Institution: University of Bristol		
Unit of Assessment: 2) Public Health, Health Services and Primary Care		
Title of case study: Rolling programme of research, centred on the National Joint Registry, to improve the outcomes of hip and knee replacements worldwide		
Period when the underpinning research was undertaken: 2012 - 2019		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting HEI:**
Ashley Blom	Professor of Orthopaedics	2003 – present
Michael Whitehouse	Professor of Orthopaedics	2011 – present
Yoav Ben-Shlomo	Professor of Epidemiology	1996 – present
Andrew Judge	Professor of Translational Statistics	2017 – present
Vikki Wylde	Associate Professor	2007 – present
Linda Hunt	Senior Research Fellow	2012 – present
Adrian Sayers	Senior Research Fellow	2007 – present
Erik Lenguerrand	Research Fellow	2012 – present
Elsa Marques	Research Fellow	2012 – present
Jonathan Evans	Academic Clinical Lecturer	2018 – present
Period when the claimed impact occurred: 2014 – 2020		
Is this case study continued from a case study submitted in 2014? No		

1. Summary of the impact

University of Bristol research utilising trials, joint registry analysis and evidence synthesis has profoundly changed the practice of joint replacement globally. It has led to:

- The abandonment of stemmed metal-on-metal hip replacements and hip resurfacing in women
- A ten-fold reduction in the use of hip resurfacing in men
- A 50% increase in use of unicompartmental knee replacements
- Increased utilisation of spinal anaesthetic and posterior surgical approach to the hip in order to decrease post-operative mortality
- Change in patient care pathways to reduce pain, improve function and adopt cost-effective treatments

These changes have led to a substantial reduction in revision rates (by approximately half) for hip and knee replacements in England and Wales, as captured by the National Joint Registry, decreased risk of mortality for patients undergoing joint replacement and improved patient outcomes.

2. Underpinning research

Research at the University of Bristol (UoB) has changed the practice of joint replacement worldwide through a comprehensive programme of research using a combination of research methods centred on the National Joint registry (NJR) for England and Wales. In addition, the research team have developed and implemented methods for monitoring surgeon, unit and implant performance, thereby ensuring iterative and ongoing improvement in the delivery of care.

1. *Identification of failing implants*

UoB research published in 2012 (1), revealed catastrophically high failure rates in stemmed metal-on-metal hip replacements, as well as in hip resurfacing in women. This led to the worldwide abandoning of these procedures. Further research conducted by the research team in 2018 found that this type of hip replacement was responsible for over 8,000 excess revision procedures at a cost of over GBP100 million in England and Wales alone.

2. *Identifying the most clinically and cost-effective implants*

There is large variation in performance between different implants that are commonly used for joint replacement. The research team utilised network meta-analysis and health economic modelling (2) to determine that the most clinically and cost-effective implants for hip replacement are implants fixed with cement and use small diameter heads. Using these implants for all patients would save between GBP252 million to GBP281 million in England and Wales in the next decade. The NJR annual reports show an ongoing decline in usage of less effective and cost-effective uncemented hip replacement stems.

3. *Reducing perioperative mortality for patients undergoing hip and knee replacement*

The research team demonstrated that partial knee replacements were associated with a lower risk of mortality than total knee replacement (3) and that they lasted on average over 25 years (4). This led to the increased utilisation of partial knee replacements. The research team's publications in The Lancet (3, 5) showed that chemical and mechanical thromboprophylaxis, spinal anaesthetic and the posterior surgical approach for the hip, all reduce the risk of mortality for patients undergoing joint replacement. NJR data show a continuous increase in use of these three co-interventions.

4. *Reducing pain after joint replacement*

Approximately 20% of patients experience long-term pain after hip and knee replacement. The UoB research has demonstrated that the injection of local anaesthetic around the surgical site during joint replacement leads to decreased long-term pain after hip, but not knee, replacement and has also established the cost-effectiveness of this intervention for hip replacement (6).

3. References to the research

1. Smith AJ, Dieppe P, Vernon K, Porter M, **Blom AW**; on behalf of the National Joint Registry of England and Wales. Failure rates of stemmed metal-on-metal hip replacements: analysis of data from the National Joint Registry of England and Wales. *Lancet.* 2012; 379(9822): 1199-204. DOI:10.1016/S0140-6736(12)60353-5

2. Fawsitt CG, Thom HHZ, Hunt LP, Nemes S, **Blom AW**, Welton NJ, et al. Choice of Prosthetic Implant Combinations in Total Hip Replacement: Cost-Effectiveness Analysis Using UK and Swedish Hip Joint Registries Data. *Value Health.* 2019; 22(3): 303–12. DOI:10.1016/j.jval.2018.08.013

3. Hunt LP, Ben-Shlomo Y, Clark EM, Dieppe P, Judge A, MacGregor AJ, Tobias JH, Vernon K, **Blom AW**, on behalf of the National Joint Registry for England and Wales. 45-day mortality after 467,779 knee replacements for osteoarthritis from the National Joint Registry for England and Wales: an observational study. *Lancet.* 2014; 384(9952): 1429-36. DOI:10.1016/S0140-6736(14)60540-7

4. Evans JT, Walker RW, Evans JP, **Blom AW**, Sayers A, **Whitehouse MR**. How long does a knee replacement last? A systematic review and meta-analysis of case series and national registry reports with more than 15 years of follow-up. *Lancet.* 2019; 393(10172): 655-663. DOI:10.1016/S0140-6736(18)32531-5
5. Hunt LP, Ben-Shlomo Y, Clarke EM, Dieppe P, Judge A, MacGregor AJ, Tobias JH, Vernon K, **Blom AW** on behalf of the National Joint Registry for England, Wales and Northern Ireland. 90-day mortality after 409,096 total hip replacements for osteoarthritis, from the National Joint Registry for England and Wales: a retrospective analysis. *Lancet.* 2013; 382: 1097-1104. DOI:10.1016/S0140-6736(13)61749-3

6. Wylde V, Lenguerrand E, Gooberman-Hill R, Beswick AD, Marques E, Noble S, Horwood J, Pyke M, Dieppe P, **Blom AW**. Effect of local anaesthetic infiltration on chronic postsurgical pain after total hip and knee replacement: the APEX randomised controlled trials. *Pain.* 2015; 156(6): 1161-70. DOI:10.1097/j.pain.0000000000000114

4. Details of the impact

According to the World Health Organisation, musculoskeletal conditions are the leading contributor to global disability. In the UK, treatment consumes 30% of NHS primary care consultations and 25% of surgical interventions. Two of the most common interventions are hip and knee replacement, with over 100,000 each performed in England and Wales annually. Hip and knee replacement rates range between 150 and 300 each per 100,000 in developed countries. Annual NHS expenditure on hip and knee replacements is over GBP1 billion and over GBP3 billion in the United States.

Around 10% of joint replacements fail, requiring complex revision surgery, and 20% of patients experience long-term pain. NICE provide recommendations on implants used in joint replacement, surgical approaches and the use of injections around the surgical site on the basis of the UoB research in order to reduce revision rates, improve outcomes and decrease pain. The UoB research showing that metal-on-metal hip replacements should not be used, and will avoid 8,000 excess revisions, led to the virtual cessation of the use of these implants in the UK, Australia and Canada by 2018.

1. Identifying failing implants and changing practice

NICE identifies acceptable revision rates as 5% at 10 years; the research team found rates far in excess of this when metal-on-metal stemmed hip replacements (1) and hip resurfacings were used. This led to the MHRA issuing a Medical Device Alert [Ai], reinforced by the British Orthopaedic Association and British Hip Society [Aii], recommending against their use in all but exceptional circumstances and that targeted surveillance should occur for any such recipients. The NICE Technology appraisal guidance [Ci] cites UoB's work (1) and evidence from the NJR annual reports [B], in its recommendations on revision rates and implants for hip replacement.

The US Food and Drugs Administration has cited UoB's research (1) and further work on the risk of cancer following implantation of metal-on-metal hip implants in its recommendations on market approval for hip replacements (FDA 2013) and Biological Response to Metal Implants [D]. The FDA now approves no stemmed metal-on-metal hip replacement systems and only two resurfacing systems for marketing in the US. Of those approved, one has strictly limited indications in the manufacturer Field Safety Notice informed by UoB's recommendations and findings. The New Zealand Medicines and Medical Devices Safety Authority (2013) and the European Commission Scientific Committee on Emerging and Newly Identified Health Risks

(2014) [E], have issued guidance citing UoB's research on the outcomes of metal-on-metal hip replacements, including research on the risk of developing cancer, in their recommendations. Prior to publication of UoB's research (1), over 1 million metal-on-metal total hip and resurfacing implants were implanted worldwide. The research team identified that the use of approximately 70,000 of these implants in the NJR were responsible for 8,000 excess revisions, at a cost of over GBP100 million. This equates to over 110,000 avoidable revisions worldwide. UoB's recommendations have led to the virtual cessation of the use of these implants (UK: 466 in 2018 vs 13,630 in 2008 [B]; Australia: 1% (2013-2018) vs 9.8% (2006-2012) (peak 17% 2007) [F]). Citing UoB's work, the FDA recommends the use of Unique Device Identifiers [G] to allow monitoring and prevent recurrence of the devastating impact of these implants. The NJR, for which the research team have been responsible for statistical analysis and specialist research for over a decade, was cited as a "global exemplar" of medical device registries by the Under Secretary of State for Health and Social Care, Jo Churchill MP, in her report to Parliament (2020).

2. Identifying the most clinically and cost-effective implants

The research on the cost-effectiveness of hip implants (2) has informed recommendations of the Analysis and Policy Observations (APO) of Australia and New Zealand 2019 [Hi], and the research on how long hip replacements last has been cited by the Dutch Institute of Health [Hii]. In the UK, the Getting it Right First Time (GIRFT) initiative is a leading NHS Improvement programme. Data utilised by GIRFT are provided by the UoB team's analysis of NJR data [I]. The programme has adopted UoB's recommendations in terms of implant selection (2, 5) [I], and change in clinical practice is demonstrated by data from the NJR which demonstrate increased use of cemented stems and abandonment of larger heads [B]. If all hip replacements performed were conducted as cemented hip replacements, this would save between GBP252 million and GBP281 million in England and Wales alone over the next decade. The success of the GIRFT programme, underpinned by UoB data, has seen it rolled out across all surgical specialties in the UK.

3. Improved patient care and reduced perioperative mortality

The UoB research has explored treatment factors that are associated with peri-operative mortality for patients undergoing hip and knee replacement. The research (1) was cited by NICE Technology Appraisal guidance [TA304] (2014) providing evidence-based recommendations on artificial hips and hip resurfacing for treating end-stage arthritis of the hip in adults [Ci], specifically in making recommendations aimed at decreasing peri-operative mortality. The latest NICE guidance on hip and knee replacement [Cii] cites the UoB research on surgical approaches and anaesthesia to improve outcomes for patients undergoing joint replacement. These recommendations have been widely adopted as demonstrated by NJR data, showing an increase in the use of mechanical and chemical thromboprophylaxis and the use of spinal anaesthetic for total hip replacement [B]. In 2011, prior to the UoB team's published research, the percentage of patients not receiving chemical prophylaxis for hip replacement was 13% (~ 13,000 patients); this fell to 2% in 2019. For knee replacement, the proportion not receiving chemical prophylaxis fell from 15% (~ 15,000 patients) in 2011 to 1% in 2019. The proportion of patients undergoing hip replacement who received a spinal anaesthetic in the period 2008-2012 was 42%, increasing to 59% in the period 2013-2017 (~17,000 more cases per annum); the corresponding proportions for knee replacement were 43% and 57% respectively (~ 15,000 cases per annum) [B]. Also, 90-day mortality rates have decreased by 7% in hip replacement and 10% for knee replacement in the period 2014 to 2019 [B].

4. Reducing pain after joint replacement

The UoB publications showing the efficacy of peri-operative wound infiltration in reducing post-operative pain (6) have contributed to widespread adoption of these techniques, particularly in rapid recovery pathways. The research team's work was cited in guidance from the Canadian Agency for Drugs Technology and Health [J] and NICE guideline NG157 [Cii] in the UK, with NICE now recommending peri-operative wound infiltration in all patients.

5. Sources to corroborate the impact

[A] i) MHRA (2017). Medical Device Alert: All metal-on-metal (MoM) hip replacements: updated advice for follow-up of patients
ii) British Orthopaedic Association (BOA) (2017). BOA/BHS Statement on Metal on Metal Hip Implants – Update from the MHRA

[B] NJR (2020). 17th Annual Report 2020: Surgical data to 31st December 2019

[C] i) NICE (2014). Technology appraisal guidance [TA304]: Total hip replacement and resurfacing arthroplasty for end-stage arthritis of the hip
ii) NICE (2020). NG157: Joint replacement (primary): hip, knee and shoulder

[D] FDA (2019) White paper: Biological Responses to Metal Implants, *Cites [1].*

[E] European Commission (2014). Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) Opinion on: The safety of Metal-on-Metal joint replacements with a particular focus on hip implants

[F] Australian Orthopaedic Association (2019). Australian Orthopaedic Association National Joint Replacement Registry 20th Annual Report

[G] FDA (2014). Unique Device Identifiers (UDIs): A Roadmap for Effective Implementation

[H] i) Grattan Institute (2019). Saving private health 1: reining in hospital costs and specialist bills, *Cites [2].*
ii) Rijksinstituut voor Volksgesondheid en Milluw (Dutch Institute of Health) (2019). Verkenning Economische Evaluaties Implantaten (Exploratory Study on Economic Assessments of Implants)

[I] i) GIRFT / BOA (2015). A national review of adult elective orthopaedic services in England
ii) GIRFT (2020). Getting It Right in Orthopaedics
GIRFT reports acknowledge Blom and use of NJR datasets

[J] Canadian Agency for Drugs Technology and Health (CADTH) (2017). CADTH Issues in Emerging Health Technologies, Outpatient (Same-Day) Total Hip Replacement, Issue 152.