub-Committee whose brief is to analyse and assess confidential data on potential outliers. This analysis is performed on a Patients Time Incidence Rate (PTIR), which is the revision ratio per 100 observed component years, first introduced by the AOANJRR. Notification for an unacceptably high rate of revision is a PTIR of twice the group PTIR, allowing for confidence intervals (Level 1 notification). When this occurs a report is filed with the Medicines and Healthcare Products Regulatory Agency (MHRA). When the PTIR is 1.5 times the group PTIR a warning letter is sent to the manufacturing company (Level 2 notification). There have been 34 prostheses or combinations identified by the National Registry since 2009.

The two other registries that internally identify prostheses with a higher than expected rate of revision are the Kaiser Permanente National Total Joint Replacement Registry (301), and the Dutch Arthroplasty Registry (LROI) (302). One other registry, the Scottish Arthroplasty Project (SAP) does not formally collect implant data but monitors operations and

subsequent complications. As outlier status is frequently associated with poor implants SAP states that their methods are applicable for indirect implant surveillance (303) (Table 1). While many registries report the survivorship or rates of revision of individual prostheses and combinations there is no formal policy of identification of specific prostheses.

Discussion

The main objective of the study was to determine if Joint Replacement Registries identified prostheses with higher than expected rate of revision and how this was performed. Four Registries had publicly available information on the devices and the threshold for reporting. Two registries identified devices internally, one by association with surgical outliers and none of the other registries had a formal method for prosthesis identification.

Surgeons rely on many sources of information when deciding which prosthesis to use and these include, but are not limited to, experience in training, colleague interaction, peer reviewed literature, scientific meetings, company sponsored events, and joint replacement registries. A considerable proportion of prostheses available have no readily available evidence of clinical effectiveness to support their use (304). Joint replacement registries, with their continuous surveillance, provide the best data for the use and outcomes of a device in the general population (3, 305, 306). Careful interpretation of this can help guide prosthesis selection in the absence of published evidence (34, 307, 308) and identification of specific outlier prostheses, as opposed to listing comparative rates of revision, highlights prostheses that are not performing as well as others within their class.

A post market surveillance system for medical devices should provide the following functions: readily identify underperforming devices, characterize and disseminate information about real-world performance, and provide data that can be used to support pre-market clearance or approval of new devices (309).

The need for registries to identify outliers along with well performing implants is therefore important but there are problems with current approaches. As revision is a relatively rare occurrence, some prostheses may be used in low volumes and there may be insufficient power to detect differences. There is also a lack of standardization of implants and their attributes which may hamper international comparisons. Registries may have different prostheses in their databases, limiting the ability to link data. The comparator and the threshold for identification also differ. Three registries use twice the rate of revision of all other devices in the same class for initial listing, one uses a single prosthesis as the comparator and one lists in order of revisions per 100 observed component years. Finally,

both the timing and the best methods to disseminate findings to the relevant stakeholders, need to be addressed.

There are several potential solutions to the above issues to further improve identification of outlier prostheses and post market surveillance of implants. Registries can consider pooling data to increase the numbers available for statistical analysis. The Nordic Arthroplasty Register Association (NARA) was established in 2007 by Sweden, Norway and Denmark to improve collaboration and was joined by Finland in 2010. This enabled a greater number of prostheses with a longer term follow-up (1995-2011) to be analysed (310). While there are examples of Registries pooling data to examine outcomes of specific prostheses (311) this has proven more difficult with regard to outlier identification. The International Consortium of Orthopaedic Registries (ICOR) commenced in 2011 and focused on two major goals: research and surveillance for hip and knee implants and worldwide implant harmonization. The consortium involved over 30 orthopaedic registries and has performed multinational investigations of total hip replacement bearing surfaces, prosthesis fixation and total knee replacement outcomes with respect to mobile and fixed bearings and stabilization. This initiative has demonstrated that registries worldwide can cooperate to monitor and improve outcomes of joint replacements (312)

The International Society of Arthroplasty Registers (ISAR) can play a significant role in coordinating data to aid in the early identification of outliers. If international registries are to compare results, then it is essential that similar data are collected (177) and there is harmonization of the device catalogues between registries. One of the current objectives of ISAR is the development of an International Prosthesis Library which can be distributed amongst all member registries, thereby allowing comparison of similar devices. There are currently 15 registries sharing this catalogue with plans to expand across all member registries. This initiative may lead to an improvement in early signal detection by close operation and the sharing of data on prostheses that have been potentially flagged by individual registries but need larger numbers for accurate analysis.

The most common comparator used is all prostheses in the same class. The threshold for identification is not uniform and needs to be standardized. Three registries use twice the expected rate of revision compared to all prostheses with the UK National Registry having an initial lower threshold of 1.5x. This may however mask prostheses that are at the higher end of the revision scale and a comparison to a group of the best performing implants may be more appropriate. Using a single implant as comparator may also present some difficulties. Comparing to the most commonly used prosthesis is one method but this may not necessarily be the best performing implant in a registry. Also the use of implants changes with time, as can the performance, and another device will need to be chosen as the

comparator. The most appropriate methods for outlier identification are currently being investigated by a working group from ISAR.

The timing of release of information on outlier prostheses is also an important factor to consider. The release of information in an Annual Report may come many months after a decision has been made on prostheses with higher than expected rates of revision. Websites that provide real time data for surgeons, industry and regulators on the performance of prostheses allow closer monitoring of joint replacement rates of revision and may alert users to seek further, more detailed reports. The timing of release of outlier prosthesis identification requires a consistent approach to be certain of the accuracy of the data, while at the same time being aware that a delay in notification may put patients at risk. Arthroplasty Watch is a website devoted to timely release of information regarding issues with all types of joint replacement. It was developed as an information project and opened in February 2013 with the purpose of collecting data on arthroplasty safety issues from a wide range of information sources on the internet and disseminating this in one single, publicly accessible site (298). The sources include arthroplasty registries, reports from regulatory authorities, manufacturers and scientific publications but there is no formal method for outlier identification.

There is no question that outlier identification plays an important role in improving the outcomes of joint replacement. This has been demonstrated by the marked reduction or cessation of use for most prostheses identified by the AOANJRR. The consequence of this identification has been the reduced exposure of patients to devices with higher than expected revision rates. Only a small percentage of devices are identified and this does not impact on surgeon choice, as there is ample evidence of many prostheses with long term low rates of revision that surgeons can use for their patients.

Another solution to avoid using devices with higher than expected revision rates would be to only use prostheses with good long term outcomes. The Orthopaedic Data Evaluation Panel (ODEP) was set up as part of the United Kingdom National Health Service to monitor data for primary hip replacement. Prostheses are classified according to level of evidence spanning a time period, with the highest rating being a 10A* for prostheses that have a 95% survivorship at 10 years (313). To qualify for this rating a hip prosthesis requires a revision rate of 5% or less at 10 years in a cohort study of a minimum 500 prostheses and Registry data supporting its use. As longer follow up has occurred the time period has extended and there now devices with a 13A rating. The AOANJRR also lists THA and TKA with 15 year rates of revision which can provide a guide to well performing implants. However if this approach is followed it may not allow for innovation. New prostheses can still be introduced if they participate in a post-marketing surveillance program such as Beyond Compliance (314).

There are some limitations to this review on registry identification of outlier prostheses. Despite a thorough search, there may be small regional registries that have local publications not readily available for review. A comprehensive attempt was made to read reports or contact all registries identified. Also, registries that were reviewed may not publically identify prostheses but may do so internally and communicate results to hospitals and surgeons thereby influencing outcomes at a local or regional level. There may also be medicolegal issues in countries that may impact on the ability to identify prostheses.

The Australian experience is that early signal detection of prostheses with a higher than expected rate of revision can lead to withdrawal of these devices from the marketplace. Consistent reporting of outlier prostheses from registries across countries would make it less likely that an under-performing prosthesis was due to patient or surgeon factors. Further research is needed to determine the optimum methods for identification including the threshold, the comparator, and the numbers required for notification of devices. Collaboration and co-operation of registries at a global level will enhance this process, thus reducing adverse outcomes for patients.

Table 1 Registries with Internal Identification of Prostheses

Registry	Identification Threshold	Comparator
Kaiser Permanente Registry	Initial threshold is twice revision rate per 100 observed component years of prostheses and follow up review by statisticians and surgeon leaders	All prostheses in same class
Dutch Registry LROI	Initial threshold is twice revision rate per 100 observed component years of prostheses with review by statisticians and surgeon leaders	All prostheses in same class
Scottish Arthroplasty Project	CUSUM Analysis of complications with prediction limit. Approximately 10% of surgeons will become outliers for at least one complication per year. Outliers associated with implants.	All surgeons performing arthroplasty

Appendix 1 List of Joint Replacement Registries

- American Joint Replacement Registry *
  http://www.ajrr.net/
  Access date: 25th Nov 2017
- Australian Orthopaedic Association National Joint Replacement Registry **
  https://aoanjrr.sahmri.com/
- Austrian Arthroplasty Register +
  Access Date: 20th May 2017
- Belgian National Arthroplasty Register*
  http://beneluxa.org/
  Access date: 20th November 2017
- Californian Joint Replacement Registry *
  http://staging.caljrr.org/
  Access date: 25th April 2017
- Canadian Joint Replacement Registry **
  https://www.cihi.ca/en/joint-replacements
  Access date: 25th April 2017
- Catalan Arthroplasty Register*
  http://aquas.gencat.cat/ca/projectes/mes_projectes/qualitat_atencio_sanitaria/racat/
  Access date: 6th May 2017
- Croatian Arthroplasty Register+
  24th May 2016
- Czech Rep. Arthroplasty Register *
  http://www.uzis.cz/
  Access date: 6th May 2017
- Danish Hip Arthroplasty Register **
  http://danskhoftealloplastikregister.dk/en/dhr/dhr-the-danish-hip-arthroplasty-register/
  Access date: 17th April 2017
- Danish Knee Arthroplasty Register *
  https://www.sundhed.dk/content/cms/99/4699_dkr-rapport-2016.pdf
  Access date: 17th April 2017
- Dutch Arthroplasty Register (LROI) **
  https://www.lroi.nl/
  Access date: 25th April 2017
- Egyptian Community Arthroplasty Register +
  24th May 2016

- European Arthroplasty Register *
  https://www.efort.org/european-arthroplasty-register-network-ear-n/
  Access date: 25th April 2017
- Finnish National Arthroplasty Register *
  https://www2.thl.fi/endo/report/#index
  Access date: 17th April 2017
- FORCE – TJR Registry **
  https://forceortho.org/
  Access date: 6th May 2017
- French Arthroplasty Register *
  http://www.sofcot.fr/Pages/Registre-des-protheses-de-hanche
  Access date: 25th April 2017
- Geneva Arthroplasty Registry +
  2nd June 2016
- German Arthroplasty Register *
  https://www.eprd.de/de/
  Access date: 25th April 2017
- Harris Joint Registry +
  20th May 2017
- Health East Joint Replacement Registry **
  http://www.healtheast.org/orthopedics/registry.html
  Access date: 6th May 2017
- Hospital for Special Surgery Hip and Knee Joint Replacement Registry +
  20th May 2017
- Hungarian Arthroplasty Register *
  http://www.ortopedtarsasag.hu/info.aspx?web_id=&sp=5
  Access date: 6th May 2017
- Indian Society of Hip and Knee Surgeons *
  http://www.ishks.com/
  Access date: 6th May 2017
- Iranian Joint Registry*
  Arch Bone Jt Surg. 2016 Apr; 4(2): 192–196
  Access date 6th May 2017
- Irish National Orthopaedic Register **
  https://www.noca.ie/irish-national-orthopaedic-register
  Access date: 6th May 2017
- Italian Arthroplasty Register Project (RIAP) *
  http://www.iss.it/binary/riap2/cont/20140407Brochure in inglese.pdf
  Access date: 6th May 2017

- Japanese Arthroplasty Register (JAR) *
  http://jsra.info/
  Access date: 6th May 2017
- Kaiser Permanente National Implant Registries *
  https://national-implantregistries.kaiserpermanente.org/
  Access date: 17th April 2017
- Lithuanian Arthroplasty Register *+
  www.lser.lt
  20th May 2017
- Malawi National Joint Registry +
  20th May 2017
- Mayo Clinic Total Joint Registry+
  20th May 2017
- Michigan Arthroplasty Registry Collaborative Quality Initiative (MARCQI) *
  http://marcqi.org/
  Access date: 6th May 2017
- National Joint Registry (NJR) for England and Wales **
  www.njrcentre.org.uk
  Access date: 17th April 2017
- New Zealand National Joint Registry **
  https://nzoa.org.nz/nz-joint-registry
  Access date: 17th April 2017
- Norwegian Arthroplasty Register **
  http://nrlweb.ihelse.net/eng/default.htm
  Access date: 17th April 2017
- Pakistan National Joint Registry **
  http://www.arthroplasty.org.pk/
  Access date: 6th May 2017
- Portuguese Arthroplasty Register **
  http://www.rpa.spot.pt/
  Access date: 6th May 2017
- RIPO – Register for Orthopaedic Prosthetic Implantation (Emilia-Romagna, Italy) **
  https://ripo.cineca.it/
  Access date: 6th May 2017
- Romanian Arthroplasty Register **
  http://www.rne.ro/rne/?lang=en
  Access date: 6th May 2017
- Scottish Arthroplasty Project **
  http://www.arthro.scot.nhs.uk/
  Access date: 25th April 2017

- Slovakian National Arthroplasty Register **
  http://sar.mfn.sk/.320.html
  Access date: 6th May 2017
- Slovenian Valdoltra Arthroplasty Register *
  http://www.ob-valdoltra.si/international
  Access date: 6th May 2017
- South African National Joint Registry +
  13th April 2016
- Swedish Hip Arthroplasty Register **
  https://shpr.registercentrum.se/en/default.aspx
  Access date: 17th April 2017
- Swedish Knee Arthroplasty Register **
  http://www.myknee.se/en/
  Access date: 17th April 2017
- Swiss Arthroplasty Register *
  http://www.siris-implant.ch/de/?id=51&L=1
  Access date: 25th April 2017

*Website ** Website and/or Report + Personal Communication if no web access or not in English

CHAPTER NINE

The Role of the AOANJRR in the Change of Practice, Policies and Outcomes of Hip and Knee Replacement in Australia

9.1 - Preface

In the previous chapters I have discussed the first three research questions examining specific themes within the overall aim and how they have led to lower rates of revision for both THR and TKR. In Chapter Nine, I address the contribution of the Registry to the change of practice and policies of joint replacement in Australia by exploring the interaction with the multiple stake holders involved. The Chapter is divided into 3 sections:

In the first section I will investigate whether there has been an improvement in the results of hip and knee replacement in Australia since the commencement of the Registry.

The second part entitled Stakeholder engagement in registry activity will discuss how the Registry has influenced key stakeholders, some of the methods by which this has been achieved and critically assess the role that the Registry has played in improving the practice of joint replacement in Australia. I will explore the interaction with surgeons, hospitals, government and regulatory bodies, industry, medical insurers and patients. Several case examples are presented to illustrate key points.

In the last section I give a brief overview of some of the Registry's' other international contributions to complement some of those already discussed in the thesis.

9.2 - Overview

So far in this thesis I have provided a description of the nature and activities of the AOANJRR, and discussed the introduction, monitoring and changes in outcomes of new materials and technologies in joint replacement. I now turn to the role of the Registry in effecting change and critically examine the evidence for this. As I will discuss, in the non-experimental setting of Registry data, evidence must be accrued from several perspectives and due caution exercised in attributing effect to cause.

As with most observational studies it is difficult to approach analyses of these large data sets from a causal perspective. A randomised trial linking cause to effect is supported by the randomisation of the treatment groups and strict adherence to the trial protocol. In general, the analytical approach that has been used for this study investigates associations, with methodologies to limit the impact of bias. Although it may be possible on occasion to make a causal inference, it is rare, if ever, to be definite about this. It has been estimated that to compare the outcomes of two prostheses with a randomised, controlled trial (RCT) it would take 4,000 patients followed for ten years in order to detect a 30% difference in the revision rate (49). It would be difficult and expensive to arrange an RCT with the numbers required to demonstrate differences in prostheses outcomes, taking into account loss to

follow up and death. Also it would not be uncommon for new prostheses to come onto the market before prior RCT's have been reported. Registries can offer some advantages over clinical trials, especially in the case of joint replacement surgery, where one of the main outcomes of interest, revision surgery, has a low occurrence. Well conducted observational studies can enable understanding of the practices, new developments and longer term effects of different exposures with the ability to evaluate large numbers of patients and evaluate multiple interventions in various patient populations (47).

A registry can achieve improvement by identifying and reporting variation in practice (best and worst). Increased adoption of best practice, whether related to prosthesis use, surgical technique, or use of technology, is not necessarily dependent on understanding the reasons why one practice is better than another. The AOANJRR has presented, in a variety of formats, data earlier than other available sources of information, data not readily available from any source other than the Registry, and these data are generalizable to the Australian population with strong external validity.(34)

There are many ways by which a change in joint replacement outcomes may be achieved and this can involve multiple stakeholders. These groups include surgeons, hospitals, government and regulatory bodies, industry, insurers, and patients. Surgeons use multiple

sources of information to make decisions about joint replacement surgery for their patients. These include personal experience, attendance at scientific and industry meetings, published literature, peer discussion and, increasingly, the use of registry data.

The primary outcome measure of the Registry is the time to first revision of a primary joint replacement. It is also a metric that can be verified, easily understood by all stakeholders, and allows comparison of different factors associated with joint replacement. There are some problems with using revision surgery as an endpoint as revisions can occur long after the index procedure and the lack of a revision operation does not always indicate a successful procedure. There may be medical or social reasons that may preclude further surgery. Patients may be too unwell to undergo further operations, they may not present to their doctor for care, or they may be offered surgery but choose not to proceed. It is therefore likely that the true failure rate for joint replacement is higher than that measured by the Registry. Revision surgery does provide an unambiguous measure of the need for further intervention and confirmation that the primary procedure, for whatever reason, has not been successful. Another metric to determine the outcome of joint replacement surgery is Patient Reported Outcome Measures (PROMS) (315, 316). The New Zealand Joint Registry has demonstrated a strong correlation between patients with poorer Oxford Hip and Knee Scores (a patient specific outcome measure with worldwide use) and revision surgery (102, 299). As the AOANJRR currently does not collect data on PROMS the time to

first revision of a primary procedure is the metric that the AOANJRR uses to compare various factors associated with joint replacement and also for international comparative studies with other registries.

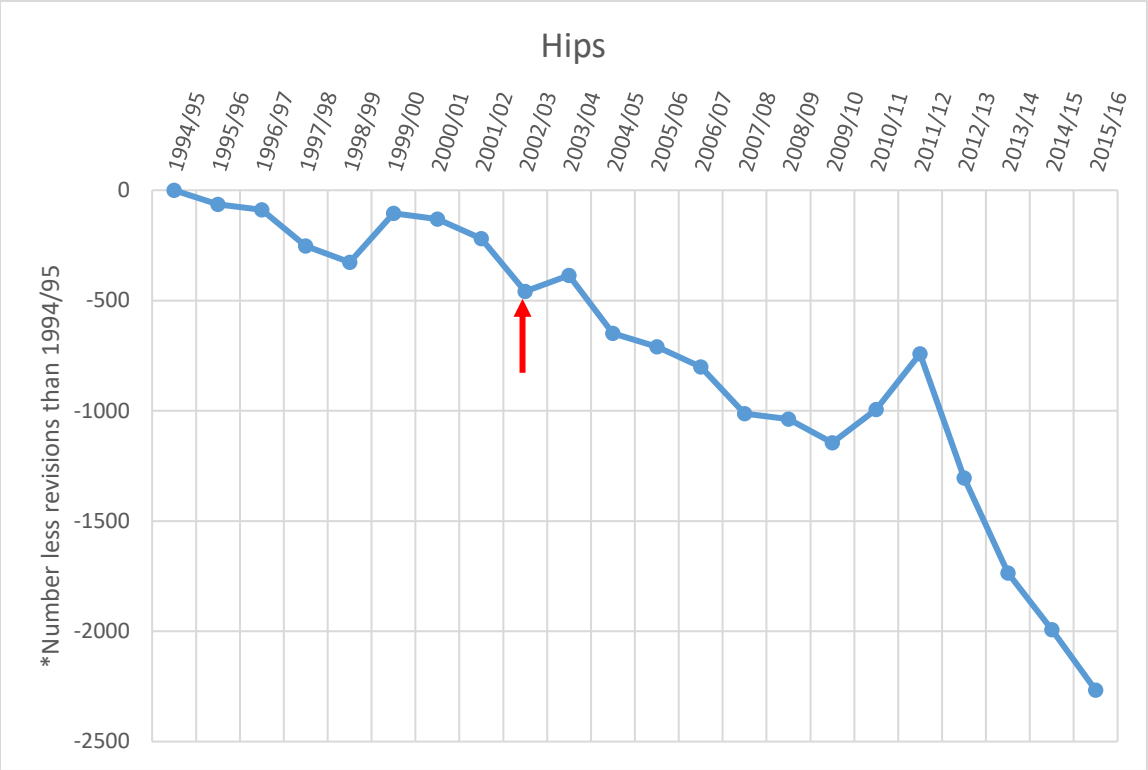
9.3 - Has the revision rate changed since the inception of the AOANJRR?

A reduction in revision rate over time can be viewed as a metric that demonstrates an improvement in the practice of joint replacement surgery in Australia. This can be measured by a reduction in the overall burden of revision surgery or a decrease in the rate of revisions of primary procedures over consecutive time periods since the Registry's inception.

The revision burden is defined as the proportion of all hip and knee replacement procedures that are revisions. This can be calculated from State Health admission and discharge data and the Registry has access to these from 1994. In Australia, the revision burden for total hip replacement has declined from 13.1% in 2002/2003 (the first year of full Registry national data) to 9.8% in 2015/2016. For knee replacements the revision burden has

declined from 9.3% in 2002/2003 to 7.4% in 2015/2016. This equates to a 25% reduction in the burden of revision for hip replacement and a 20% reduction for knee replacement over the respective periods and means there were 7,000 fewer hip revisions and 8,400 fewer knee revisions performed in 2015/2016 if the proportion of revisions had remained at their respective rates before the commencement of full national data collection. There was a small increase in hip revision in 2011 as a result of the increased rate of revision of patients who had large head metal on metal hip prostheses. These prostheses are no longer available, with the Registry having played a major role in their removal, as discussed later. Figures 1a and 1b demonstrate the revision burden for hip and knee replacement from 1994/1995 until the latest available data for 2015/2016. They show a reduction in revisions since the commencement of the Registry national data collection and reporting. There may be other reasons that have contributed to the reduction in revision burden though these are unlikely to be present in the Australian context. Access to hospital care improved with the Australian Government Private Health Insurance Rebate (317), introduced in 2000, but this would affect both primary and revision procedures equally. Improvements in anaesthesia, multi-modal pain therapy, and peri-operative care, over this time period make it less likely that patients would be denied access to revision surgery.

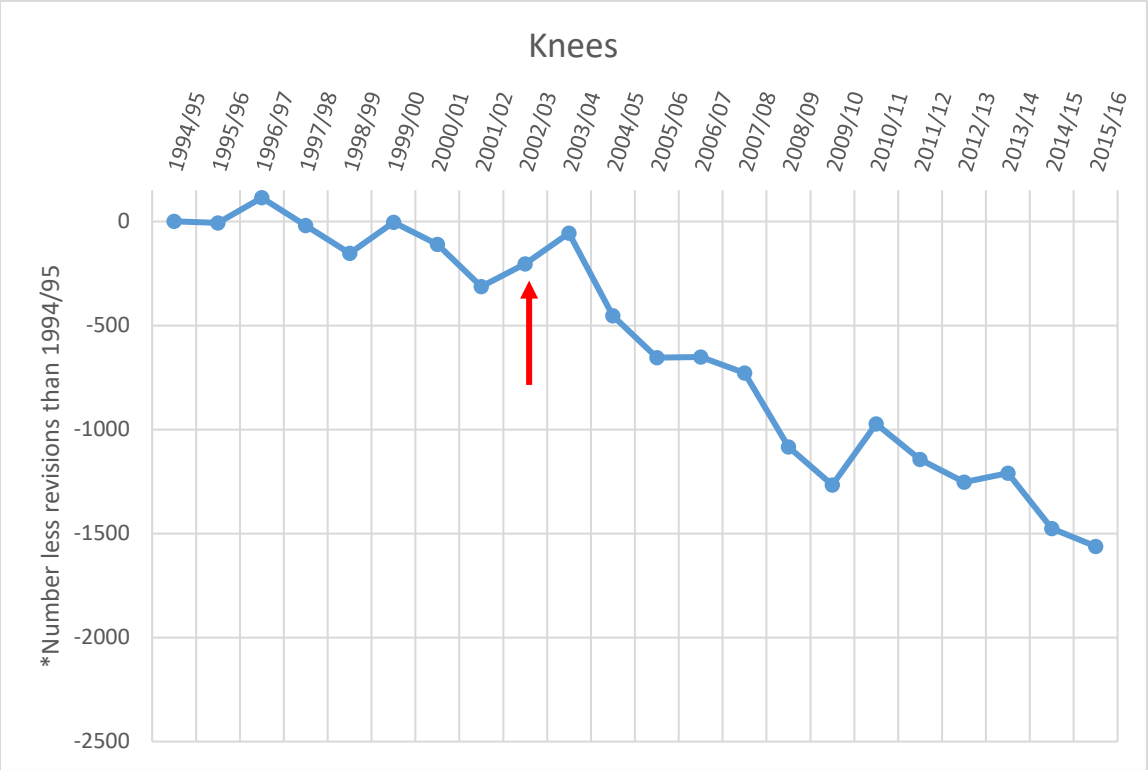
Fig 1a Revision Burden for Hip Replacement



*Y axis is the number of fewer revisions than 1994/1995 if the proportion of hip revisions had remained the same as 1994/1995 (14.7%).

↑ Commencement of full national data collection of AOANJRR.

Fig 1b Revision Burden for Knee Replacement



* Y axis is the number of fewer revisions than 1994/1995 if the proportion of knee revisions had remained the same as 1994/1995 (10.0%)

↑ Commencement of full national data collection of AOANJRR.

Source: Figures prepared from Government admission and discharge data held by AOANJRR and based on material prepared by AOANJRR for Economic Evaluation of Clinical Quality Registries, Australian Commission of Safety and Quality in Health Care November 2016

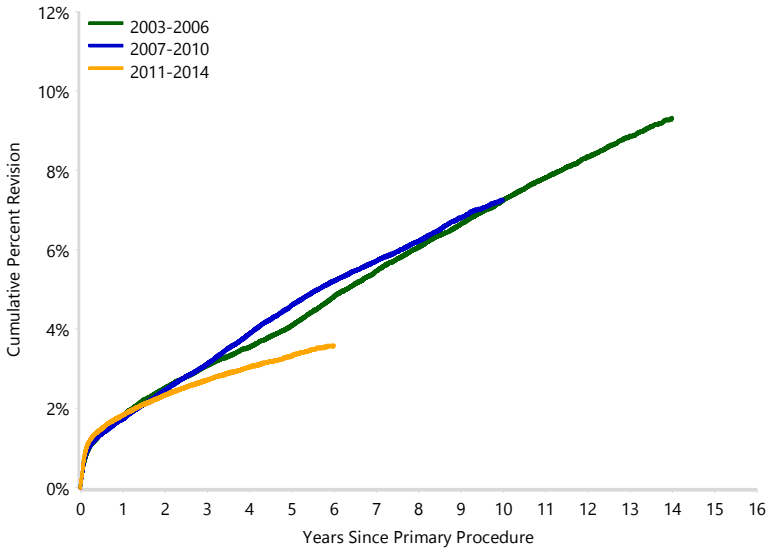
In contrast to Australian figures, the revision burden has increased for TKR in the U.S.A.(318, 319). Bozic et al utilised data from the Nationwide Inpatient Sample (NIS) to evaluate approximately 8,000,000 discharge records from 1051 hospitals in 45 states. The database gives a representative sample of all US hospitals and the 45 states covered 96% of the population. From 2006 to 2010 the authors demonstrated an increased revision burden for knee replacement (9.1% to 9.6%) and a small fall in the burden of revision hip

replacement (15.4% to 14.6%) over this time period. The revisions for TKR were due to mechanical loosening, implant failure and joint infection. Nineteen percent of both TKR and THR revisions were performed in patients <55 years of age and the authors stated that an increasing proportion of primary TKR performed in younger patients (12, 318) may contribute to the revision burden. While it is difficult to directly compare the reasons for revision listed in registry data with administrative datasets based on the use of ICD-9-CM diagnosis codes, there is a larger proportion of TKR and THR revised for mechanical and implant issues in the NIS dataset than the AOANJRR. The AOANJRR has also consistently reported on the association between a younger age and higher revision rates for TKR, and the proportion of primary TKR performed in Australia in patients <55 years of age remains small (6.9%) and there has been little change in that proportion since 2003. It is important to note that there was no nationwide joint registry in the U.S.A. over the time period reported in this study.

Another method of demonstrating improvement in outcomes of THR and TKR is by examining revision rates over consecutive time periods, a method that has been used by the Swedish registries. Three consecutive time periods of four years were chosen from the commencement of full national data collection: 2003-2006, 2007-2010, and 2011-2014. This allowed for calculation of revision rates up to six years for the latter group. In Australia the cumulative percent revision at six years for primary THR has declined from 4.8% for the

time period 2003-2006 to 3.6% for THR performed between 2011 -2014. A similar reduction is also seen for TKR over the same period with a decrease in the rate of revision from 5.1% for procedures performed from 2003 -2006 compared to 3.8% for procedures performed from 2011-2014.(Fig 2a and 2b)

Figure 2a Cumulative Percent Revision of All Hip Replacements by Procedure Year



HR - adjusted for age and gender

2003-2006 vs 2011-2014

- 0 - 3Mth: HR=0.86 (0.80, 0.93),p<0.001
- 3Mth - 6Mth: HR=1.15 (0.99, 1.34),p=0.061
- 6Mth - 1.5Yr: HR=1.39 (1.26, 1.52),p<0.001
- 1.5Yr - 3Yr: HR=1.42 (1.28, 1.57),p<0.001
- 3Yr - 5.5Yr: HR=1.77 (1.61, 1.95),p<0.001
- 5.5Yr - 6.5Yr: HR=2.99 (2.59, 3.45),p<0.001
- 6.5Yr+: HR=4.38 (1.10, 17.51),p=0.036

2007-2010 vs 2011-2014

- 0 - 3Mth: HR=0.88 (0.82, 0.94),p<0.001
- 3Mth - 1Yr: HR=1.10 (0.99, 1.21),p=0.067
- 1Yr - 1.5Yr: HR=1.32 (1.16, 1.50),p<0.001
- 1.5Yr - 3Yr: HR=1.67 (1.52, 1.83),p<0.001
- 3Yr - 6.5Yr: HR=2.36 (2.16, 2.58),p<0.001
- 6.5Yr+: HR=3.69 (0.92, 14.73),p=0.064

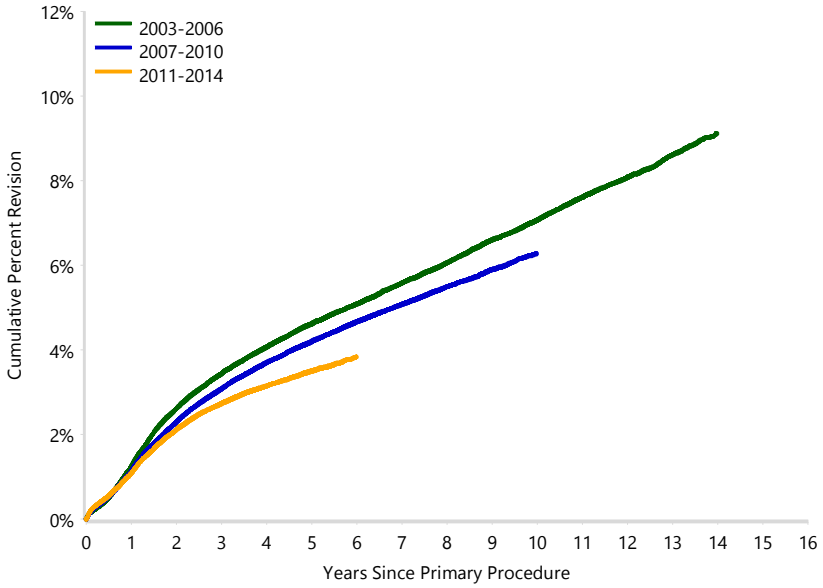
2007-2010 vs 2003-2006

- Entire Period: HR=1.02 (0.98, 1.05),p=0.310

Number at Risk	0 Yr	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs
2003-2006	99854	91622	87580	83915	80311	76738	73051	69438
2007-2010	118830	109421	104687	100252	95791	91490	87347	80470
2011-2014	141004	130230	125409	116001	80106	48981	21704	0

Number at Risk	8 Yrs	9 Yrs	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs	16 Yrs
2003-2006	65957	62622	59430	54541	37593	22394	9610	0	0
2007-2010	54775	32728	14057	0	0	0	0	0	0
2011-2014	0	0	0	0	0	0	0	0	0

Figure 2b: Cumulative Percent Revision of All Knees by Procedure Year



Number at Risk	0 Yr	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs
2003-2006	115185	112661	109713	107084	104243	101239	97985	94406
2007-2010	147750	144916	141667	138567	135391	131925	128221	120968
2011-2014	184612	181379	177836	169642	120202	75376	34312	0

Number at Risk	8 Yrs	9 Yrs	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs	16 Yrs
2003-2006	90775	86738	82477	76370	51755	30227	13075	0	0
2007-2010	83222	50926	22107	0	0	0	0	0	0
2011-2014	0	0	0	0	0	0	0	0	0

Source: ad-hoc request prepared by AOANJRR for thesis 2017

9.4 - Stakeholder Engagement in Registry Activity

Provision of information to surgeons

Changing behaviour in a healthcare setting involves complex interactions between stakeholders (320). While it would appear reasonable that audit of outcomes and feedback of information might prompt healthcare professionals to change practice, this has not been found to be consistently effective (321). Jamtvedt et al conducted a systematic review of the effects of audit and feedback on a variety of randomized controlled trials involving healthcare professionals (322, 323). The authors concluded that audit and feedback can be effective in improving practice. The effect is likely to be larger if compliance with recommended practice is lower and if feedback is more intensive or multifaceted. Developing strategies to implement effective change should incorporate multiple interventions including education, audit and feedback, multi stakeholder collaboration and professional development (324, 325). Using data from registries to improve both short and long term outcomes for joint replacement surgery should be a priority (326). The AOANJRR has endeavored to provide accurate information to all stakeholders regularly, and in numerous forms.

The Registry has provided this information to surgeons in multiple ways, including the published Annual Report, regular Scientific Presentations of Registry data, the provision of surgeon specific information through *ad hoc* reports, and on the AOANJRR Website. The Annual Report was first published in 2000 (327) and outlined the aims of the AOANJRR:

- Determine demographic and diagnostic characteristics of patients undergoing joint replacement surgery nationally
- Provide accurate information on the use of different types of prostheses in both primary and revision joint replacements
- Evaluate the effectiveness of different types of joint replacement prostheses and surgical techniques at a national level
- Compare the Australian joint replacement experience to that of other countries
- Provide confidential data to individual surgeons and hospitals to audit their joint surgical techniques to achieve successful outcomes

As with all observational data collections the initial reports were largely demographic in nature, giving a thorough snap shot of the practice of hip and knee replacement in Australia in the preceding years. The first two aims of the Registry were therefore established early and continue to be relevant with the 17th Annual Report released in 2017.

With increasing data and time, comparative analyses and more in depth reporting was first published in the 2005 Annual Report, thereby achieving the third aim of the initial Report. Opportunities to compare at an international level have been strengthened with the development of the International Society of Arthroplasty Registries. Close co-operation of Joint Registries from many countries has allowed benchmarking and development of early signal detection of devices, thus fulfilling the fourth aim. The final aim, provision of information to surgeons and hospitals, has been an ongoing project of the Registry and will be discussed further.

The Annual Report, in its printed version, is distributed to all surgeons performing arthroplasty in Australia and, in 2017, was sent to over 1600 surgeons. The Registry recorded 1,174 surgeons who had performed at least one procedure in 2016 and the Report is also sent to surgeons who have ceased operating, but still have an interest in the field of joint replacement. The Annual Report has also been available on the AOA website since 2001. The Annual Report is available to trainee surgeons within the AOA accredited training scheme. Lectures on interpretation of AOANJRR data have been embedded in the Victoria and Tasmanian State Training Program since 2012, and are now part of the national training curriculum.

The Annual Reports have had almost 2,000 citations since 2004 (Table 1) and are increasingly viewed on the Web (Table 2). The 2016 Annual Report has been viewed over 30,000 times since release.

Table 1: Cumulative number of citations of AOANJRR publications by year

Year	Cumulative No. Citations
2004	157
2006	161
2007	173
2008	363
2009	489
2010	964
2011	1334
2012	1604
2013	1717
2014	1816
2015	1956
2016	1968
2017	1990

Table 2: Number of downloads of AOANJRR Annual Report by year

Title	Download Count
Annual Report 2000	770
Annual Report 2001	496
Annual Report 2002	730
Annual Report 2003	706
Annual Report 2004	866
Annual Report 2005	1013
Annual Report 2006	983
Annual Report 2007	1687
Annual Report 2008	1822
Annual Report 2009	2364
Annual Report 2010	2574
Annual Report 2011	2492
Annual Report/SR 2012	20733
Annual Report/SR 2013	31797
Annual Report/SR 2014	17635
Annual Report/SR 2015	15597
Annual Report 2016	30,204

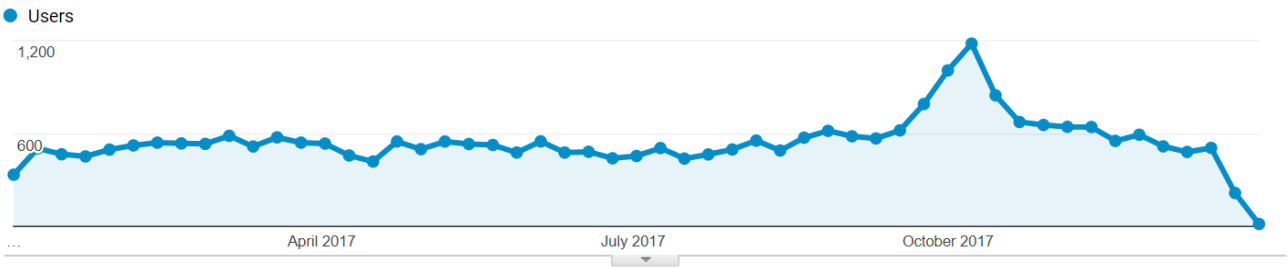
Presentations at Scientific Meetings

The Annual Report is released in September of each year and therefore a specific limitation of the Report is that data are up to date as of 31st December of the previous year. While the Report provides the most complete synopsis of the Joint Registry activity on the whole population, provision of data in more up to date fashion is potentially more beneficial to surgeons.

Presentations at Scientific Meetings are a powerful method for the Registry to disseminate up to date information. A formal Registry session has been incorporated into every AOA Annual Scientific Meeting (AOA ASM) since 2006. More than half of all orthopaedic surgeons register for the ASM, and, along with industry representatives, the Registry plenary session on a Wednesday morning is one of, if not the most, well attended. Commencing in 2007, the Registry has presented a preview of the latest findings to the Annual Meeting of the Arthroplasty Society of Australia, approximately 5 months prior to the official Report release. This session summarises that year's Report, highlighting new chapters and any significant changes in outcomes. This has enabled feedback from the peak arthroplasty body in the country and a two way exchange of information. Issues that have been discussed include adjusting outcomes for surgical volume and complexity, suggestions for new analyses, and feedback from surgeons using prostheses that have been identified

with higher revision rates. The Director and Deputy Directors also present Registry data at multiple meetings throughout Australia including State Branch Meetings, Continuing Orthopaedic Education Meetings, industry sponsored joint surgery meetings, and academic university meetings centred on Registry sciences. In this way up to date data is available for dissemination sometimes many months prior to the formal Report being distributed. Following the release of the Annual Report and AOANJRR Australian Orthopaedic Association Annual Scientific Meeting presentations there is a spike in *ad hoc* requests from surgeons and an approximately 100% increase in web site access, which may be attributed to the release of the Registry Report. (Fig 3)

Figure 3 – AOANJRR Web Access following Annual Report and Scientific Meeting



Source: Google analytics from AOANJRR 2017

Over the past ten years Registry staff have given over 350 scientific presentations at state, national, and international conferences. Information from the Registry Annual Reports, particularly the figures, is also widely used by both Australian and

international surgeons and researchers when giving presentations[8]. The Registry has won awards from the American Academy of Orthopaedic Surgeons (AAOS)[9] and the European Federation of Orthopaedics and Traumatology[10] and was recently invited to contribute to a major symposium entitled 'The Benefits of National and Regional Arthroplasty Registries' at the world's largest orthopaedic meeting, the AAOS, in March 2018. The proceedings from this symposium will be published in Instructional Course Lectures 68 (AAOS Press).

Surgeon *Ad Hoc* Requests

Commencing in 2001 the Registry has allowed surgeons, academic institutions, governments and industry to specifically request data from the Registry. The requests are discussed at the Registry Working Group meetings, data analysis is performed by the Registry statisticians, and the reports are reviewed by the Registry Working Group before release to the stakeholder. Although requests were few in

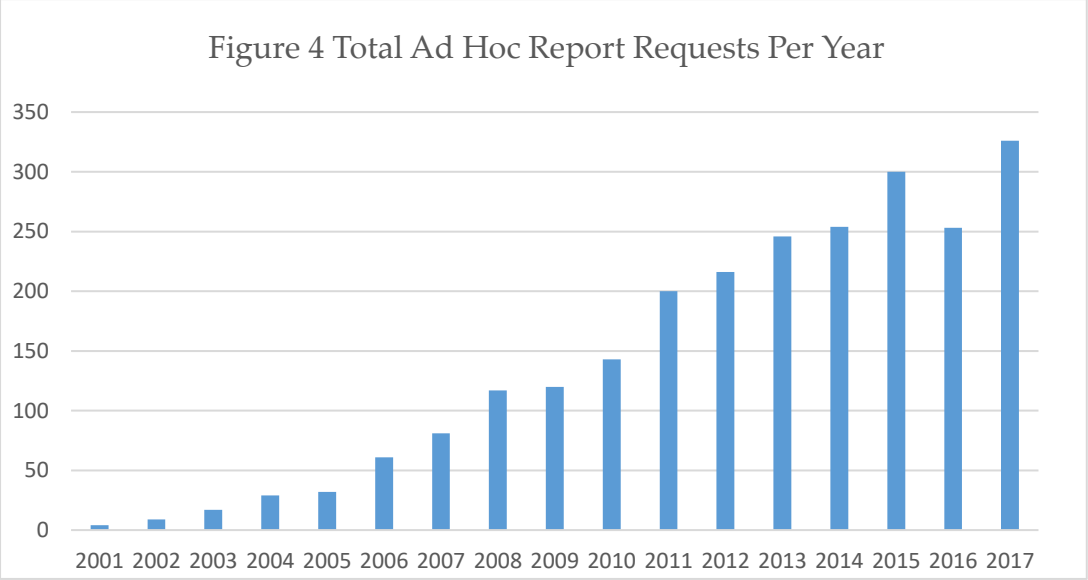
[8] Personal Communication: Dan Berry, former president, American Academy of Orthopaedic Surgeons and previous Director, American Joint Registry

[9] Best *Poster Outcome of Metal on Metal articulation in primary Conventional THA: Analysis of 17,775 procedures*.American Academy of Orthopaedic Surgeons ASM, San Diego USA February 2011

[10] Best Poster EFORT Jacques Duparc Award *The Outcome of revised Resurfacing Arthroplasty* 14th EFORT Congress, Instanbul, 2013

the first few years following the commencement of the Registry, there has been a steady increase in both the number and complexity of the *ad hocs*.

Overall the number of *ad hoc* requests has risen from 17 in 2001 to 326 in 2017. Fig 4. The importance of these and the attribution of the Registry to the improvements of joint replacement are discussed with respect to each of the specific stakeholders. A list of the numbers of requests and the stakeholders requesting them is provided in Appendix 1.



Source: Data from AOANJRR Board Report to the AOA. Adelaide, Australia; 2017, updated Feb 2018

With regard to surgeon *ad hoc* requests there has been over a fivefold increase from 2006 (26) to 2017 (169). One of the most common requests from surgeons is for the provision of a full data analysis of the surgeon's performance in a more detailed way

than is provided on the web portal. Information includes full demographics of the surgeon's practice, reasons and types of revisions, a list of prostheses they use, hospitals where they treat their patients and revisions by year of implantation. On a number of occasions surgeons have also provided their own databases for cross checking and linkage with the Registry. Prior to 2008 a surgeon's individual code number was not linked to their name and from June 2008 surgeons were given the opportunity to link their data thus enabling them to have a more complete picture of their activity from the beginning of Registry data collection.

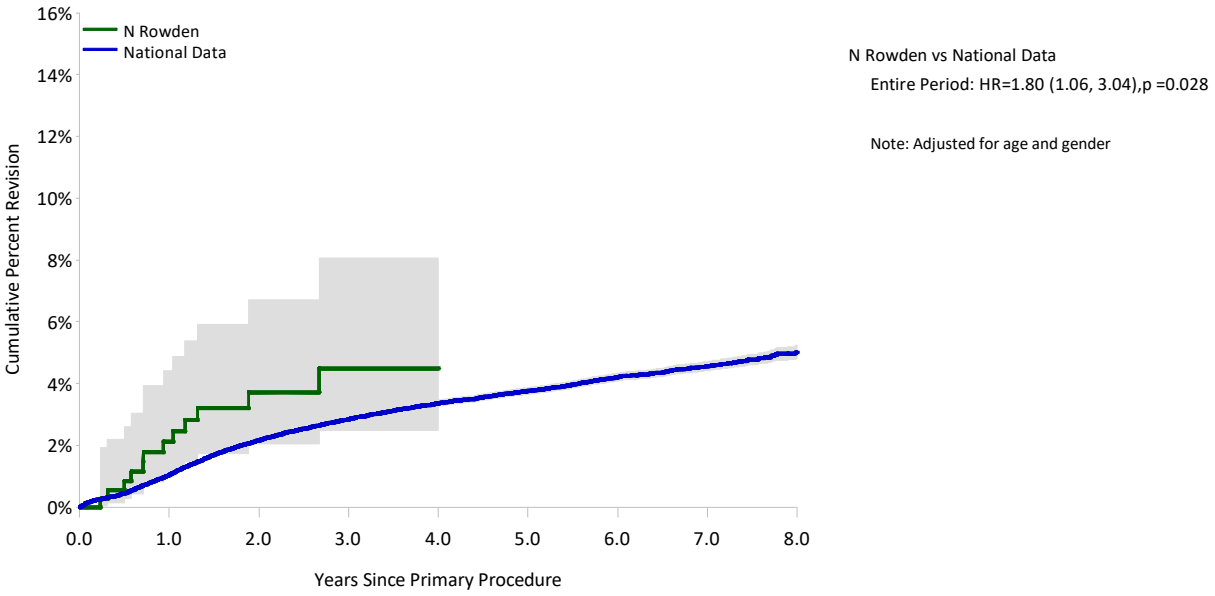
Feedback from surgeons who have been supplied analyses of their own data from the Registry indicates that the process is an important element in the way they practice and this process will often motivate change, especially if they are outside the norms of national outcomes.

Case Example

Mr. Rowden is a surgeon performing a high volume of knee replacements. He had kept comprehensive records of his knee replacements and had provided his own database for cross checking and linkage with the Registry. He submitted an *ad hoc* request to analyse his data in full in 2009 and became aware of his own higher than

expected revision rate for total knee replacement. His revision rate for total knee replacement was double the national rate (1.6 revisions/100 observed component years compared to 0.8 revisions/100 observed component years) This report also demonstrated that he had a higher rate of revision for patella femoral pain and a higher proportion of revisions were for patella only. Mr. Rowden did not routinely resurface the patella during TKR. As a result of this information he changed his surgery to resurface the patella in all cases. Mr. Rowden then reviewed his results regularly. A further *ad hoc* request analyzing data up till December 31st 2015 demonstrated a significant improvement in revision rates for total knee replacement, reducing from 1.6 to 0.77 revisions/100 observed component years. Figures 5a and 5b illustrate this change. Figure 6 demonstrates the cumulative percent revision of TKRs performed by Mr. Rowden before and after change, compared to the national rate, and clearly illustrates the significant improvement in the outcome of his TKRs.

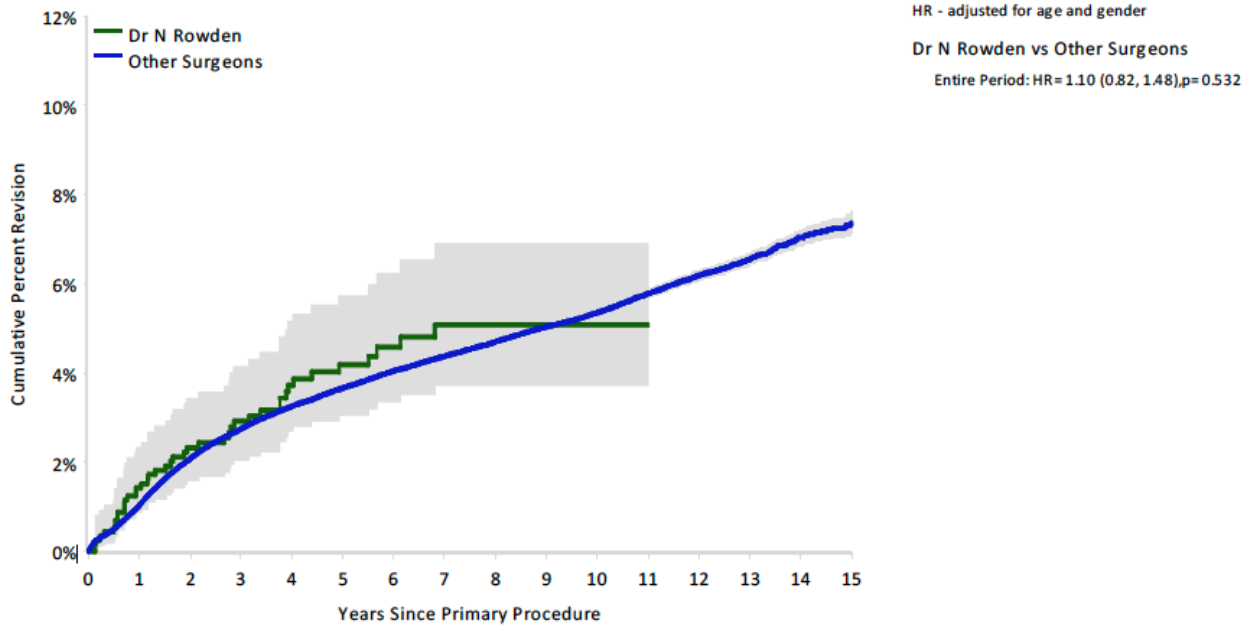
Fig 5a Cumulative Percent Revision of Primary Total Knee Replacement by Mr. Rowden



Source: ad-hoc request number 390 June 2009 based on AOANJRR data up till December 31st 2008

Data provided with kind permission of Mr. Rowden.

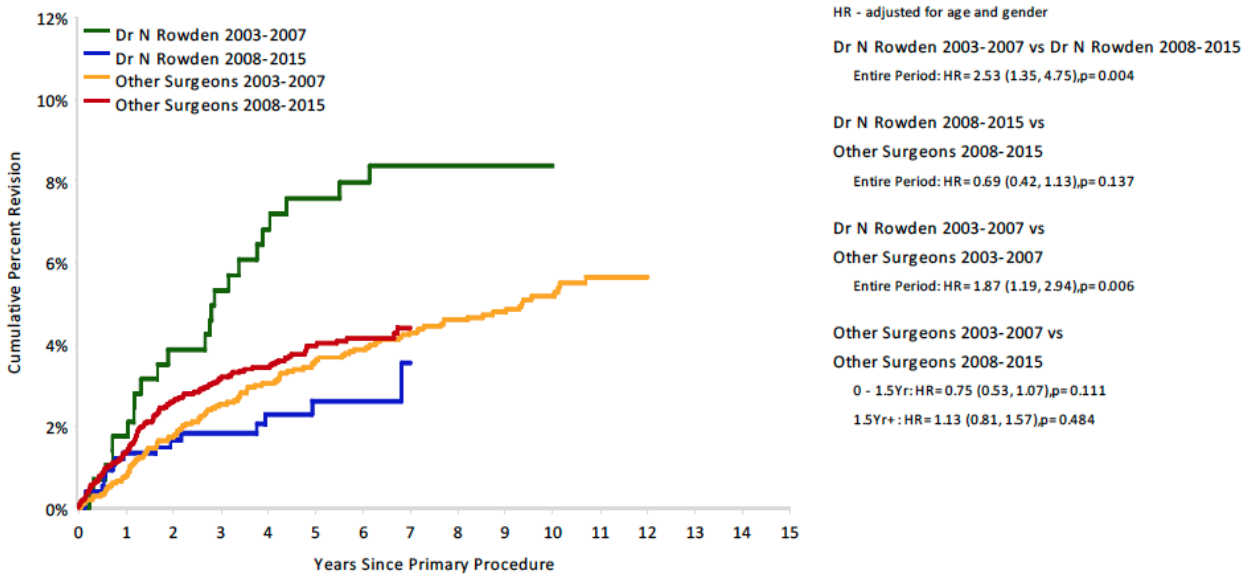
Figure 5b: Cumulative Percent Revision of Primary Total Knee Replacement by Mr. R, after routine resurfacing of the patella



Source: ad-hoc request number 2024 September 2016 based on AOANJRR data up till December 31st 2015

Data provided with kind permission of Mr. N Rowden

Fig 6 Cumulative Percent Revision of Primary Total Knee Replacement by Surgeon and Procedure Year



Source: ad-hoc request number 2024 September 2016 based on AOANJRR data up till December 31st 2015

Data provided with kind permission of Mr. Rowden

This improvement in outcomes occurred directly as a result of his surgeon portal feedback, practice audit through the Registry and subsequent change of practice.

There are multiple reasons why surgeons may not know the outcomes of all their patients and these include, but are not limited to, the following:

- Follow up of patients is time consuming and contacting patients for a follow up on a regular basis reduces available consulting time for new patients.

- Patients may be unhappy with their result and they seek other surgeons for advice. Although it is generally accepted practice to provide information back to a treating surgeon, it is not uncommon for patients to specifically request that no further information is provided to the initial surgeon. Therefore the treating surgeon for the initial operation may have no knowledge of the outcome of that patient's procedure.
- Patients move interstate, may be difficult to contact and also may not wish to be involved in follow up studies. The Registry is able to monitor all revision surgery regardless of who performed the surgery or where it was performed, although information is only provided back to the treating surgeon of the primary procedure if they were involved in the revision procedure.

The Registry has analysed the data on the proportion of surgeons who perform both the primary and revision procedure for THR and TKR and the surgery is carried out approximately only 65% of the time for both hip and knee procedures by the surgeon involved in the primary procedure. The reasons the treating surgeon does not perform the revision procedure in over a third of their cases could be due to referral by the initial treating surgeon to surgeons who specialize in revision surgery, because the patient has moved, or the patient does not wish to be treated by their first surgeon. These figures illustrate that a substantial number of procedures are performed by a surgeon not involved in the primary operation and the

importance of feedback to enable the treating surgeon to be aware of their patient outcomes. Only the Registry can provide this information.

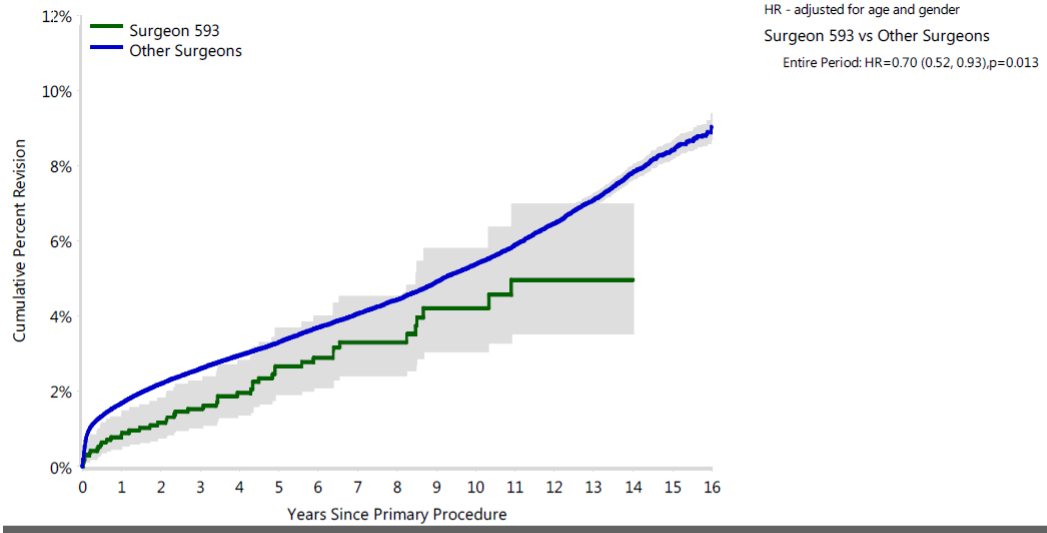
Surgeon Specific Internet Access and Comparative Analysis of Surgeon Performance

The AOANJRR developed a web portal for members who had consented to access their data and this was launched in April 2009 (328). In the first month after the introduction of the Web portal in April 2009, 112 surgeons accessed their site. This information is available to surgeons who have linked their identification number to their name, thus enabling the Registry to confirm that the specific procedure belonged to that individual surgeon. The information is provided in table form of all classes of both hip and knee replacement performed by the surgeon, including numbers of primary procedures, the numbers of procedures that have been revised and the revisions per 100 observed component years. Surgeons can break down their activity by class of device and by hospitals in which they performed the surgery and there are tables for the type of revision performed and the reason for the revision. The national revision rate per 100 observed component years is also provided to give surgeons some indication of their overall performance.

Feedback back from surgeons was extremely positive; and refining and improving surgeon reporting has been a major focus of the Registry. An initial workshop was held with Registry staff, statisticians and AOA Board Members in 2016 with the aim of exploring methods by which this could be done that would be easily understood by surgeons, and relatively straightforward to implement at a national level. It was decided that the provision of funnel plots used to display variation in revision was the best way to providing a visual representation of surgeon performance. A funnel plot is a scatter plot where each point represents a single surgeon's rate of revision with the X axis representing volume of procedures performed (individual procedures performed by the surgeon and recorded by the Registry). The Y axis is a measure of performance given by a standardized proportion of the ratio of the number of revisions observed to the number of revisions expected, multiplied by the overall proportion of revisions. The degree of variation is displayed on the graph with both 95% upper confidence limits and 99.97% upper confidence limits, which indicate the confidence limits around the overall revision rate for all procedures. This overall revision rate is represented by a separate green line and each surgeon is recorded in the scatter plot. The individual surgeon whose data is displayed is then represented by a green diamond that demonstrates their performance with respect to their peers. Funnel plots are provided for several options associated with both THR and TKR including overall outcomes for all diagnoses and all types for revisions, and outcomes for specific revision diagnoses such as prosthesis dislocation, or revision for infection within two years. This enables surgeons to identify their

performance, compare themselves to the national average and examine the reasons for revision. The provision of the funnel plots along with a detailed analysis as provided in a typical *ad hoc* report, was made available to surgeons in August 2017 (135). The report on individual surgeon variation and hospital variation was also presented in the 2017 Annual Report. These detailed surgeon reports and funnel plots will be provided on a yearly basis and are expected to increase to biannual within the next two years. Figures 7a, 7b, 7c, 7d demonstrate the author's own outcome of THR with a standard Kaplan Meier survival curve and funnel plots demonstrating comparative performance.

Figure 7a: Cumulative Percent Revision of Primary Total Conventional Hip Replacement performed by the author. (Excluding Large Head (>32mm) Metal on Metal, All Diagnoses)



Number at Risk	0 Yr	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs
Surgeon 593	1723	1571	1398	1222	1063	922	769	621
Other Surgeons	365101	318524	279375	242824	209616	179025	150413	124619

Number at Risk	8 Yrs	9 Yrs	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs	16 Yrs
Surgeon 593	486	371	290	232	167	113	64	23	0
Other Surgeons	102320	83581	67546	53067	39430	27017	16299	7396	1885

Figure 7b: Funnel Plot of Primary Total Conventional Hip Replacement (Excluding Large Head (>32mm) Metal on Metal, All Diagnoses, Revision for Any Reason)

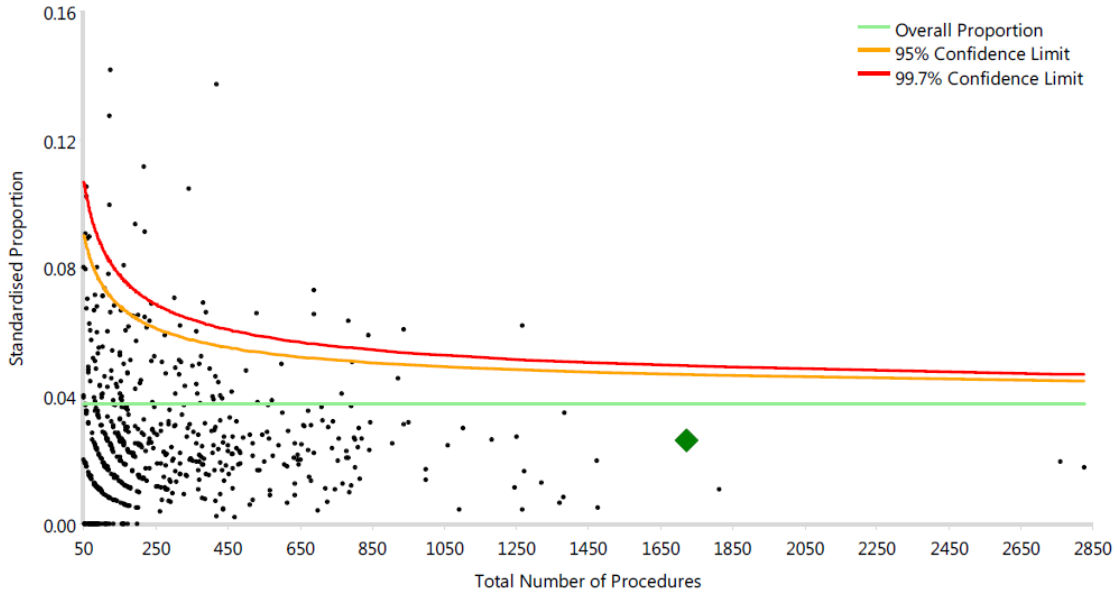
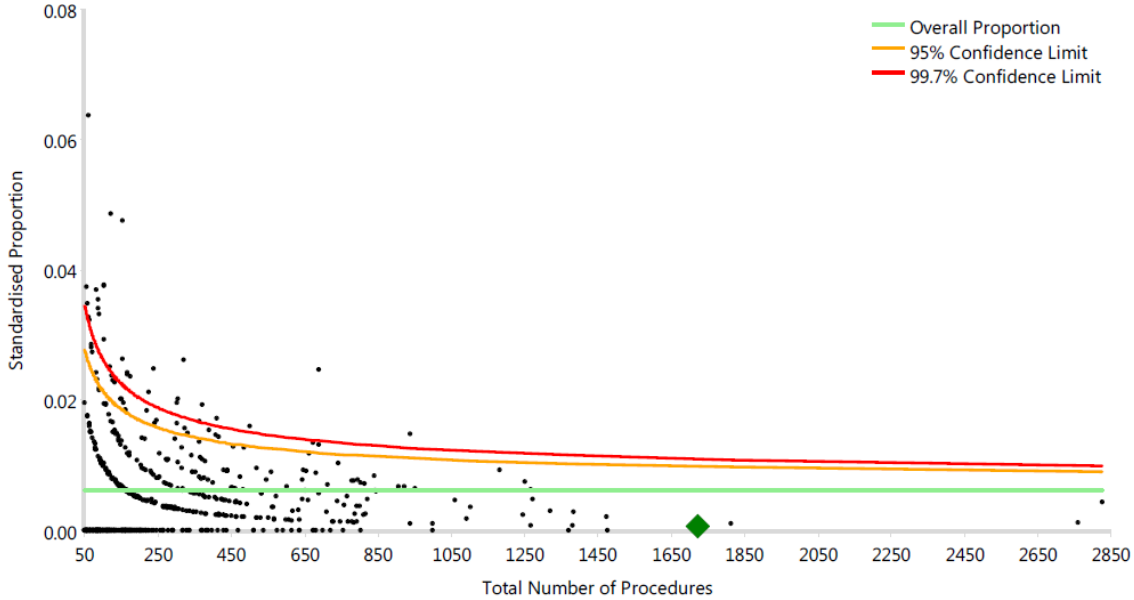
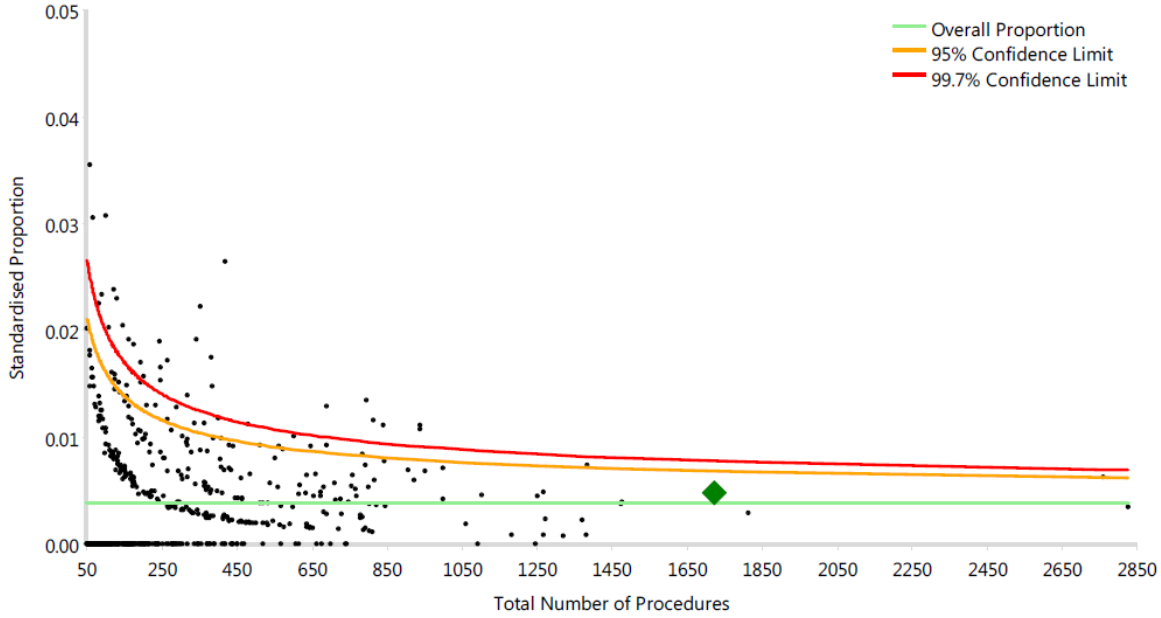


Figure 7c: Funnel Plot of Primary Total Conventional Hip Replacement (Excluding Large Head (>32mm) Metal on Metal, All Diagnoses, Revision for Prosthesis Dislocation within 2 Years)



Source: Surgeon Reports Dec 2017 prepared for all surgeons on comparative outcomes of THR and TKR. Green diamond is author

Figure 7d: Funnel Plot of Primary Total Conventional Hip Replacement (Excluding Large Head (>32mm) Metal on Metal, All Diagnoses, and Revision for Fracture within 2 Years)



As a surgeon who regularly reviews and publically presents his own data I am pleased with the overall rate of revision of my primary THR compared to the population, and, particularly for the low rate of revision for dislocation (one in 16 years). However the rate of revision for periprosthetic fracture is the same as for the population and is the most common reason why my THRs are revised. This is an acute event following a fall sometime after a successful procedure. Only half these patients are treated by me as they are often taken to the nearest hospital emergency department as distinct from the initial hospital. While I have no revisions for aseptic loosening of the femoral prosthesis that I use, this feedback has prompted me to examine other types of femoral stems that have good long term results but different design characteristics that may lessen the occurrence of fractures when patients fall

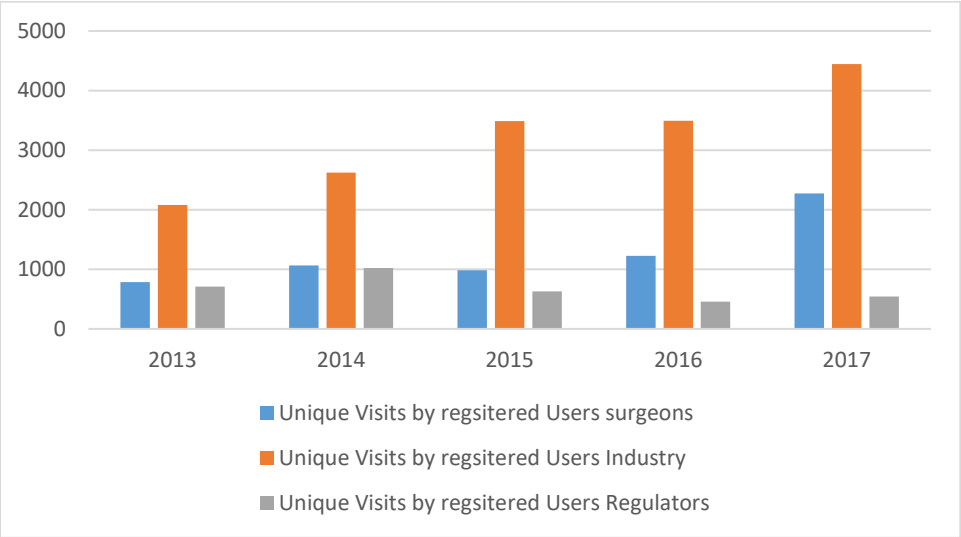
over. It will also form the basis for a separate publication as my concerns appear to be replicated by other registries and surgeons.

Monitoring surgeon use of Registry reports

While it is one thing to provide surgeons with information it is becoming an increasingly important part of the Registry to monitor the use of activity and to try and determine subsequent benefits.

The AOANJRR has been able to track surgeon activity on online access to the Annual Report and surgeon web portal (which are separate activities from *ad hoc* requests) since 2013. This provides an additional source of information to the hard copy version of the Annual Report, distributed to over 1100 surgeons. These data have been available since 2013 and demonstrate over a 100% increase in visits to the web portal by surgeons (Fig 8). In 2013, 193 surgeons (of 980 surgeons who had performed at least one joint replacement) had 786 unique visits to the web portal. In 2017 this had risen to 545 surgeons (of 1,211) who visited the web portal on 2,271 occasions.

Fig 8 Unique visits to Website by registered users for surgeons, industry and regulators



Source: AOANJRR Internal Reporting Site prepared 2017

There has been increasing use of personal Registry data by surgeons and this reflects the increased confidence they have with the ownership, accuracy and analysis of the information provided. The Registry is the best source of critical information for surgeons and its penetration of the target audience is very high. The provision of these data by the Registry is the only way that surgeons can obtain feedback on their own outcomes, with the exception of the very small numbers of academic surgeons involved in research and follow up studies (329). The use of the Registry as a Quality Assurance Activity and the protection from identification means surgeons are now readily using the information for self-audit, Continuous Professional Development (CPD), and peer presentations. The true challenge for the Australian Orthopaedic Association is therefore to engage those surgeons who do not look at Registry data and it is hoped that the newly released surgeon variation and funnel plot

presentation will aid this process. The AOA has recommended access of a surgeon's individual reports with funnel plot data be counted as a specific requirement of ongoing CPD for those surgeons performing joint replacement. It is encouraging to note that, as of March 2018, 387 surgeons of a total of 756 who had performed at least one joint replacement in 2016, had downloaded their report[11]. It will require a few years before the effect of this improved feedback can be studied.

Prosthesis Use

One of the major benefits of the Registry is the ability to compare the performance of prostheses within an entire population. Post market surveillance is important because most prostheses are released into the market with minimal supporting clinical data (330). Surgeons ultimately decide which prostheses they feel are best for their patient though the clinical evidence for this choice may be lacking. Previous chapters of this thesis have examined the reporting of specific prostheses or combinations of prostheses with higher than anticipated rates of revision (HTARR). The reporting of outcomes on entire classes of devices by the Registry is another major way in which the Registry identifies variation which can lead to the adoption of best practice. There are multiple examples where reporting of data by the

[11] Source; Memo from AOANJRR to AOA board April 2018

Registry appears to be associated with a change of practice that has led to a reduced revision burden for hip and knee replacement. This has been achieved by not only reducing the use of certain classes of devices but also reporting the outcome of devices with respect to age and gender. Some prosthesis outcomes are dependent on these variables and providing these data enables surgeons to make an informed choice. Some examples of a beneficial change in practice include:

- There was a clear reduction in the use of cementless Moores Hemi-arthroplasty for fractured neck of femur following the report of an almost threefold increase in the rate of revision compared to a cemented Thompson's prosthesis (Annual Report 2003) (331).
- The use of unicompartmental knee replacement markedly reduced after the Registry reported twice the rate of revision compared to total knee replacement (Annual Report 2004) (182) and this was particularly evident in younger patients. Unicompartmental knee replacements represented 19% of knee replacements performed for osteoarthritis in 2003 and this proportion has gradually reduced to 5.1% in 2016. The use of unicompartmental knee replacement has remained at approximately 15% in some countries (332).
- A whole class of conventional THR has been classified as 'Exchangeable Neck Prostheses' by the Registry and the AOANJRR is the only registry to report on the outcomes of this class. These devices offered the opportunity for surgeons

to adjust leg length and off set with potential greater accuracy. The AOANJRR first reported that this class of devices had over twice the rate of revision as conventional fixed neck prostheses in the 2010 Annual Report (333). The use of primary THAs for OA with exchangeable neck prostheses peaked in Australia at 6.6% of all primary THR in 2010.and their use has steadily decreased since that time. In 2016 only 1.1% of all procedures for THR used an exchangeable neck. The Registry evidence suggests that the continued use of femoral components with an exchangeable neck in primary THA undertaken for OA can no longer be justified (206).

- Resurfacing hip replacement is classified as a separate class of primary hip replacement and surgeons initially used these devices in all ages and in both females and males. Outcomes analysis by the Registry reported a higher failure rate in females and older patients (Annual Report 2007)(200) and when femoral head sizes smaller than 50mm diameter were used in both females and males (Annual Report 2008)(199). This led to a change in practice with Australian surgeons implanting resurfacing hip replacements largely in males under the age of 65. Continued reporting of resurfacing hip arthroplasty and its comparative outcomes compared to conventional hip replacement has led a marked reduction in its use in Australia from a peak of 8.9% of primary THR in 2005 to 0.9% in 2016 (AOANJRR Annual Report 2006 and 2016) (16, 191).

- Continual reporting of the method of femoral fixation for conventional hip replacement has demonstrated an increased rate of revision for cementless implants in patients over 75 years of age. This age category is the only age group that has a higher proportion of cemented compared to cementless femoral stems, reflecting, in part, surgeons responding to ongoing provision of data by the Registry.
- The Registry has identified that the use of patella resurfacing in total knee replacement has led to a lower rate of revision over time, particularly with posterior stabilized implants. This has led to increased use of patella resurfacing in Australia with more total knee replacements having a resurfaced patella than un-resurfaced from 2010 onwards (Annual Report 2011) (185).

Case example: Large Head Metal on Metal Total Hip Replacement

In 2007 the Registry was the first body to identify a significantly higher rate of revision for the ASR Hip Resurfacing System and the following year the ASR XL Acetabular System (1). The identification of these particular prostheses was associated with a substantial reduction in the use by surgeons and the subsequent withdrawal of the prostheses from the Australian market in December 2009. Confirmation from other studies and from both the New Zealand and the National

Joint Registry of the United Kingdom resulted in the world wide withdrawal of the prostheses in August 2010 (96, 199, 200, 334-336). This was a prime example of the AOANJRR influencing the global outcome of joint replacement surgery. This also demonstrates how a single registry's data is strengthened by other sources including other registries and clinical studies.

The identification of this device led to a closer examination of all prostheses that had a large head metal on metal bearing (defined as a femoral head greater or equal to 32mm diameter). This class of large head metal on metal devices was introduced with little clinical data and was employed to address several factors. These included revision of resurfacing hip arthroplasty due to fracture to avoid revising the acetabulum, to reduce revision for wear related issues as metal on metal bearings had reportedly low wear characteristics, and to use large diameter femoral heads to reduce the risk of hip dislocation. The Registry first reported on the outcomes of bearing surfaces in THR in the 2008 Annual Report (199). The Registry has tracked the use of different bearing surfaces for THR over time but more importantly provides a comparative performance of the different surfaces. The 2008 Report detailed outcomes on five different combinations, Ceramic on Ceramic, Ceramic on Polyethylene, Metal on Metal, Metal on Polyethylene and a small number of cases where the Registry was unable to identify the bearing surface. Metal on Metal

bearing surfaces of all sizes had a higher rate of revision than Metal on Poly at all time points at seven years follow up.

In the 2009 Annual Report (337) the Registry examined the effect of bearing surfaces for conventional THR with respect to femoral head size. When the head size was greater than 28mm Metal on Metal bearing surfaces had the highest rate of revision but this was not evident with head sizes of 28mm. The effect of head size was analysed in more detail in the 2010 Annual Report (333) and several variables were studied including head size, age and gender. To further evaluate the effect of head size with Metal on Metal bearing surface, analysis was undertaken comparing four head size groups (≤28, 30-32, 36-40, >40mm). The two larger head size groups were associated with an increased risk of revision compared to the two groups with head sizes 32mm or less and the Registry then defined large head Metal on Metal as head sizes greater than 32mm. This naming convention for large head was adopted internationally. The higher risk of revision for those prostheses with large head sizes became evident after two years. There was also an interaction between age and head size. The risk of revision for large head sizes was higher regardless of age and this risk was greater the younger the patient. Females also had a higher rate of revision but again only for large head sizes. The reasons for revision of large head Metal on Metal were also examined and compared to Metal on Polyethylene. There was a higher incidence of revisions for loosening/lysis and metal sensitivity for the Metal

on Metal group. In order to determine if the higher revision rate of articulations with large head Metal on Metal was prosthesis specific, the Registry analysed all prostheses head/acetabular combinations with more than 200 procedures with both Metal on Metal or other bearing surfaces. There were 12 combinations that met these criteria and many of these devices contributed to the higher revision rate, lending further weight to the argument that the large metal head bearing surface was a problem and it was not just the ASR hip. This information was clearly demonstrated in the 2010 Annual Report. The use of larger head Metal on Metal bearing surfaces peaked in 2009 and then there was a 85.7% reduction in the use of large head Metal on Metal in the year after the 2010 Annual Report compared to the peak in 2009 (Fig 11 and Table 3).

Figure 11. Use of Metal on Metal Total Conventional Hip Replacement by Head Size over time

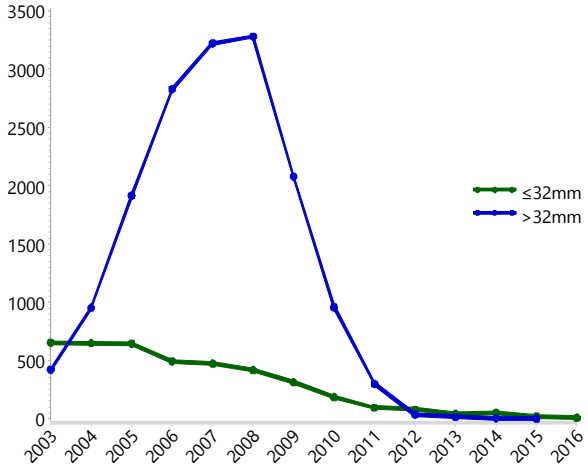


Table 3: Metal on Metal Total Conventional Hip Replacement by Head Size

Procedure Year	≤32mm		>32mm		TOTAL	
	N	Row%	N	Row%	N	Row%
≤2002	1706	85.2	297	14.8	2003	100.0
2003	653	60.8	421	39.2	1074	100.0
2004	647	40.5	952	59.5	1599	100.0
2005	643	25.1	1915	74.9	2558	100.0
2006	493	14.8	2828	85.2	3321	100.0
2007	472	12.8	3222	87.2	3694	100.0
2008	417	11.3	3280	88.7	3697	100.0
2009	311	13.0	2077	87.0	2388	100.0
2010	184	16.2	955	83.8	1139	100.0
2011	94	24.0	298	76.0	392	100.0
2012	78	69.6	34	30.4	112	100.0
2013	41	74.5	14	25.5	55	100.0
2014	51	91.1	5	8.9	56	100.0
2015	18	94.7	1	5.3	19	100.0
2016	8	100.0	.	.	8	100.0
TOTAL	**5816**	**26.3**	**16299**	**73.7**	**22115**	**100.0**

Source: Demographic data prepared from AOANJRR 2017

In Australia there has been no recorded use of large head Metal on Metal since 2015 when just one was used.

While there were other publications and registry reports of adverse outcomes of large head Metal on Metal bearings, (22, 23, 25, 26) the AOANJRR was the first Registry to report these findings and, as a consequence, the use of this bearing surface declined in Australia before other countries (98, 338).

Hospitals

Hospitals are increasingly using Registry reports of their overall joint replacement activity. Each hospital performing joint replacement surgery in Australia (currently 305) receives a hard copy of the report and notification of online access. Acknowledgement is also made of the Registry hospital coordinators, who facilitate data collection and respond to Registry queries. Unlike surgeons, industry, government and regulators, hospitals do not have registered access to their own hospital data but can request this in the form of *ad-hoc* reports. In 2001 there were 3 requests and in 2017 this had increased to 45. There have been a total of 236 *ad-hoc* reports provided to hospitals though some of the larger hospitals have had more than one request. Epworth Healthcare, the largest hospital group in the state of Victoria (author's employer) has used reports for audit and to benchmark against other healthcare institutions of equivalent size and similar case complexity. They have also chosen to post figures from the Registry reports on the hospital website showing the hospital performance (Figs 11a,b) (339). While the results show significantly lower rates of revision than the national average for THR, resurfacing hip replacement and unicompartmental knee replacement, for TKR the hospital has a higher rate. The data have been presented at audit meetings, and the reasons for the higher rate have been a combination of prostheses not performing as well as others (but not identified with a HTARR) and a large proportion of TKR performed

by high volume TKR surgeons who did not re surface the patella. There has been a change of some prostheses and the high volume surgeons now routinely re surface the patella. Further audit meetings have demonstrated an improvement.

Figure 11a Cumulative Percent Revision of Primary THR at Epworth HealthCare

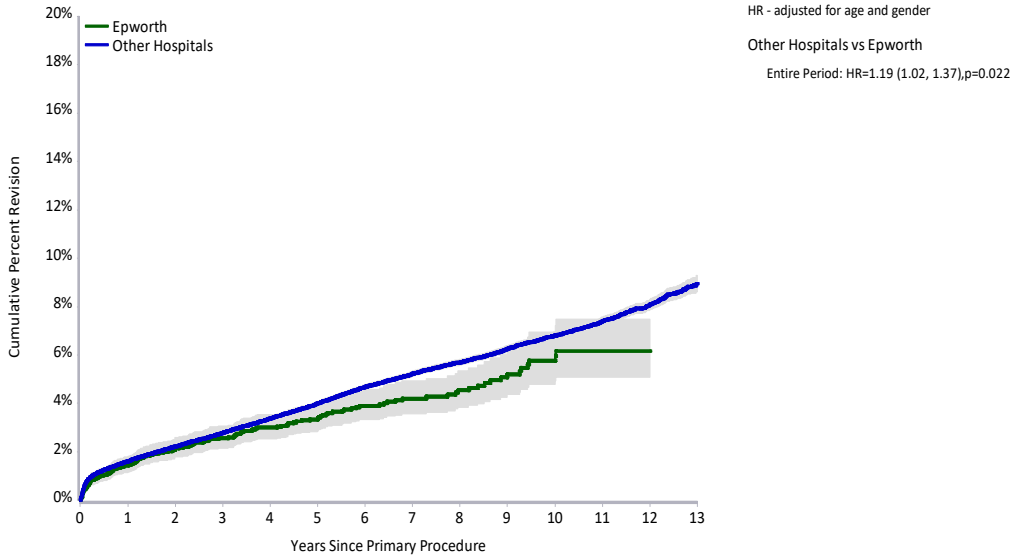
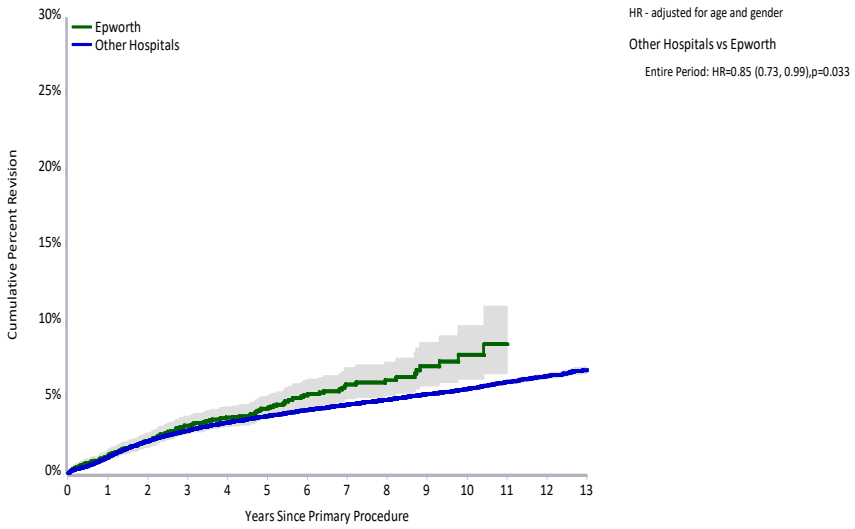
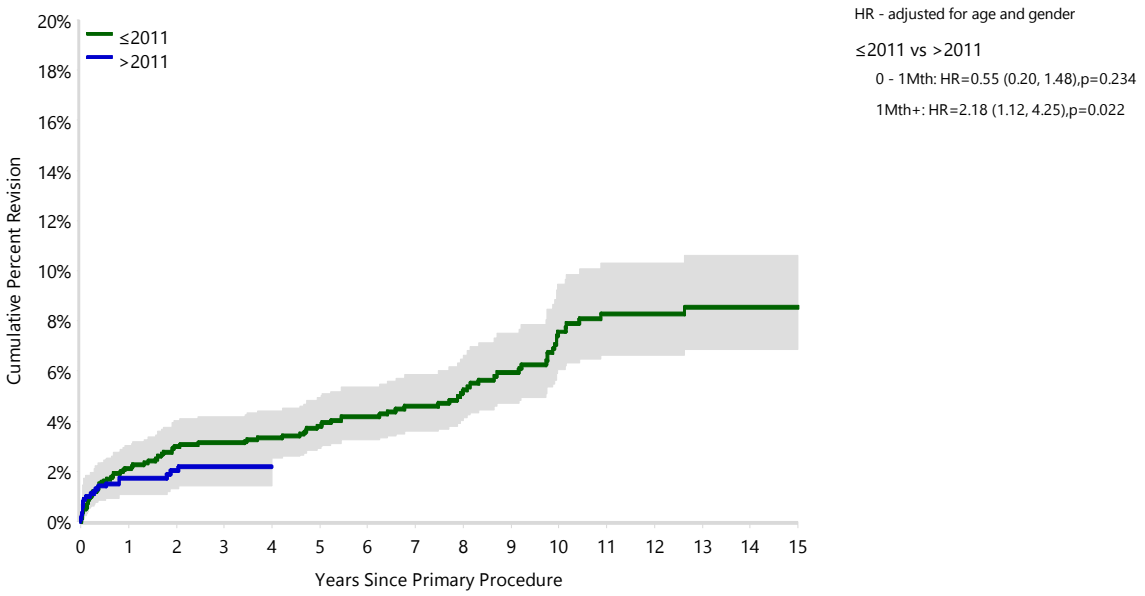


Figure 11b Cumulative Percent Revision of Primary TKR at Epworth Healthcare



Another example of the change in practice as a result of information provided by the Registry involves another hospital performing large numbers of joint replacements, including a number of devices that had been previously reported by the Registry with a HTARR. At the yearly hospital audit meeting all surgeons are asked to present the outcomes of their individual joint replacement data as well as the overall hospital data. The Director or a Deputy Director of the Registry attends these audits and provides interpretation of the data and feedback. As a result of the use of some prostheses with a HTARR at the hospital, the hospital board instituted a policy in 2011 prohibiting the use of any HTARR device reported by the AOANJRR. As a result of this intervention the outcomes of the hospital audit have markedly improved as demonstrated by a reduction in the cumulative percent revision before and after the board's decision (Figure 12).

Fig 12 Example from One Hospital. Cumulative Percent Revision of Primary Total Conventional Hip Replacement by Time of Primary Procedure (All Diagnoses, Excluding Large Head (>32mm) Metal/Metal)



Source: data on file AOANJRR 2017, permission granted for use of de-identified information

More recently, Ramsay Healthcare, the largest provider of private hospital beds in Australia, has commissioned reports on each of their 35 hospitals that perform joint replacement surgery. Multiple public hospitals have also requested data from the Registry to present at internal hospital audits.

Government and Regulatory Authorities

The AOANJRR has worked closely and co-operated with government since its inception. The Registry was initially declared a Federal Quality Assurance Activity in March 1999 by the then Federal Minister for Health and Aged Care and the Activity status has been renewed in 2001, 2006, 2011 and 2017. This Quality Assurance Legislation is part of the Health Insurance Act of 1973 and was amended in 1992 to include Quality Assurance Confidentiality. The Act operates on the underlying assumption that quality assurance activities are in the public interest and the Declaration ensures that Registry data are free from subpoena and are held in absolute confidentiality. This prohibits disclosure of information identifying individual patients or healthcare providers to any organization including the government. This protection provided by the Quality Assurance Activity assures surgeons, hospitals and government that the information supplied to the Registry remains confidential and secure. The Registry has received increased funding from Government to cover day to day operating costs and this is likely to be as a result of the ongoing Quality Assurance activities promoted by the Registry and improvement in joint replacement outcomes.

State Health Departments have submitted 107 *ad-hoc* requests since 2001 and these have been overwhelmingly for demographic data and prosthesis use. These reports

are utilized for public hospital purchasing contracts and to investigate regional variation. The author, along with Hospital Directors of Orthopaedic Departments, has been a member of the Victorian Department of Health prosthesis review committees and has given advice on the clinical interpretation of the Registry data.

The Registry has also worked closely with the Therapeutic Goods Administration (TGA) which is part of the Australian Government Department of Health. The TGA is responsible for regulating therapeutic goods across a wide range of medicines, vaccines and medical devices. The manufacturers of medical devices have an ongoing responsibility to report adverse outcomes to the TGA. However, there are inherent issues with the accuracy of post market surveillance, as previously discussed in Chapter Four (221). The Registry has worked closely with the TGA to develop a robust reporting of all hip and knee prostheses implanted in Australia and the TGA has had access to its own AOANJRR web portal from 2010. This web portal enables staff to view the outcomes of all devices which are reported in outcomes per 100 observed component years. The TGA can independently identify devices or classes of devices which they believe warrant further investigation, and request an in depth *ad hoc* Report from the industry sponsor responsible for the prostheses. These types of requests have increased in detail and complexity and the Registry Working Group has provided clinical input to these reports. The TGA can take regulatory action to suspend a prosthesis from the Australian Registry of Therapeutic Goods

(ARTG) when they deem that the safety of the prostheses is not acceptable. These recalls are accompanied by a notification to surgeons and hospitals that have implanted the relevant devices and are undertaken in a voluntary fashion. The relationships with the TGA have been built over a period of time and reflect the increased understanding of the value of the data.

There have been changes to the regulatory framework for approval of new implants within the European Union, USA and Australia (340-343). One of the major drivers of these changes has been the significantly higher rate of revision of the ASR hip resurfacing hip system and ASR XL large head Metal on Metal THR as detailed earlier in this chapter. Problems with these devices were first reported by the AOANJRR, as were subsequent issues with all large head Metal on Metal THR. In August 2013 the TGA released the Regulation Impact Statement: *Changes to premarket assessment requirements for medical devices* (344). This identified the need for an increased level of premarket scrutiny for higher risk implantable medical devices prior to approval, the need for transparency and for conformity of assessment. The report's conclusion was to improve premarket assessment and subject implantable devices to a full TGA conformity assessment. All prostheses which have a load bearing role within the human body are now required to be "up classified" (TGA terminology) from Class IIb to Class III. This upgrading has meant that clinical information on the outcome of the devices must be presented to the TGA, and the

Registry has responded to both Industry and the TGA with multiple *ad hoc* Reports on device outcomes(340). Industry have used these *ad hoc* requests for both the local regulators and also to provide information for the European regulators for devices that are common to both markets.

The Registry has also had a vital, advisory role to play with the Government's Prostheses List Advisory Committee (PLAC) and Hip and Knee Clinical Advisory Groups. The Advisory Committee on Medical Devices (ACDM) provides independent medical and scientific advice to the Minister of Health and the TGA on the safety, performance and manufacturing of medical devices in Australia and Registry reports on orthopaedic devices are a major source of current information (345).

The Registry has identified outlier prostheses through the process of Higher Than Anticipated Rates of Revision (HTARR). As a result of this process, a large number of devices have been removed from the market (Additional Discussion, Chapter Four). However, as well as providing information on these devices that are not performing as well as others, the Registry has also had a major role to play in providing information for benchmarking of devices. The Orthopaedic Device and Evaluation Panel (ODEP) was established in the United Kingdom in 2002 by the National Health Purchasing and Supply Agency with the aim of providing a strict

benchmark standard for assessing the quality of hip prostheses. The principal benchmark standard was better than 90% survivorship at 10 years (10A) for individual acetabular and femoral prostheses. In 2010 the AOANJRR suggested that the benchmark for a superior outcome (ODEP 10A*) should be raised from 90% survivorship at 10 years to 95% survivorship at 10 years. This was subsequently been adopted by ODEP in 2014. As discussed in the Industry section many companies use AOANJRR data for applications to ODEP.

The Registry first published data on the cumulative percent revision of prostheses with a 10 year follow up in the 2011 Annual Report This time point was widely regarded by the international orthopaedic community as an important milestone in assessing the performance of prostheses. With the increasing length of follow up the Registry will continue to report on these devices. In the 2017 Annual Report the outcomes of over 36 hip prosthesis combinations and 24 knee prosthesis combinations with a 15 year follow up are tabled. These data provide information to all stakeholders on the longer term outcome of prostheses.

Australia introduced a benchmarking system for both total hip and total knee prostheses in 2007. Those prostheses that are eligible to receive a 10-year benchmark are awarded a Superior Performance Suffix (SCP) if they achieve the required criteria at 10 years (95% survivorship at 10 years) The purpose of this was to

encourage the continued use of prostheses identified as performing well in the longer term. The Registry has provided data for the recognition of SCP and these prostheses are rewarded with an increased premium from Health Insurance Funds of up to 20% over the established standard re-imbursement. Once again, the use of these data, which is only available through the Registry, promotes the use of better performing prostheses.

Industry

The relationship between the Registry and Industry has improved over the past 15 years such that now there is close cooperation with mutual benefit for both parties. Initially this was not the case and the Registry was viewed with some suspicion, particularly with regard to the early identification of implant failures. In 2004, implants with a HTARR were first identified. At this stage manufacturing companies were given the chance to respond and explain if there might be an alternative explanation for why the device was not performing as well as others. This explanation was incorporated in the Annual Report without further Registry comment, but this practice ceased in 2006 for a number of reasons including a delay in company response and also a tendency to apportion blame on anything other than the device. The Registry created a link for companies to log on to their own specific website in 2009 and this has led to greater industry involvement with Registry data.

Industry can track data on their own website and then request detailed *ad hoc* reports from the Registry if they have evidence that a prosthesis or combinations are not performing as well as expected. This also involves cooperation with the TGA as previously explained. The Registry has been able to provide companies with accurate data on implant use and revisions of their components. Prior to this they relied on post market surveillance with adverse event report or feedback from sales representatives. However, it is quite common for revision procedures to be performed by another surgeon with the use of a prosthesis different from that of the original company and therefore, without detailed feedback from the Registry, industry would be unaware of their true implant revision rate. Several of the industry websites now have a direct link to the AOANJRR website though there are disclaimers that state there is no organisational affiliation and industry does not necessarily endorse the content (346-348).

Case Example

The 2006 Annual Report identified that the outcome of Hip Resurfacing procedures (HR) was related to gender and age, and in the preceding year, HR comprised 8.9% of all primary THR. In 2008 the Registry reported that the size of the femoral head of the HR was also related to the outcome, with smaller head sizes (< 50mm) having a higher rate of revision. The Registry was the first to report these findings and this led

to a marked change in utilization of these devices by Australian surgeons with male patients < 65 years making an increasing proportion of all HR procedures. By 2010 the proportion of males receiving HR had increased from 71.2% in 2003 to 91%, with 95% under the age of 65. The Birmingham Hip Resurfacing (BHR) prosthesis (Smith & Nephew) had almost 70% of the hip resurfacing market share at this stage and Smith & Nephew reacted to this information. It issued an Instructions for Use statement to recommend the use of the BHR in males < 65 years of age and withdrew smaller resurfacing femoral heads from the market (before any regulatory authority guidelines) (347). This was an example of follow through from an industry perspective and reflected a mounting respect for Registry data quality.

The Registry has also worked closely with industry to provide them with reports for submission to regulatory authorities, both nationally and internationally, for re-imbursement. Up until 2017, better performing prostheses in Australia (termed superior clinical performance) were awarded a premium price of 10% above the list price for implants with less than 5% rate of revision at ten years. Industry used reports based on Registry data for applications for superior clinical performance. Reports are also used for benchmarking and to obtain device ratings through ODEP in the United Kingdom. This promotes the use of devices with good outcomes which is one of the key strategies of the Registry. From 2001 till December 2017 there have

been 936 requests for *ad hoc* reports from industry and these comprise 39% of all the Registry requests. (Appendix 1).

Over the past 18 months the Registry has worked closely with senior executives of the four major industry manufacturers to develop standardized, automated reports. This will allow industry unlimited access to their own products, and be available on a regular basis as a downloadable file. All the information required by the companies to satisfy regulatory and re-imbursement submissions, and to monitor the performance of their implants will be provided.

The AOANJRR Governance sub-committee has recommended to the AOA Board that industry can also utilise these reports for a wide range of other activities including white papers, advertising, and provision of industry specific reports to surgeons and hospitals. The use of above activities using *ad hoc* reports had previously been prohibited and this change reflects the more mature relationship between the Registry and Industry. There still strict rules in place for accurate use of the data[12]. Industry has come to respect the scientific veracity of the Registry and the close co–operation of both Registry staff and Industry leaders has fostered this. No

[12] Source AOANJRR extraordinary Governance Board meeting, White paper prepared for AOA Board April 2018

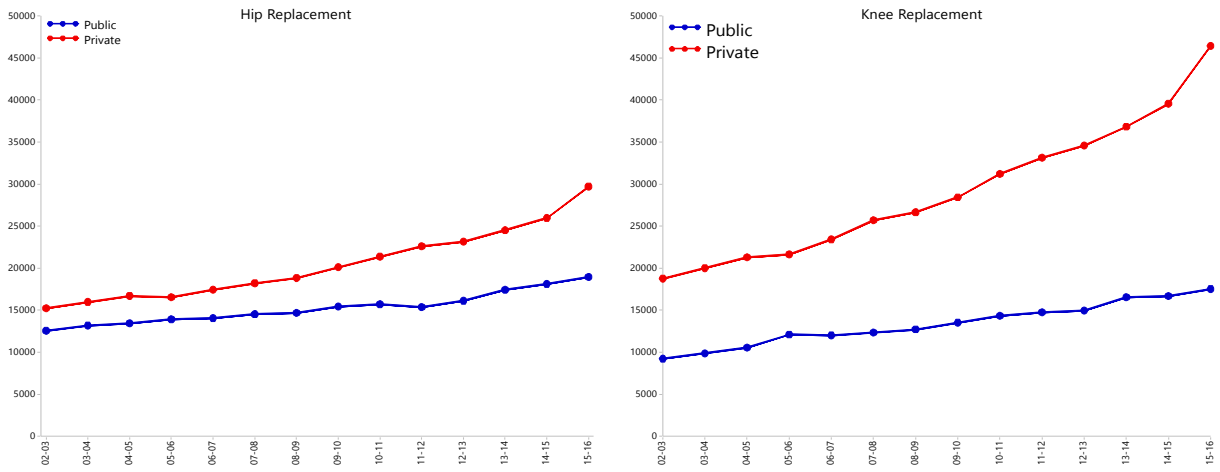
stakeholders involved in the orthopaedic field wish to see a repeat of the ASR failure, with the dramatic health problems suffered by patients and the subsequent huge litigation payouts awarded against industry. The ability of Industry to access real time reports of devices in an unlimited fashion may help to minimise this from ever happening again in future.

While it is pleasing to see the increased cooperation of Industry with the Registry it should be recognised that the objectives of companies may differ compared to those of the Registry. A commercial entity must satisfy shareholders as well as regulatory authorities whereas the Registry primarily serves the Australian public. There are strict guidelines in place that stipulate regulations for the members of the Registry with regards to commercial influence. These are incorporated both within Government legislation, which forbids any Registry personnel form divulging identified information, and with the AOA code of conduct which Registry directors sign upon appointment (Appendix 2).

Medical Insurance Companies

For the 2015/2016 financial year, 59% of THR and 71% of TKR were performed in private hospitals (349) and the trend for more surgery to be performed in private hospitals compared to public has been consistent for over 20 years.

Figure 13 Number of Hip and Knee Replacements by Public and Private Sector and Year



Source: Data adapted from AOANJRR Supplementary Report, Demographics of Hip, Knee and Shoulder Arthroplasty 2017

For companies to be reimbursed, all prostheses inserted in private hospitals have to be approved by the Prostheses List Advisory Committee (PLAC), though this is not the case for public hospitals, which have separate State Government contracts for re-imbursement. The Registry has been represented on the Federal Government Department of Health Committee to examine ways to reduce costs associated with the health industry. The Minister has decided to reduce benefits payable by health

insurers for joint prostheses by 10%. The Registry has strongly encouraged the use of well performing devices as a way of also reducing costs. Mindful of the need not to stifle innovation, but still adhere to appropriate pre market testing, the Registry has been involved in organising the concept of developing clinical trials hosted within registries. 'Registry nested clinical trials' may support industry and insurers to work together to safely introduce new devices into the market (350).

In the introduction to this chapter, I have discussed how revision surgery is the metric that the Registry uses to measure the outcome of joint replacement. This approach is limited in that it only identifies a subset of patients that have had an unsuccessful procedure and the use of PROMs is another method that may be employed to achieve further improvement in joint replacement. PROMs may be a valuable tool to aid in the move towards a value based healthcare system with more emphasis on patient outcomes. In 2017, Medibank, the largest private health insurer in Australia, approached the AOA and the AOANJRR to partner in developing a pilot study to investigate the feasibility and effectiveness of collecting national PROMs data[13]. The AOA PROMs Pilot Project commenced in November 2017 and incorporated advice from international experts in the field. Data collection is expected to commence in June 2018. This project has been made possible by funding

[13] Source; Pilot Project on the collection of PROMs and other outcome data within the AOANJRR prepared for AOA Board February 2017 Commercial in Confidence

from a variety of medical insurance companies. The reputation and track record of the AOANJRR as a clinical quality registry has been a major reason for the insurers to collaborate with the Registry in this important project. This project will have important implications for collecting and reporting of PROMs associated with other medical interventions.

Patients

Health literacy is defined as the skills and abilities needed to gain access to, understand, and use health related information. There is a growing importance of providing information to the public to involve them in shared decision making (351), though the evidence for the effectiveness of this is mixed (352). The author has been involved in research that has examined the use of multimedia with regards to surgery and the provision of easily understood information has demonstrated clear benefits to patients (353-355). Other studies using decision aids have supported this concept (356, 357), and health professionals should take steps to ensure patients have access to a variety of health information. This has been an increasing focus of the Registry.

The AOANJRR Governance committee has a formal appointment of a patient advocate and currently the Registry has a patient champion who regularly speaks at public forums. The widespread newspaper, television, radio and social media coverage of the ASR hip revisions involved the Director of the AOANJRR, and exposed the Registry findings to a much wider public audience. Concerns about the type of THR and bearing surface became (and still are) regular questions that patients ask during consultations.

It is now common practice for patients to refer to the internet for information regarding joint replacement. The Registry provides a publically accessible Lay Report annually (358). This is, by far, the most commonly accessed supplementary report provided by the Registry and the 2017 Lay Report was downloaded over 900 times in the first three months following release[14]. The introduction to the Lay Report states;

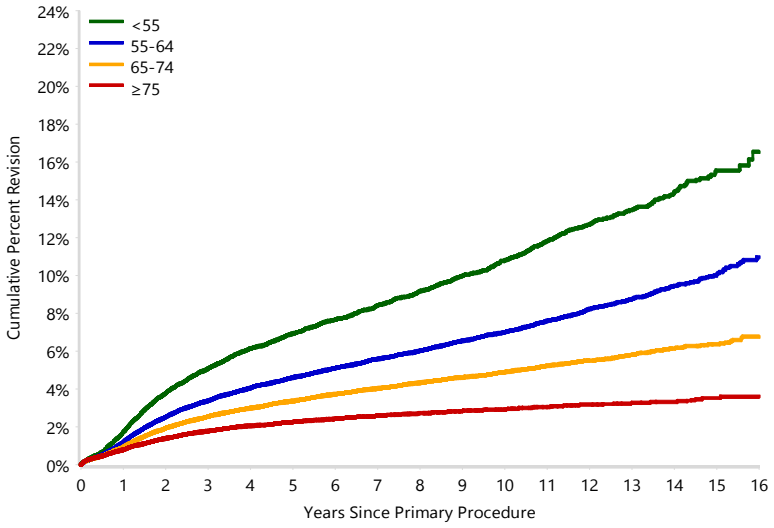
- *The Lay summary is provided to ensure that a clear, concise and easily understood explanation of the published findings is available to all those who may be interested. The Australian Orthopaedic Association (AOA) believes this is especially important*

[14] Source: AOANJRR material prepared for Department Of Health 2018

because of the high level of community interest in the Registry and the need to ensure that reports are accessible to all.

Surgeons are also increasingly using the Registry to interact with patients in consultations to provide them with accurate, up to date and unbiased data[15]. Registry data can be used to show each patient the typical outcomes for other patients with similar demographic and comorbidity profiles. An example of one of the most commonly used figures is the outcome of TKR with respect to age.

Figure 14 Cumulative Percent Revision of Primary Total Knee Replacement by Age



Source: Fig KT10 AOANJRR Annual Report 2017

[15] Source: Discussion at Australian Arthroplasty Society ASM 2015

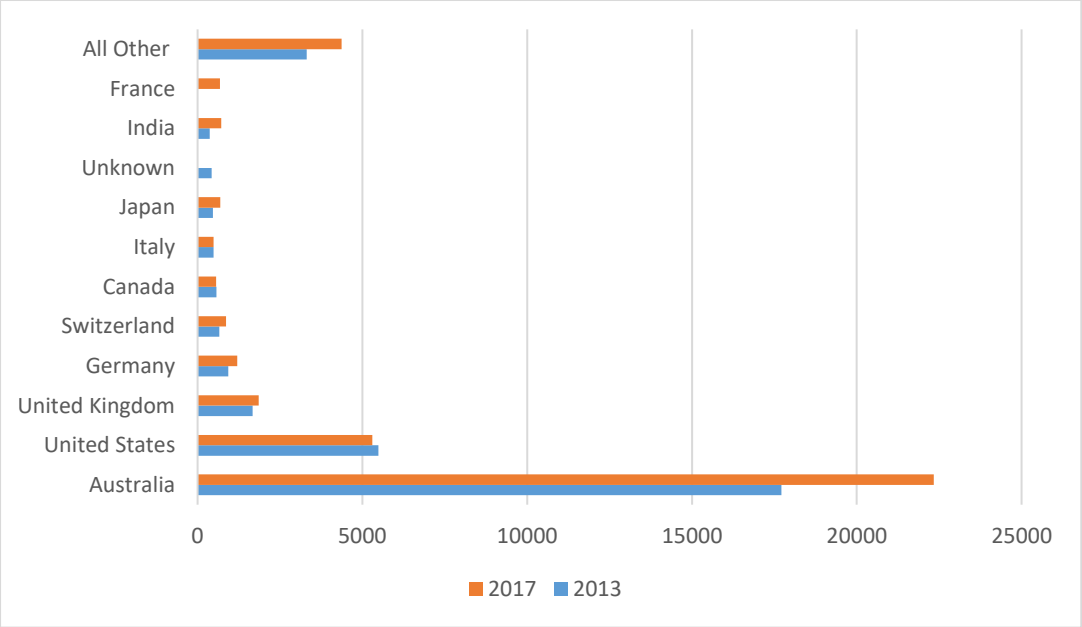
It can be difficult to convey the concept of revision of a joint replacement during a consultation with younger patients, particularly when explaining that it is preferable to delay TKR and maximise other non-operative methods of treatment for knee arthritis for as long as reasonably possible. Patients younger than 55 years of age have a higher rate of revision than older patients and this can be clearly seen and understood by patients. Other figures from the Registry Annual Report that are frequently used in surgeon/patient interactions are the benefits of cemented femoral stems in older patients, the differences in rates of revision between TKR and unicompartmental knees and to demonstrate the likely risk of complications following surgery.

Figures based on Registry data are a way to ensure that patients are well-informed and have realistic expectations for their procedure outcomes considering their own unique circumstances (354). Helping patients become more involved in the shared decision-making process enables surgeons to work towards increasing patient satisfaction (359).

9.5 - International Contribution of the AOANJRR

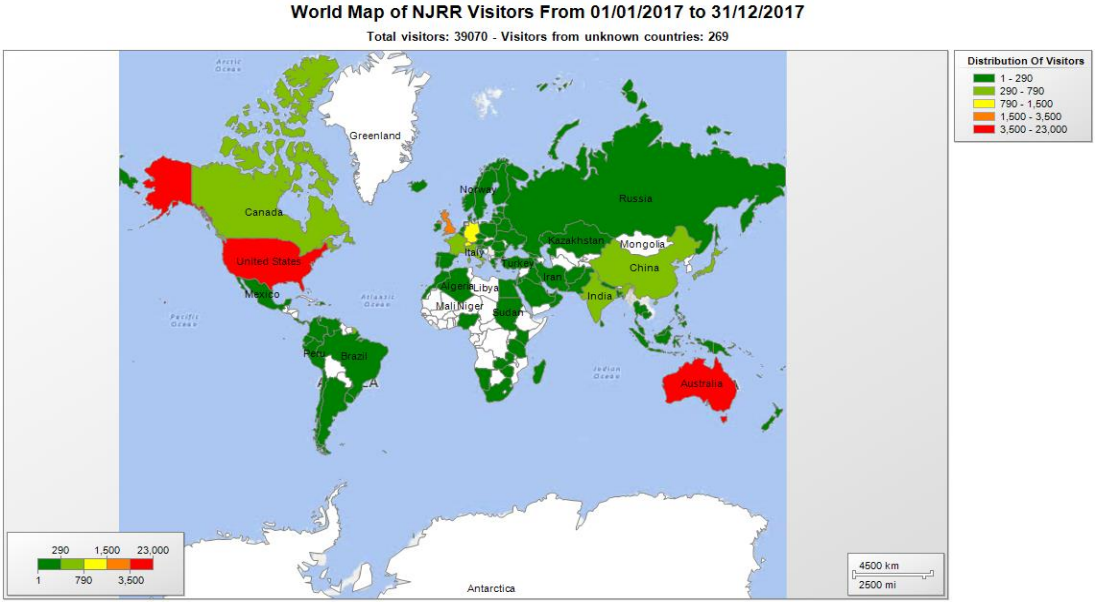
The Registry is able to use Google analytics to monitor worldwide access to the Annual Report. Australia provides over 50% of all activity followed by the U.S.A., United Kingdom and Germany. The global access by the top 10 countries is shown in Figure 9, demonstrating the change from 2013, when data were first collected, to 2017. Apart from the United Kingdom, access is highest by those countries that do not have registries, or registries not long enough established to provide more than demographic data. Recently the Registry has collaborated with Chinese orthopaedic surgeons to produce editorial articles summarizing the most recent information from the Annual Report with a focus on the application to the Chinese population (360, 361).

Fig 15 Global Access by Top 10 countries



Source: AOANJRR Internal Reporting Site prepared 2017

Fig 16 World Map of Visits to the AOANJRR Website for 2017



Source: Google analytics report prepared by AOANJRR 2017

While the primary aim of the Registry has been to improve the outcomes of joint replacement for Australian patients, there are numerous examples of the

international influence of the Registry and many of these have been discussed throughout the previous chapters. There are other areas where the AOANJRR has made major international contributions and three are discussed below:

1. Implant harmonisation: For international comparative outcomes research in joint replacement, it is important that implants have a standard terminology and their respective attributes are the same (catalogue and lot numbers) throughout the world (49, 362). The Registry Director, Professor S Graves and the AOANJRR data management staff and statisticians have made a major contribution to hip and knee implant harmonisation with the initial creation of an International Prosthesis Library (IPL). This Library of implants is currently in use in 11 registries throughout the world. An IPL Governance Committee has been established as part of the International Society of Arthroplasty Registries (ISAR) and, in June 2017, a memorandum of understanding was signed on behalf of the Advanced Medical Technology Association (AdvaMed) and ISAR. AdvaMed supports the commitment of members of its orthopaedic manufacturing sector to provide ISAR with hip and knee arthroplasty attribute data and to update data as appropriate when new devices come onto the market. ISAR has subcontracted with the American Joint Registry to implement and manage the IPL and will distribute this library to member registries. The library will facilitate outcomes analysis

and be important for the early signal detection of devices for post market surveillance across international registries.

2. The US Food and Drug Administration (FDA): Section 510(k) of the Food, Drug and Cosmetic Act requires device manufacturers to notify FDA of their intent to market a medical device at least 90 days in advance. This is known as Premarket Notification, also called PMN or 510(k). This allows FDA to determine whether the new device has substantial equivalence to a device already in the market (363). New hip and knee devices are often introduced into the US Market under Section 510(k) but historical precedent may not be adequate for pre-market assessment. The introduction of large head metal on metal THR through this process is a sobering example, and is well described in an article in the New England Journal of Medicine (364). The AOANJRR has co-operated closely with the FDA, and allowed access to a secure web portal of our Registry database in 2010. This enabled the FDA to access another source of information to aid in their assessment and monitoring of devices.

3. International Prosthesis Benchmarking: The AOANJRR has pioneered a method for identifying implant outliers that has now been adopted by at least four large international registries. It has also been closely associated with the

development of a system to rank the performance of hip and knee prostheses and establish a global benchmarking standard.

In conclusion, notwithstanding the limitations of observational data, Chapter 9 presents abundant evidence that suggests that the AOANJRR has had a substantial influence on the practice of orthopaedic surgeons, the processes of government agencies and industry, and the outcomes of joint replacement for patients.

9.6 - Appendices

Appendix 1 *Ad Hoc* Requests Summary

Year	Government	Hospital	Industry	Surgeon	Other	Follow up reports	Total
2001	1	3					**4**
2002	2	2	2	3			**9**
2003		7	2	7	1		**17**
2004	2	8	7	11	1		**29**
2005	1	15	5	11			**32**
2006	3	17	15	26			**61**
2007	2	10	23	37		9	**81**
2008	3	5	45	39	3	22	**117**
2009	2	6	51	47	3	11	**120**
2010	4	10	66	50	5	8	**143**
2011	15	10	85	76	2	12	**200**
2012	21	27	60	105	1	2	**216**
2013	12	10	123	98	3	0	**246**
2014	11	17	117	107	2	0	**254**
2015	15	30	129	123	3	0	**300**
2016	9	14	100	129	1	0	**253**
2017	4	45	106	169	2	0	**326**
Total	**107**	**236**	**936**	**1038**	**27**	**64**	**2408**

Appendix 2 Author Contract Extract with Terms and Conditions in relationship to commercial dealings.

9 LIAISON WITH INDUSTRY

9.1 The Deputy Director shall report any liaison with the Orthopaedic prostheses industry to the Director and as required through the AOANJRR Committee (and where relevant to the AOA CEO) as part of his report to the Director and the AOANJRR Committee (as required) and whenever necessary in otherwise responsibly carrying out his designated role.

9.2 The Deputy Director must not entertain or engage in any commercial undertakings with the orthopaedic prostheses industry nor accept any benefits from industry.

9.3 It is noted that the Deputy Director is involved in attracting research grant funding for approved human ethic trials. The Deputy Director warrants that he is not a beneficiary and that all funds are made available to the Epworth Research Foundation. It is also noted that the Deputy Director has declared all association with industry to the Commonwealth and is an approved Commonwealth Clinical Advisory Group representative on behalf of AOA 9.4 The Deputy Director must make an annual declaration to the AOA to the effect that he has no direct or indirect commercial dealings with industry and receives no direct or indirect benefits from the orthopaedic prostheses industry.

CHAPTER TEN

Summary and future research

The aim of this thesis was to study the impact of the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) on hip and knee replacement in Australia, determine whether joint replacement outcomes had improved since the introduction of the Registry, and critically assess the role of the Registry in this process.

Chapter one outlined the global burden of hip and knee arthritis, and THR and TKR are effective treatments when non operative measures have failed. Joint registries provide an excellent method of monitoring outcomes of these procedures. Chapter two summarised a brief history of registry development, discussed the processes involved with the AOANJRR and assessed the quality, strengths and limitations of the Registry. In Chapter three I examined the literature with respect to the aim of the thesis and the specific research questions. There is evidence that both national and regional joint registries can improve outcomes of joint replacement though these do not necessarily extend beyond their respective borders. There has been no formal examination of the impact of the AOANJRR apart from an economic assessment of the Registry. As expected, there was minimal literature pertaining to the research questions and these questions sought to address specific topics that the Registry monitored and reported on, and to link these in part with improved joint outcomes.

Chapter four addressed research question one and described the process by which the Registry identifies outlier prostheses. The Registry was the first to formalise a method for this and it has had a significant national and international impact. As a result many implants have been removed from the market, several international registries have adopted this method, (Chapter eight) and it has indirectly led to the formation of an international working group to investigate early signal detection of devices. This process has also been integrated into the regulatory framework of the TGA.

Research question two examined a specific technique of implanting a TKR and the resulting paper five was the first to demonstrate that the use of computer navigation resulted in a reduced rate of revision for younger patients. The methods for collecting this type of data, as distinct from implant identifiers has enabled the Registry to monitor a range of new techniques, including custom designed instruments, and robotic surgery. The regular feedback of improved outcomes of navigation has led to increasing use of navigation in Australia (not apparent in most other countries) and is likely to contribute to the reduced revision burden for TKR.

Research question three examined the impact of XLPE, a modified bearing surface designed to reduce wear, on the outcomes of TKR and THR. Papers six and seven demonstrated reduced rates of revision for the majority of prostheses using XLPE

compared to conventional polyethylene. Regular analyses of the benefits of XLPE in the Annual Reports from 2008 onwards has contributed to the majority of prostheses now using XLPE instead of conventional polyethylene. Again Registry data has influenced Government policy with a superior performance suffix for XLPE and a recent decision from the PLAC to remove all conventional polyethylene from re-imbursement.

Research question four examined the interaction of the Registry with the multiple stakeholders required to implement effective change of practice. I have demonstrated both a reduction in the revision burden for THR and TKR since the inception of the registry and a steadily reducing rate of revision over successive time periods. Multiple examples of registry interactions with stakeholders are discussed and the argument is presented that all these have contributed to improvements in the practice of joint replacement as a result of the Registry.

Future Research

Data Linkage

The Registry has continually endeavoured to meet the aim of improving joint replacement practice by increasing the number of analyses, improving feedback to all stakeholders and striving to provide the information in as timely a manner as possible. One of the major strengths of the AOANJRR is the use of a minimal dataset which contributes to the almost complete capture of all joint prostheses implanted in

Australia. The Registry is aware though, that other sources of information have the potential to expand and improve the analysis of our data. In order to address this limitation the AOANJRR applied for, and was awarded in 2017 an NHMRC Grant (1148106) with the University of South Australia entitled '*Enhancing joint replacement outcomes through data linkage'*. This will enable the Registry to link to other existing health data including the Department of Human Services Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) data, Australasian Association of Cancer Registries (AACR), state-based hospital data and Australasian Rehabilitation Outcomes Centre (AROC) database, and will permit more extensive and detailed analysis of the outcomes of THR and TKR. A working group of clinicians, statisticians and health services researchers has been formed to investigate key factors associated with joint replacement outcomes. These include prosthetic joint infection, long term morbidity and mortality associated with joint surgery, cancer risk, opioid use, and rehabilitation outcomes.

Registry Nested Trials

One of the criticisms by industry directed at joint registries is that they may stifle innovation and the introduction of new prostheses. An area of future research that the Registry is currently investigating is implementing Registry nested trials which involve imbedding randomised or clinical trials within a Registry framework. This has many potential benefits including, comparing a new device with all other devices or just the best devices, an accurate measure of the outcome of the device in a population independent of designers, surgeons and industry, and potential

substantial cost savings for industry in introducing a new device as the organizational framework of the Registry can be utilized for the clinical trials.

Obesity

Obesity is an increasing problem for the community and can impact on the outcomes of joint replacement. The Registry did not commence collecting data on height and weight up until 2015 so analysis of outcomes related to BMI was not possible for this thesis. Future research will examine the effects of multiple co-morbidities associated with joint replacement as outlined above and obesity is one such factor. In the 2018 AOANJRR Annual Report the Registry reported for the first time the rates of revision with respect to the six classes of BMI, as classified by the World health Organisation (365). For all hip replacements the majority of procedures are undertaken in patients who are normal or pre-obese (60.5%). This differs from patients undergoing knee replacements where the majority of patients are either pre-obese or obese class1 (62.3%). The Registry reported increased early rates of revision for patients with a higher BMI undergoing hip replacement, with revision for infection being the commonest cause for patients with obese class 1 and higher. For knee replacement the rate of revision is increased for patients with obese class 3 compared to a normal BMI, and the rate of infection increases with increasing BMI class. The relationship between BMI and joint outcomes will be explored in more detail when the Registry has longer follow up to examine whether this higher early rate of revision continues to increase.

Patient Reported Outcome Measures

While the Registry uses cumulative percent revision as a hard end point to determine the outcome of the primary procedure, lack of revision does not necessarily indicate a successful procedure and the use of Patient Reported Outcome Measures (PROMs) provides another aspect of the results of surgery which may help to improve outcomes. The Registry has commenced a national pilot project of PROMs on patients undergoing hip and knee joint replacement in over 50 hospitals in Australia. This will help the Registry to further understand other measures of success or failure which have been discussed as a limitation in Chapter nine. The collection of PROMs will also include an economic benefit and will further explore whether PROMs are related to a joint revision. This work has now commenced.

Health Economic Research

Health economic analysis is a vital part of any research into medical interventions with joint replacement being no exception Now that it is established that the outcomes of hip and knee replacement have been improved by the AOANJRR, an economic analysis of the Registry warrants further research but was outside the scope of this Thesis. As mentioned in Chapter 5.3 one project is underway to analyse the cost effectiveness of computer navigation in association with the Health Economic Department at the University of Melbourne

Future research will directly inform the health system and clinical policy and will likely result in further improvements for patients undergoing joint replacement surgery in Australia and globally.

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