PERIPROSTHETIC FEMORAL FRACTURES IN TOTAL HIP ARTHOPLASTY

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ABSTRACT

Introduction

Periprosthetic Femoral Fractures (PFF) are a complication of Total Hip Arthroplasty (THA) which are technically challenging to treat and associated with significant morbidity. There is a lack of epidemiological evidence relating to these common fractures, which are thought to be an increasing problem in orthopaedic practice. This thesis aims to assess the temporal trends, the risk and risk factors as well as the outcome of treatment of PFF in THA.

Methods

This thesis used a combination of systematic review of existing evidence and analysis of the National Joint Registry (NJR), the world's largest arthroplasty registry. Temporal trends of revision arthroplasty for PFF were assessed using NJR data to calculate "revision burden" and incidence of first revision in terms of implant-years at risk, by year. The risk and risk factors for PFF were assessed using a systematic review of high volume observational studies followed by analysis of NJR data of primary THAs performed in England and Wales. A novel flexible parametric approach was used to assess risk factors and estimate 'real-life' probabilities of revision for PFF in the presence of multiple competing risks (death and revision for indications other than PFF). A systematic review of treatment of PFF in the presence of a loose femoral stem (Vancouver B2 and B3 fractures) was performed to compare outcomes based on treatment modality including implants used and fracture type.

Finally, outcomes of first revision surgery for PFF were analysed based on NJR data using flexible parametric competing risk models to determine risk factors for failure and estimate the risk of further revision and death.

Thesis Findings

The results of the temporal trends study indicated that both revision burden and incidence of first revision for PFF have demonstrated an increase in England and Wales despite showing decreases for other indications for revision.

For intra-operative fracture, increasing age, female gender and cementless stem fixation were associated with a higher risk of PFF based on systematic review and NJR data. For post-operative fractures, the NJR data indicated that increasing age, male gender and primary THA for neck of femur fracture were associated with a higher risk of revision for PFF. Implant factors were complex with significant difference in risk between stem designs as well as implant-brand specific differences. The results provide “real-life” estimates of probability of PFF revision for patient-implant groups.

The systematic review of treatment of Vancouver B2 and B3 fractures demonstrated overall poor outcomes particularly when revision arthroplasty was not used. A suggested minimum dataset for studies reporting outcomes of periprosthetic fracture was devised to improve comparisons between institutional studies. Analysis of NJR data relating to first revisions for PFF, suggested higher overall mortality compared with other common indications

for revision. Risk of further revision was significantly higher after first revision for PFF compared to revision for aseptic loosening.

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GLOSSARY

ASA	American Society of Anaesthesiology
CI	Confidence Interval
NJR	National Joint Registry
OA	Osteoarthritis
PFF	Periprosthetic Femoral Fracture
SD	Standard Deviation
PROMS	Patient Reported Outcome Measures
THA	Total Hip Arthroplasty

DEFINITION OF COMMON TERMS

Acetabular Component	The part of the hip replacement which is inserted into the acetabulum.
Arthroplasty	Operation where a native/natural joint is replaced with an artificial one. Total hip arthroplasty and total hip replacement can be used synonymously.
Arthroplasty/Joint Registry	National or Regional bodies responsible for collecting and monitoring arthroplasty provision.
ASA Grade	American Society of Anesthesiology scoring system to assess fitness for surgery: 1=fit and healthy, 2=mild disease, 3=incapacitating systemic disease, 4=life threatening disease, 5=expected to die within 24 hours with or without surgery.
Bearing Surface	The two surfaces that articulate with each other in a joint replacement.
Bilateral Arthroplasty	Joint replacement on right and left in the same individual.

Brand (of prosthesis)	The manufacturers product name for an implant, e.g. The Exeter V40 femoral stem.
Cemented	Prostheses designed to be fixed to bone using cement.
Cementless	Prosthesis designed to be fixed to bone without cement.
Femoral Stem or Stem	The part of the hip replacement that is placed into the femur.
Modular	Individual component composed of more than one piece. e.g. modular acetabular shell with a modular liner.
Primary Hip Arthroplasty	The first time a total joint replacement is performed on an individual joint in an individual patient.
Revision Hip Arthroplasty	Surgical procedure to remove and usually replace one or more components of a hip replacement.

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1 Introduction

1.1 Total Hip Arthroplasty

1.1.1 The Hip Joint

The hip is a ball and socket synovial joint, with stability conferred primarily by the nature of the matched contact between the spherical shape of the femoral head and the cup-like acetabulum. Secondary stabilisers include the hip joint capsule, ligaments and muscle groups crossing the joint.[1] The load supported by the hip joint is greater than three times body weight while ambulating on a level surface.[2]

1.1.2 Total Hip Arthroplasty (THA)

Total Hip Arthroplasty (THA) is widely seen as one of the twentieth century's most important developments in the field of surgery and has one of the largest effect sizes of any medical intervention. Philip Wiles of London's Middlesex Hospital developed and undertook the first THA in 1938.[3] The pioneer of modern day hip arthroplasty is Sir John Charnley, who in 1957 designed a low friction THA consisting of a stainless steel sphere articulating in a polytetrafluoroethylene cup.[4] However, it was not until he developed the ultra-high molecular weight polyethylene cups in the 1960s that more successful outcomes of THA were achieved (Figures 1 & 2). In addition, he introduced the use of polymethylmethacrylate bone cement to fix THR prostheses to

bone. Results of Charnley's first generation THA demonstrated survivorship of 81% and 77% at 25 years follow-up, demonstrating good outcomes were achieved even with early THA design and operative technique.[5,6]

In the early years of THA surgery, the indications were narrow and the vast majority of patients were elderly with severely restricted function. Indications have since widened, partly due to low failure and complication rates which have led to a higher number of younger patients with moderate limitation in quality of life related to the hip, undergoing THA.[7]

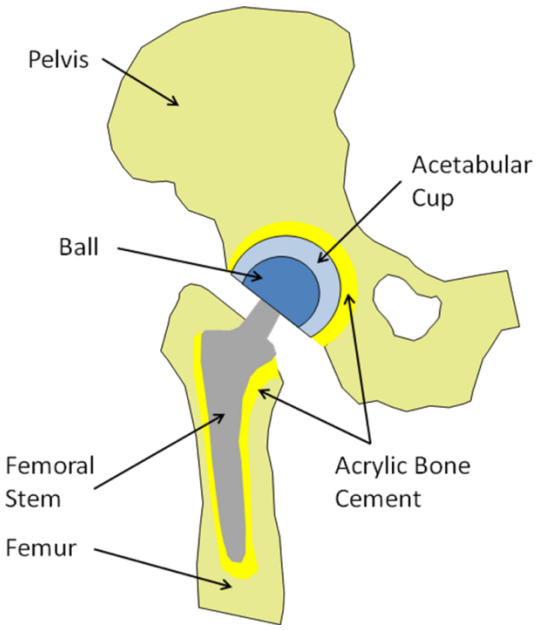


Figure 1-1 Schematic of THA Design (Reproduced from [8])



Figure 1-2 Charnley's low friction arthroplasty – cemented metal stem with polyethylene cup

1.1.2.1 Cemented THA

Cemented THA relies largely on the interface between bone and cement in order to provide robust fixation and transmit torsional and other forces between the implant and bone. As the surgeon is responsible for manufacturing the bone-cement-implant composite at the time of surgery, the process is dependent on technique.

1.1.2.1.1 Cementation Technique

The method of cementation has changed significantly over the years with first generation techniques focussing little on preparation of the femoral and acetabular bony surfaces. The sequelae of this were inadequate cement penetration into cancellous bone and a deficient, incomplete cement mantle. Bone cement acts more like a grout rather than a glue, with implant fixation occurring via mechanical interlock as opposed to adhesion. Cement pressurisation has been demonstrated to enhance its bony penetration leading to higher tensile and shear strengths at the interface between bone and cement [9,10]. It has also been shown that cleaning of the bony surfaces prior to cement

insertion further improves cement penetration, resulting in superior shear strength.[11,12]

Retrograde cement insertion using a cement gun and a femoral cement restrictor to plug the intramedullary canal and augment cement pressurisation were introduced as part of the second generation cementation technique. Third generation cementing techniques currently employed involve cleaning of the endosteal bone with pulsatile lavage, vacuum mixing to reduce cement porosity and sustained cement pressurisation.

1.1.2.1.2 Cemented Stem Design

Cemented femoral stem design is guided by two distinct philosophies; 'polished/loaded taper' or 'forced closed fixation' and 'composite beam' or 'shaped-closed fixation'.[13-15] Both philosophies aim to allow transmission of axial and torsional load to the cement mantle and bone while avoiding detrimental peak stresses and extreme micro-motion. Furthermore, with regards to cemented stem design they intend to provide a mechanically stable construct even with repetitive loading over a long period. Figure 1.3 is a photograph of the two of the most commonly used cemented stems in the UK; the Exeter stem which is a polished taper design (Stryker, UK) and the Charnley Stem, a composite beam type stem (DePuy-Synthes, USA).



Figure 1-3 The Exeter Stem, Stryker, UK (left) and the Charnley Stem, DePuy-Synthes, USA (right)

Polished taper stems are tapered in two or three planes, allowing the stem to be wedged in the cement mantle during axial loading[16-18] and decreasing the peak stress along the proximal to distal cement mantle.[19] The taper design allows initial subsidence of the stem until "radial compressive forces are created in the adjacent cement and transferred to the bone as hoop stress" which balance the axial loads and prevent further subsidence.[15] A distal centraliser filled with air is attached to the stem tip, allowing the stem to subside to a stable position and hence preventing excess stress in the adjacent cement mantle around the tip.

Polished taper stems are generally polished to facilitate gradual subsidence to a stable point. Stem features which prevent subsidence within the cement mantle are not compatible with the polished taper design. These include the use of collars, canal filling or anatomic shape and rough surface finish.[13] Figure 1.4 shows a radiograph of a cemented polished taper stem demonstrating the taper design allowing gradual subsidence within the cement mantle.



Figure 1-4 Post-operative radiograph of a cemented polished tapered stem (CPT, Zimmer, Warsaw, Indiana, USA)

The composite beam philosophy requires rigid fixation of the stem to the cement. The cement acts as a grout filling the gaps between the rough surface of the prosthesis and the trabeculae of the bone. This forms a cantilever construct with forces transmitted between the stem and bone via the cement grout. Any subsidence will lead to destruction of the cement mantle and interfere with the strength of the interface. This results in both the direct loss of polymethylmethacrylate, and micromotion that produces both polymethylmethacrylate and metal debris which can eventually cause implant failure.

Both straight and anatomical stems based on the composite beam principle have been demonstrated to be successful.[20-22] The cement mantle surrounding the femoral stem can be either thick or thin, which is determined by the size of the prosthesis compared to the broach (instruments of sequentially increasing size used in THA to widen the femoral intramedullary canal to allow insertion of the stem). A stem which is canal filling is not undersized compared to the last broach used and is inserted with a thin layer of cement. With this type of design, areas of stem contact with cortical bone help provide implant stability. Figure 1.5 demonstrates an example of composite beam cemented fixation.

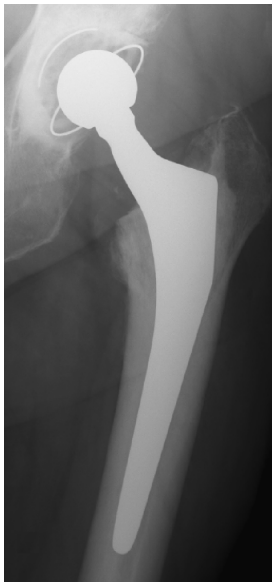


Figure 1-5 Radiograph of a composite beam type stem (Vectra, Biomet, Warsaw, Indiana). Notice the line-to-line fixation with a thin cement mantle.

Despite it appearing logical that rough surface finish in composite beam designs would improve stability, in practice, micromovement of the stem can lead to the formation of cement and metal debris. In the case of canal filling stems, this can be particularly detrimental as the debris can be transmitted from areas of stem-cortex contact to the bone cement-bone interface, leading

to osteolysis and ultimately stem loosening. Furthermore, rough surface finish results in higher shear and tensile stresses at the cement bone interface. Hence, polished stem designs are preferred even for stems based on a composite beam philosophy.

Although individual cemented stem products can be grouped into polished taper or composite beam in terms of design philosophy, there are small but potentially significant difference within these groups which may influence their properties once implanted in bone and hence the overall outcome.

1.1.2.2 Cementless THA

Cementless THA design was introduced initially to tackle the early failures due to loosening of cemented THAs caused by osteolysis, which was thought at the time to be caused by 'cement disease'. Hence, focus was shifted to designing THAs which do not require cement for fixation.

The design of cementless THA components is such that they provide sufficient initial stability while promoting bone osseointegration onto or into the prosthesis[23]. The surfaces of implants are either manufactured with a porous coating or as a minimum a rough surface to help hold the implant in place. Following biological bony fixation which can take some months, the implants enable normal transfer of biomechanical forces across the joint.

1.1.2.2.1 Cementless Stem Design

Currently used cementless femoral stems are either fully or partially coated (in the metaphyseal region) with a porous surface (Figure 1.6) aiming for bony ingrowth or ongrowth. Early designs of fully porous coated cylindrical stems were associated with greater proximal stress shielding (decrease in bone density as a result of decreased loads or stress placed on the bone by an implant), bone loss and increased cortical atrophy. Proximal coated stems which remained cylindrical distally were designed to improve this by promoting physiological loading and therefore reducing stress shielding.[24]



Figure 1-6 Fully porous coated stem (Corail, DePuy, USA) (left) and partially coated (Osteonics, USA) (right).

Cementless stems are generally broader than cemented to allow a press-fit when inserted. They rely on metaphyseal fixation, metaphyseal-diaphyseal junction fixation, diaphyseal fixation or a mixture of the three.[7] In addition, despite the availability of many cementless stems, the overall shape can be classified as either anatomic, tapered or cylindrical. Anatomic stems are curved in the antero-posterior plane to match the natural bow of the femur.

The concept behind the anatomic shape is to enhance initial stability of the stem and therefore enable bony ingrowth. Tapered stems are based on proximal cancellous bone ingrowth and initial three-point fixation to confer early stability. Cylindrical cementless stems rely on cortical support distally to gain initial stability. Fixation distally also protects against torsional forces due to a higher lever arm. Cylindrical stems are therefore canal-filling, requiring a higher diameter.

1.1.2.2.2 Stem Collars

Both cementless stems and composite beam cemented stems may have a collar at the neck, which is designed to rest on the calcar (the inner medial bony cortex). The primary aim of collars is to prevent undesirable stem subsidence within the femoral canal. By transferring load directly from the implant to the calcar or the medial cement mantle for cemented stems, theoretically they may decrease stress shielding in the proximal femur. However, there is some controversy over whether collars add a useful advantage in terms of outcome. A number of prospective randomised trials have found no significant difference in implant survival at up to 11 years between collared and collarless designs.[25-27]

1.1.2.2.3 Bone Quality and Structural Phenotype of Proximal Femur

The Dorr classification was designed to aid the assessment of proximal femoral bone quality from radiographs and guide surgeon decision-making for using cemented or cementless femoral stem fixation in THA.[28] Dorr suggested three distinct morphologies using a combination of quantitative and qualitative

measures. The quantitative measurement used is the ratio of the canal diameter at the level of the lesser trochanter divided by the canal diameter 10 centimetres below this level (canal ratio). The qualitative component relies on a visual assessment of the bony cortices on antero-posterior (AP) and lateral radiographs. Table 1.1 demonstrates the Dorr femoral phenotypes and the suggested THA stem fixation for each.

Table 1-1 Dorr Classification of Proximal Femoral Bone Quality and Structure

Dorr Type	Canal Ratio	Bony Cortices	Suggested Stem Fixation
A	<0.5	Cortices seen on both antero-posterior and lateral radiographs	Cementless
B	0.5-0.75	Thinning of posterior cortex on lateral radiograph	Cementless
C	>0.75	Thinning of both cortices on both radiographic views	Cemented

1.1.2.3 Acetabular Component Design

In terms of design, the traditional cemented polyethylene cup has changed very little over the years. The flange around the cup (Figure 3) is an added feature introduced to allow cement containment and thus aiding pressurisation.



Figure 1-7 Flange around polyethylene cup (Exeter Contemporary Cup, Stryker, USA)

Cementless acetabular cups were designed to address the problem of loosening of cemented cups. Charnley's results demonstrated that 14% of cemented cups showed radiographic signs of loosening at 12-15 years.[29] Most cementless acetabular components are fully porous-coated to allow bony ingrowth and biologic fixation, and are press-fit for initial stability. Cementless cups with screws and pegs are also available for stability.

1.1.2.4 Bearing Surfaces in THA

The bearing surface refers to the articulation between the femoral head of the THA and the acetabular cup component. The ideal bearing has minimal wear characteristics and an adequately large head to confer a low risk of dislocation. Any debris resulting from the bearing surfaces should not lead to an adverse reaction in the host tissues. Low friction should be a property of the materials used in order to reduce forces applied to the implant-bone interface and the articulation should not generate any noise. In addition, the materials should be strong enough to resist fracture and not at high risk of developing scratches.

The main bearing couplings used in THA include:

Hard-on-soft couples:

- Metal (femoral head) on conventional non-cross-linked ultra-high molecular weight polyethylene (UHMWPE) – high rates of wear
- Metal (femoral head) on highly cross-linked polyethylene – significantly lower rates of wear compared to UHMWPE
- Ceramic (femoral head) on highly cross linked polyethylene – lower wear compared to metal.

Hard-on-hard couples:

- Metal-on-metal (MoM) – significantly lower wear rates than metal on polyethylene but MoM wear debris leads to host inflammatory response which is strongly associated with the development of

pseudotumours in local tissues and early THA failure. Systemic dissemination of metal ions has also been widely reported.

- Ceramic-on-Ceramic – lowest wear rates but due to brittle properties of ceramic, there is higher risk of component fracture.

1.1.2.5 Trends in Usage of Cemented and Cementless THA Designs

As the volume of THAs performed worldwide increases, trends in implants used continues to evolve. In the US, cementless THA has been reported to account for 93% of all THAs[30] with good published outcomes in the literature[31]. In other countries, there is variation in use of cementless and cemented THA. In Sweden, for example, 85% of THAs were cemented in 2010.[32] Troelson and colleagues reported an increase in cementless THA fixation in 7 countries based on national arthroplasty data between 2006 and 2010.[32] In England and Wales, the proportion of fully cemented (stem and acetabulum) THA has almost halved and that of fully cementless nearly doubled between 2004 and 2017[33]. Interestingly, over the same time period the use of hybrid (cementless acetabulum, cemented stem) implants has risen 3-fold[33] (Figure 1.8). This is likely related to a combination of perceived higher rates of acetabular loosening with cemented polyethylene cups[34,35], excellent long term survivorship of cemented stems[36] and increased use of alternative bearing surfaces such and ceramic-on-ceramic.[33]

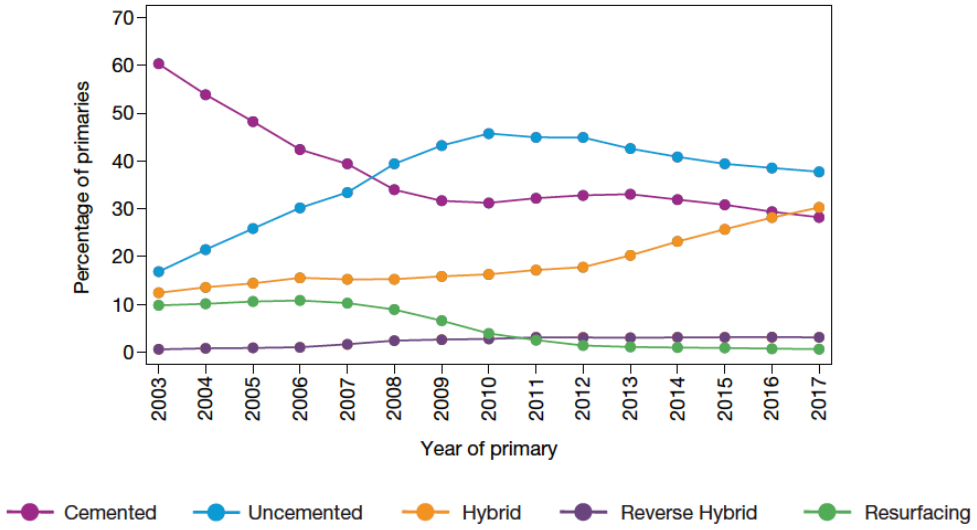


Figure 1-8 Temporal changes in primary hip arthroplasty by fixation in England and Wales[33]

1.2 Failure of THA

1.2.1 Outcome Assessment

Outcome assessment in the earlier years of THA was largely surgeon-based using scoring systems. The Merle d'Aubigne and Postel score, which was modified by Charnley[37], and the Harris hip score[38], are still commonly used scores which were adopted to assess outcome after THA. The keys limitation of surgeon-based scores is that they combine clinical, radiological and subjective patient reported outcomes which cannot be added quantitatively to provide a comparable measure.[7] They also do not necessarily measure outcomes which are important to the patient.

Dobbs introduced survivorship analysis in orthopaedics in 1980[39] as a method of assessing the long-term outcome of arthroplasty procedures. Revision of Implant (surgery to remove and replace the original joint replacement) is the universally defined endpoint for survivorship analysis in arthroplasty and allows comparison of outcomes for different implants and between different patient groups. However, a limitation of survivorship analysis with revision surgery as the end-point is that it does not take into account patient satisfaction, symptoms, function or radiographic measures of implant failure.

As significant restriction in quality of life related to the hip is the primary indication for THA, patient reported outcome measures (PROMS) developed using item response theory are widely accepted as the best way of evaluating satisfaction after surgery and quality of life status. There are a variety of validated generic quality of life PROMS scores including short form 12 (SF-12)[40] and disease specific such as Western Ontario and McMaster University Osteoarthritis Index (WOMAC)[41]. In addition, PROMS specific to the hip joint have been developed and validated for THA. The most commonly used in the UK is the Oxford Hip Score[42]. In Randomised Controlled Trials, PROMS provide a useful outcome measure but are not always achievable in long-term observational or epidemiological studies. Furthermore, as they are not patient-specific, they do not take into account patient expectation with regards to outcome, which in younger, physiologically fitter patients are often significantly different from expectations in older less mobile individuals. In

addition, the 'Ceiling Effect' makes it difficult to distinguish between well-functioning individuals.

1.2.2 Arthroplasty Registries

Arthroplasty registries were initially developed to monitor performance of new prostheses used in joint replacement surgery. However, the breadth of data collected and an increase in volume of information available has led to wider uses. The key objectives of an arthroplasty registry are to provide robust information relating to the practice of joint replacement surgery in the region the registry is active, audit outcomes and allow an analysis of factors contributing to outcome at national, unit and individual surgeon level.[43] Rising healthcare costs and an increasing need to demonstrate cost-effectiveness of interventions have led to some use of arthroplasty registry data to guide implant selection. The Australian Orthopaedic association have estimated that information from their registry could lead to a reduction in revision rates equating to a saving of $10 million per year.[43]

There are national joint registries establishes in Australia, New Zealand, Finland, Norway, Sweden and the UK. There are numerous stakeholders in registry data, which includes surgeons, patients, purchasers and policy makers.

1.2.2.1 The National Joint Registry (NJR)

The National Joint Registry of England and Wales (NJR) is the largest arthroplasty registry in the world with over 2 million primary and revision

arthroplasty procedures recorded. It was established by the Department of Health in 2002 and is presently operated by the Healthcare Quality Improvement Programme (HQIP). Northgate Information Solutions Ltd. are currently responsible for collection and storage of NJR data and Bristol University is contracted to produce the Annual Report. A levy is added to to the price of each arthoplasty sold in England and Wales to cover the costs associated with operating and developing the NJR.

Information relating to the patient, implants, hospital, surgeon and procedure are recorded on a minimum dataset (MDS) collection form (Appendix 11.1) Since inception of the NJR, completion and submission of the MDS forms have been mandatory for every arthroplasty and revision arthroplasty performed within NHS and in the independent sector (England and Wales). Linking patient records using patient identification numbers allows matching of revisions with primary arthroplasties recorded in the registry so that duration from primary to revision and cause of failure can be established. Information on mortality is available based on data from the Office of National Statistics (ONS) which is thought to be very reliable since death registration is mandatory within 5 days and burial or cremation are not permitted without the required documentation. Recent NJR data quality audit (2017) indicated very few missing arthroplasty records for primary compared to revisions with 95.69% (96.04% hips, 95.34% knees) and 90.27% (90.43% hips, 90.11% knees) of primary and revision procedures recorded in the NJR respectively.[33]

1.2.2.2 Strengths of Arthroplasty Registry Data

The quantity of generated longitudinal data relating to the arthroplasty population contained within a registry are second to none. They can provide information regarding temporal changes in terms of implant use, surgical factors as well as patient factors. Problems are often highlighted by registry data at an early stage, which allow appropriate changes to practice being made. The most well publicised success of the NJR was identification of early failure of the ASR XL hip replacement (DePuy, USA), which was later recalled. NJR data demonstrated 8% cumulative revision at 3 years.[44,45] In contrast, single-centre cohort studies or case series lack the volume of cases using specific implants necessary to provide a meaningful comparison of survivorship or risk estimates for failure and mode of failure. Similarly, randomised controlled trials (RCTs) for the purpose of survivorship analysis in arthroplasty typically require large sample sizes and long-term follow up to make clinically relevant comparisons, which is at significant cost. However, some very important research questions generated partly from registry analysis often do proceed to development of a RCT.[46]

1.2.2.3 Limitations of Arthroplasty Registry Data

A criticism of registry data is the reliance on the breadth of variables collected on the MDS which somewhat limits the ability to determine the aetiology of observations. Institutional databases tend to collect more detailed information on each patient undergoing arthoplasty with rigorous outcome data including radiographic and Patient Reported Outcome Measures (PROMS) together with

demographic and comorbidity information. Although the generalisability outside the institution is questionable, important observations other than the firm outcomes of revision and death which typify registry data can be made. Some technical aspects of THA are not captured by registry data including the morphology and bone quality of the proximal femur (Dorr classification). This is often used as a guide to determine the fixation choice for the femoral stem (cemented/cementless) and therefore this data would be useful when analysing outcomes and failure. Decision-making surrounding revision surgery is complex and factors, which are outside the remit of registry data collection, may influence the decision to proceed with revision arthroplasty; until a revision procedure has occurred the primary procedure remains successful. The final major limitation of registry data is the observational nature of the data. It is an excellent resource for assessing and establishing associations, however causation can only be really hypothesised.

1.2.3 Common Modes of Failure of THA

1.2.3.1 Aseptic Loosening & Osteolysis

Aseptic Loosening (implant loosening in the absence of infection) is a common mode of failure in THA. It results from bone resorption mediated by osteoclastic activity at the cement-bone or bone-implant interface. As an example, the articulation between a metal (cobalt-chromium) femoral head and a polyethylene cup produces wear particles in the range 0.3 to 10μm. These wear particles trigger an immune response, which increases osteoclastic activity. Malpositioning of components is a significant cause of excessive

early wear leading to loosening and failure.[47] However, activity level and implant design also have a role.

1.2.3.2 Dislocation

Recurrent dislocation is a frequent indication for revision THA and is also a common reason for failure even after revision THA. Component malposition and hip abductor muscle deficiency are reasons for instability. Other risk factors include previous fracture, age, component sizing, polyethylene wear, patient compliance and surgical approach.[48-51] Using larger head sizes and dual-mobility cups have become popular in attempts to reduce dislocation risk.

1.2.3.3 Infection

Deep infection of a THA is a complication, which results in significant patient morbidity. Treatment can involve multiple operations in addition to antibiotics. The common organisms implicated in THA infections are *staphylococcus aureus* and *staphylococcus epidermidis*.[52] The main established risk factors are advancing age, obesity and multiple comorbidities.[53-56]

1.3 Periprosthetic Fractures in THA

1.3.3 Definition

Periprosthetic fractures in THA refer either to a fracture of the femur or acetabulum with a THA in situ. Periprosthetic fractures can also be divided into those occurring intraoperatively and those occurring post-operatively.

1.3.4 Classification Systems

The most widely used radiographic classification system for periprosthetic femoral fractures around hip arthroplasties is the Vancouver classification.[57] It has been validated extensively and is useful in guiding clinical decision making with regards to treatment.[58-60] The features of the Vancouver classification include the anatomical location of the fracture, the stability of the stem (i.e. whether it remains well-fixed or is loose), and the extent of bone loss in the proximal part of the femur (see Figure 1.9). Type A fractures are defined as through the trochanters of the femur (A-G –greater trochanter, A-L – lesser trochanter), and do not traverse the shaft of the femur or the stem of the THA femoral component. Type B fractures are through the femur at the level of the stem. In B1 fractures the stem remains well fixed. B2 fractures have a loose stem in addition to the fracture and B3 fractures have a loose stem and poor bone stock in the proximal femur. Type C fractures are those occurring through the femur distal to the tip of the femoral stem.

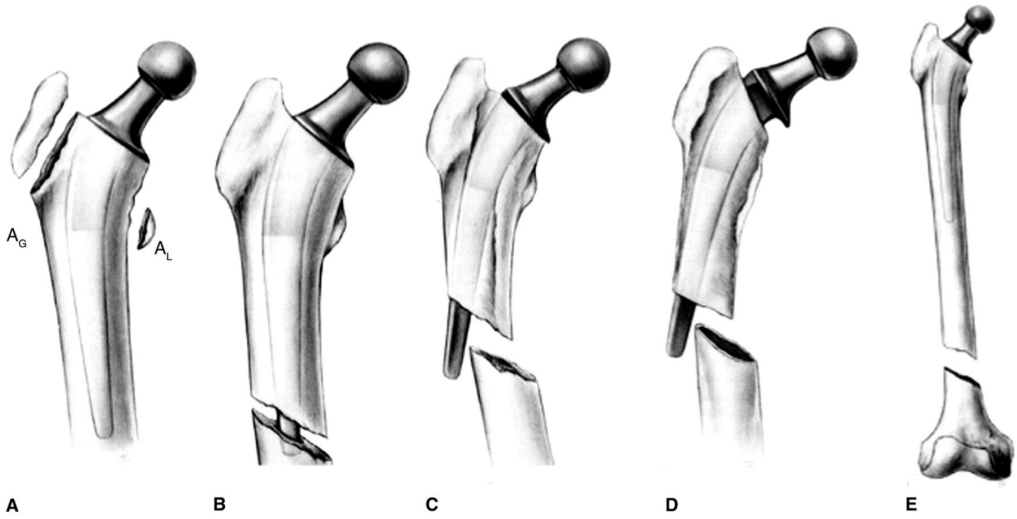


Figure 1-9 Vancouver Classification of Periprosthetic Femoral Fracture (Reproduced from [61]). (A) Type A Fracture, (B) Type B1 Fracture, (C) Type B2 Fracture, (D) Type B3 Fracture, (E) Type C Fracture.

1.3.5 Treatment

Despite non-surgical treatment, including prolonged traction, playing a role in the treatment of periprosthetic fractures, particularly in the earlier years of hip arthroplasty surgery,[62,63] surgery forms the mainstay of treatment for the majority of patients and fracture types.

1.3.5.1 Type A Fractures

Type A fractures are typically associated with avulsion of either the greater or lesser trochanter often secondary to osteolysis.[64] Hence, treatment is advised to address the osteolytic process, generally with exchange of the polyethylene liner. The lytic lesions can be bone grafted and if the fracture is unstable, stabilisation with internal fixation techniques are utilised. In asymptomatic patients with minimally displaced or undisplaced Type A fractures, non-operative treatment is advocated.

1.3.5.2 Type B1 Fractures

As B1 fractures have a well-fixed femoral stem, internal fixation without implant revision is the widely preferred option for most cases. There are a variety of internal fixation techniques used. Methods using cerclage cables and wires alone do not provide sufficient biomechanical stability.[65] A range of plate fixation options are available including the dynamic compression plate (DCP) and dynamic condylar screw (DCS) plates, which are 'simple' plate-screw constructs which aim to compress the fracture and have reported good outcomes.[66-68] Other options such as the Mennen clamp-type plate (CMW Laboratories, Exeter, UK), have performed poorly with high incidence of biomechanical failure.[69-71] Both the DCP and DCS plate are designed such that they can be used with bicortical (crossing both bony cortices) and unicortical screws (crossing only the near cortex) for use around the stem (i.e. proximally). In cases, particularly where a canal-filling, well-fixed cementless stem remains in situ, adequate stability with unicortical screws may not be achieved, hence plate designs where cerclage cables can be used in conjunction aim to overcome this problem and provide far cortical fixation.[72,73] Laboratory results using plate-cable-screw combinations suggest constructs where a plate with proximal cables and distal bicortical screws are used have lower biomechanical strength when compared to a plate with proximal unicortical screws and distal bicortical screws or a plate with proximal unicortical screws and cables and distal bicortical screws.[74,75] Similar results have been demonstrated in clinical studies using the Dall-Miles cable-plate system.[72,73]

Locking plates are used increasingly in fixation of periprosthetic fractures. They have the advantage in that they do not rely on compressive friction between the plate and bone for stability. This allows both preservation of blood supply and as stability is gained from the fixed-angle interlock between screw and plate, unicortical fixation is sufficient and pull-out strength is theoretically higher. The majority of modern locking plates have the both locking and non-locking screw options (such as the LCP, Synthes, Philadelphia, USA) which allow compression across the fracture site as well as the ability to place screws anterior or posterior to the femoral stem without disrupting the cement mantle as can occur with a fixed-angle locking screw.

Some observational studies have been reported overall good results using locking plates.[76-81] However, the results of a systematic review reporting outcomes of Vancouver B1 fracture treatment (all level IV observational studies) suggest a higher rate on non-union when locking plates are used compared to conventional compression/cable plate fixation.[82] In contrast, another systematic review of all periprosthetic femoral fractures after THA treated with internal fixation found non-locked plates to be associated with an 11 times higher risk of non-union compared to locked plates.[83] It is likely that an effect size of this magnitude represents heterogeneity in the study populations and differing methods of fixations.

Allograft struts of cortical bone are often used to augment stability and promote bony union. They are typically used in conjunction with a plate, to provide biplanar stability.[84] Both biomechanical[84,85] and clinical studies[86 87] support their use. Reported union rates and 10-year survivorship of allograft bone have been close to 100%.[86-89] Potential disease transmission and expense are disadvantages.[90]

It has been suggested that for a subgroup of B1 fractures, revision arthroplasty with a long stem bypassing the fracture site, sometimes augmented by internal fixation methods, provides a better treatment option. There is evidence from biomechanical studies that revision with a long stemmed prosthesis combined with allograft strut gives superior strength and stability for transverse fractures near the stem tip.[75,91] However, there are few clinical studies, which provide evidence for superior patient outcome with revision arthroplasty in B1 fractures. The published reports are largely case series with low patient numbers with B1 fractures.[92,93] Furthermore, erroneous misclassification of B2 fractures (with loose femoral stems) as B1 fractures has been suggested to be a possible reason for poorer outcomes of internal fixation in reported series of B1 fractures.[94]

1.3.5.3 Type B2 & B3 Fractures

Revision arthroplasty with or without internal fixation strategies is required for Vancouver B2 and B3 fractures. A long stem which bypasses the fracture

by at least twice the diameter of the femoral cortex is recommended.[95] This simultaneously addresses both the loose femoral component and the fracture, providing intramedullary stability (shorter lever arm compared to extramedullary techniques such as plate fixation).

Consensus with regards to revision surgery is difficult to achieve for multiple reasons. Firstly, implants used for primary THA varies between surgeon to surgeon as well as centre to centre. The type of primary arthroplasty used is likely to influence the choice of implants for revision surgery, specifically in terms of whether to use a cemented or uncemented prosthesis. Secondly, surgical experience varies with respect to use of implants particularly newer prostheses. Thirdly, the evidence for comparative benefits of specific revision implants for periprosthetic fracture surgery is largely from observational series with small case numbers.

Cementless extensively porous-coated stems, which rely on diaphyseal fixation, have shown excellent survivorship in revision THA,[96-100] even in the presence of reduced femoral bone stock.[96,101] Comparative results have suggested that fully porous-coated stems perform better in terms of survivorship and incidence non-union than both long cemented stems and proximally porous-coated stems.[102]

Revision femoral stems which are designed for fixation in the distal femur include cementless tapered fluted stems, which were initially popularised in Europe in the mid to late 1980s; provide axial stability by virtue of the taper, and the fluted element (splines) provide rotational stability.[103-106] The Wagner stem (Sulzer-Medico, Baar, Switzerland) was the first of this type of stem and was a non-modular, mono-block (one piece) in design.[107] Despite reports of good overall survivorship,[104,105] subsidence and a high incidence of dislocation were noted problems.[105] The development of modular revision stems was aimed at reducing the incidence of instability and subsidence. There are relatively few studies reporting the results of modular tapered fluted stems, which overall suggest good outcomes.[108-112]

Femoral stems, which are locked distally with screws are also aimed at providing distal fixation. The earlier designs of this type of stem were not porous coated,[113] but more recent iterations are porous-coated.[114-116] In such designs, the distally locked screws act until the stem is stabilised by bony ingrowth.

Femoral bone loss as in Vancouver B3 fractures requires treatment, which provides sufficient initial as well as long-term stability. Long stems have been used with 'allograft bone-prosthesis' composites.[109] Impaction grafting of allograft bone is a technique which aims to reconstitute the bone loss with packed small chips of allograft bone, creating a scaffold in which a long

femoral stem can be cemented in place.[117] Tumour-type 'mega-prostheses', are generally reserved for salvage cases.

1.3.5.4 Type C Fractures

Treatment of Type C fractures can involve both internal fixation strategies as detailed above as well as revision surgery if they occur in association with a loose stem. When revision arthroplasty is undertaken, particularly long stems are required to bypass the fracture sufficiently. Similarly, long plates are necessary to provide adequate stability. The stress riser created between the plate and the distal part of the stem is a potential reason for failure in Vancouver C fractures.

1.4 Periprosthetic Femoral Fractures in THA: Existing Evidence and Rationale for Thesis

1.4.1 The Magnitude of the Problem

The rate of primary THA has shown a steady increase. In the USA, rates of primary THA between 1990 and 2002 increased by 50% from 47 per 100,000 population to 69 per 100,000 population.[118] Between 2005 and 2010, a 16% increase in primary THAs was seen.[119]

It has been projected that the annual number of primary THAs performed in the USA will reach 572,000 procedures by 2030. This indicates an increase of 174% between 2005 and 2030.[118] Based on similar predictive modelling using National Joint Registry (NJR) data from England and Wales, Patel and colleagues suggest an increase in annual numbers of primary THA to 186,893 procedures, which corresponds to a rise of 134% between 2012 and 2030.[120] The authors reported that these figures are based on a constant proportional growth in incidence and suggested the incidence of primary THA by 2030 is likely to be higher if there is acceleration in proportional growth due to a rise in population and widening indications for arthroplasty and improvements in implant design.[120]

Similar rising demand with regards to revision THA has been projected. Kurtz and colleagues predict a 137% increase in annual numbers between 2005 and 2030 in the US, corresponding to 96,700 revision THAs by 2030.[118] In England and Wales, predictions in annual numbers of revision THAs by 2030 of 137,056 (in 2012 the actual number of revision THAs was 10,048) have been made.

The increase in numbers of primary and revision THAs suggests that PFF, as one of the commonest indications for revision hip arthroplasty, is also a growing problem. There are few studies that have attempted to estimate incidence of PFF. The largest studies to date have been based on data from the Swedish Hip Arthroplasty Register.[121,122] Lindahl and colleagues performed an epidemiological analysis of periprosthetic femoral fractures around THA using data from the Swedish National Hip Arthroplasty Register.[121,123-126] This was initiated in 1979 as a nationwide prospective registry, recording patients

undergoing primary THA. Periprosthetic fractures were reported to the registry. Lindahl reported that annual incidence ranged between 0.045% and 0.13%, with an overall pattern of increasing incidence between 1979 and 2000[121]. A more recent updated analysis of the Swedish data,[122] which defined incidence of PFF as the number of new fractures divided by the number of alive patients with a THA in situ at the end of the specific year, suggested an incidence of 1.4 per 1000 primary THAs in 2011, which was an increase from 1.0 in 2001-2002.

According to the Swedish Registry, from 4 years onwards periprosthetic fracture is the second most common indication for revision. A risk analysis per patient years demonstrated a rise in risk of periprosthetic femoral fracture as year-on-year following primary THA. Based on the Swedish dataset, by 10 years post primary THA, the overall proportion of patients who had sustained a periprosthetic femoral fracture was 0.64%.[121] In contrast, using the Scottish Arthroplasty Project, Meek reported the proportion of patients with a fracture to be 1.7% at 10 years following primary THA.[127]

The Mayo Clinic total joint registry is single-institution based registry in the US. The registry contains over 100,000 primary and revision joint replacements performed at the Mayo Clinic, Rochester, Minnesota, from 1969 onwards. Detailed patient information including radiographs in addition to robust follow-up at 1, 2, 5, 10 years post arthroplasty and 5 years thereafter is clearly a strength of the database.[128] Recently published results of their 20-year longitudinal data indicated a cumulative probability for post-operative periprosthetic femoral fracture of 1.6% at 10 years and 3.5% at 20 years.[129] For intra-operative fractures, they reported a proportion of 1.7%.

It is evident that some level of variation exists in the quoted risk of PFF, even based on the largest studies to date and this may be reflective of heterogeneity in patient groups, surgical factors as well as differences in statistical techniques used to assess risk. A systematic analysis of the existing data is clearly required to develop an understanding of the risk and risk factors for PFF.

An investigation at a national level requires the use of national arthroplasty registry data. There are few national registry studies specifically investigating periprosthetic fractures after THA. The largest studies are all are considerably smaller populations than that of England and Wales, which is significant not only in terms of volume of arthroplasty patients but also variation in practice.

1.4.2 Risk Factors for PFF

1.4.2.1 Gender

There are mixed observations from early case series of periprosthetic femoral fractures in the literature. Some have reported a slight female preponderance [63,130-132] whereas others demonstrate the converse.[133]

Lindahl's analysis of the Swedish registry reported an almost equal gender distribution of periprosthetic femoral fractures after primary THA, with 52% females.[126] Interestingly however, using Kaplan-Meier survivorship analysis and a Cox proportional-hazards regression model, the Scottish registry study suggested a higher risk of periprosthetic fracture after primary THA in females (Hazard Ratio 2.9).[127] The Mayo clinic found no difference in risk related to gender in their recent cohort of primary THAs.[129]

1.4.2.2 Age

With regards to age as a risk factor for sustaining a periprosthetic fracture after THA, there is also mixed results. Cook reported a 2.9 times higher risk of fracture in THA patients over 70 compared to those aged under 70.[134] Conversely, Lindahl (Swedish Arthroplasty Registry) found a greater risk of fracture in younger, more active individuals.[125] The Mayo clinic reported based on their cohort (32644 primary THAs), that age did not influence fracture risk.[129] Singh performed a multivariate-adjusted regression analysis which also showed no influence of age on risk of fracture in a cohort of 14,065 primary THAs.[135]

1.4.2.3 Implant Characteristics

Abdel reported a 14 times higher occurrences of intra-operative femoral fractures during cementless (3%) compared with cemented THA, in the Mayo cohort (0.2%).[129] Earlier reports have shown a similar pattern for intraoperative periprosthetic fractures.[121,136,137]

With regards to post-operative fractures, the data from Finnish arthroplasty registry showed an increased fracture risk when the Exeter stem (Stryker, USA), a double-tapered collarless polished cemented stem, was used.[138] Malchau reported large numbers of Exeter (Stryker, USA) and Charnley (DePuy, USA) stems in the fracture group in Sweden, whereas the Lubinus (Link, USA) was underrepresented. These three stems were the most commonly used cemented stems in Sweden. Malchau suggested that the

anatomic design of the Lubinus may protect against fractures.[139] An inadequate cement mantle combined with malpositioning of the Charnley stem and increased hoop stresses in the cement mantle due to the Exeter's taper design were suggested as possible reasons for predisposition to fracture.[139]

The recent paper by Abdel and colleagues from the Mayo clinic, USA, reported a strikingly higher risk of late postoperative periprosthetic femoral fracture in uncemented compared to cemented stems.[129] The authors speculated that the use of cementless stems preferentially in younger, more active patients who are at higher risk of trauma is a potential contributing factor. The Nordic registry data also reports a higher risk of periprosthetic femoral fracture within two years following primary THA with uncemented stems especially in older patients.[140]

1.4.3 Outcomes of Treatment

The decision making and treatment of periprosthetic femoral fractures is complex. A number of studies have indicated a poorer functional outcome and higher mortality after revision for periprosthetic fracture compared with other indications for revision.[102,130,141] Bhattacharya reported a mortality rate after periprosthetic femoral fracture treatment of 11%.[142] Furthermore, in the same study a delay to surgery of greater than 2 days following admission was associated with significantly higher mortality. High mortality after periprosthetic femoral fracture treatment was also reported by other authors, Lindahl (9% in first year), Shields (17.7% in first year).[123,143] Drew calculated the combined risk of either death or re-operation in the first year after periprosthetic femoral fracture to be as high as 24%.[144]

The Swedish Registry studies are to-date the largest observational series, which includes all modalities of treatment (i.e. internal fixation, revision surgery, combination of both). The authors report a first year reoperation rate of 10% following PFF.[123,124] A high failure rate of Vancouver B1 fractures treated with internal fixation alone was explained by potential incorrect classification of B2 fractures (with a loose stem) as B1 fractures. A 32% failure rate of B2 fractures treated with fixation alone was also reported. 25% of Vancouver C fractures treated with fixation alone also failed.

As many of the studies reporting outcomes of periprosthetic femoral fractures are single-centre observational case series of one or two specific treatment methods, attempting to determine the risk factors for poor outcome is difficult. Age, lower BMI and Vancouver C fractures have been implicated with higher risk of failure,[144] but there is little evidence regarding potentially reversible factors.

1.5 Overall Aims & Objectives

Aims

To perform a detailed analysis of periprosthetic fractures in THA using existing evidence from high volume studies and data from the largest arthroplasty database in the world (NJR).

To develop and apply flexible parametric competing risks models to NJR data in order to provide accurate estimates for probability of event and cause-specific hazards in the presence of multiple competing risks.

Objectives:

1) To perform a systematic review of high volume observational studies reporting incidence and risk factors for PFF in THA.
2) To examine the trends in the incidence of revision surgery for periprosthetic femoral fractures after THA in England and Wales using National Joint Registry (NJR) data.
3) To determine the patient and implant related risk factors for intra-operative and post-operative PFF revision after THA.
4) To compare the risk of PFF revision after THA based on patient and implant factors
5) To perform a systematic review of surgical treatment of Vancouver B2 and B3 periprosthetic femoral fractures.
6) To investigate the outcomes after revision surgery for PFF in THA.

1.5.1 Hypotheses

1) Periprosthetic femoral fractures in THA are increasing in incidence, and there are identifiable patient and implant related risk factors, which are independently associated with fracture risk.
2) Outcomes in terms of mortality and risk of further revision after PFF treatment are poor and worse than other common indications for revision after primary THA.

1.6 Summary of Methodology

1.6.1 Study Design

Each objective required a different study design. For objective 1 and 5 (systematic reviews), structured processes were used following the Centre for Reviews and Dissemination (CRD) guidelines and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist. For objectives 2, 3, 4 and 6 cohort study design with time-to-event survivorship analysis techniques based on NJR datasets was used.

1.6.2 Overview of Statistical Analysis Techniques

Traditionally, analysis of arthroplasty registry data involves survival methods, where the outcome of interest is 'time to revision/re-operation', which represents the time from the date of insertion of the implant until the date on which the revision/re-operation is performed. In this way, revision/re-operation is the primary indicator of failure of a joint replacement. Although

revision/re-operation is dependent on many factors including the fitness for surgery of the patient, it provides a firm end-point for analysis, particularly in epidemiological studies.

One of the features of survival data is that if an observation is not observed within the time frame analysed, there would be incomplete observations, which are known as censored events. Right censoring is the most common and occurs if a subject does not experience the event during the study period, is lost to follow-up or withdraws from the study. Death is another reason for censoring.

The risk set at a specific point in time includes individuals/implants that at that time are at risk of experiencing the event (i.e. revision/failure). These are the individuals that have survived up to that point. An individual/implant will leave the risk set either by experiencing the event, or when they are censored.

The two main measures of interest in epidemiological studies are the risk of the event occurring (probability) and the rate of its occurrence (hazard).

1.6.2.1 Non-parametric Methods

The Kaplan Meier is a non-parametric method which is frequently used in survivorship analysis of joint replacements [145].

Log rank tests are used to compare survivorship between different groups and the cumulative hazard function is often estimated non-parametrically using the Nelson Aalen estimator.

1.6.2.2 The Cox Proportional Hazards Model

The usual method for regression analysis to assess the effect of different covariates on the hazard function (or rate of revision/failure in arthroplasty data) is the Cox Proportional Hazards (PH) model.[146] The main assumption of the Cox model is proportional hazards. This implies that the hazard ratio remains constant over follow-up time and can be reported as a single number. From this proportional hazards assumption, it follows that an increase or decrease between any of the groups is constant over time.

The Cox PH model is a semi-parametric method. For single event survivorship analysis, (ie. event=revision surgery) there is a direct association between the hazard and survival functions, therefore the Cox PH model is able to determine the effect of covariates on survival.[147] However, in large population-based data, used in this thesis, the assumption of proportional hazards is not always reasonable. This assumption can be tested using graphical techniques such as plotting the 'Schoenfeld residuals' against time.[148]

Another disadvantage for the Cox PH model in large database studies is that it does not provide an estimate of the underlying baseline hazard, which is needed to understand the process of the condition which, in this study, is periprosthetic femoral fractures in THA.

1.6.2.3 Flexible Parametric Survival Model with Competing Risks

In survivorship analysis, competing risks are present when an individual or implant is at risk of more than one mutually exclusive event, for example,

revision surgery and death where death is considered to be a competing risk. The occurrence of a competing event may prevent the event of interest from occurring. It is therefore logical to perform an analysis that takes into account these competing risks. In arthroplasty registry studies, competing risks analysis have been adopted by a few studies.[149-152] In such studies, the single competing risk of death has been accounted for. For the purpose of our study examining revision arthroplasty for periprosthetic femoral fracture, the competing events that need to be accounted for are both death and revision for all other indications.

There are two key approaches to competing risk modelling. The first is to initially model the cause specific hazards and transform these to determine the cumulative incidence function. The second approach is to model the cumulative incidence function directly through a method proposed by Fine and Gray.[153] In this thesis, the first approach was used as both the cause-specific hazards and cumulative incidence provide a better understanding of risk factors for periprosthetic fracture and their effect on the collective THA population.

Unlike a non-parametric approach used in some other arthroplasty registry studies,[149,150] a flexible parametric model avoids the assumption of proportional hazards and provides a model that can easily incorporate time-dependent effects.[153]

Hence, for the reasons detailed above, flexible parametric survival models were used, which allowed us to obtain both the cause-specific hazards for revision surgery for periprosthetic fracture and the cumulative incidence

function, within a competing risks structure. This required the development of specific analysis code for competing risk models with multiple competing risks. Approaches to modelling competing risks are discussed in further detail in Chapter 4.

2 The Risk and Risk Factors for Periprosthetic Femoral Fractures in Total Hip Arthroplasty: A Systematic Review of High Volume Observational Studies

2.1 Introduction

Intra-operative and post-operative periprosthetic femoral fractures (PFF) in Total Hip Arthroplasty (THA) result in significant morbidity. According to the Swedish Arthroplasty Register, from 4 years following primary THA onwards, periprosthetic fracture is the second most common indication for revision [121]. Furthermore, the cost of revision for PFF is considerably greater than other indications for revision[154] and it has been associated with higher mortality rates.[142,155] Comparing revision with primary THA, the risk of post-operative periprosthetic fracture is believed to be higher.[127] Similarly, intraoperative fractures are more common in revision THA[156] and with predicted number of revision THAs in the US reaching 96,700 by 2030[118], the frequency of intraoperative PFF is likely to grow.

Traditionally, revision is used as the universal end-point for arthroplasty survival analysis and allows comparison of outcomes for different implants and between different patient groups. It is becoming increasingly important to quantify the risk of negative outcomes in THA, largely to provide an estimate of disease burden, to establish risk factors and to compare event rates between groups of THA patients. It is also necessary to provide easily understandable numerical revision risk estimates when counselling patients who are

candidates for primary or revision THA, which has medicolegal implications [157]. Heterogeneity within cohorts is a fundamental problem in attempting to estimate the risk of periprosthetic fracture in THA from smaller studies. Although, this problem is not eradicated in larger epidemiological studies, it is significantly reduced and confounding factors can be identified and adjusted for more easily.

Studies providing estimates for overall risk and projected risk of revision are therefore increasingly reliant on arthroplasty registry and other national-level databases. One of the strengths of epidemiological data is the volume of information available. Multivariate regression techniques allow an assessment of the effect of covariates on the risk of revision and depending on study design, these are commonly presented as Hazard Ratio (HR), Risk Ratio (RR) or Odds Ratio (OR). Most recent survival analysis techniques can account for competing risks (such as death) within a multivariate model and transform the hazard function to provide a comparable estimate of probability of revision for patient groups using the Cumulative Incidence (CI) function.

Despite the benefits of using arthroplasty registry data, one of the limitations with studying post-operative PFF in THA is that the majority of registries record only the PFFs treated with revision, which infers that periprosthetic fractures treated with internal fixation without revision are not represented in these registries. Hence, the data can only provide the risk of revision for PFF and not the risk of PFF as a whole. Therefore, for providing estimates of risk

of PFF, it is also useful to use data from large institutional databases containing detailed information of cohorts of arthroplasty patients.

Several risk factors for intra-operative and post-operative PFF in THA have been suggested in the literature including increasing age[134], cementless femoral components,[158] polished taper designs[139,159] and female preponderance.[135] However, other studies demonstrate conflicting evidence.[121,133,158] Therefore, there is a need to systematically review the evidence in relation to study design and size, to ensure appropriate conclusions on factors associated with PFF and the magnitude of associations can be made.

The aim of this systematic review was to estimate the overall risk of periprosthetic femoral fracture in primary and revision THA, to identify key risk factors and determine the magnitude of their influence on fracture risk.

2.2 Methods

We followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist for systematic reviews.[160] The review was registered on PROSPERO, an international prospective register of systematic reviews.

2.2.1 Data Sources

A comprehensive electronic search of Ovid MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials and Database of Systematic Reviews from the earliest available year of indexing up until May 2017 was conducted. As an example, the key terms utilised in the Ovid Medline search are shown in Appendix 11.2. The electronic search was supplemented with a manual search of the reference lists of all retrieved review articles for any other relevant citations. Abstracts of all citations were screened independently by two authors and full texts of articles were obtained to decide on inclusion of relevant studies.

2.2.2 Study Selection

Cohort, case-control and cross-sectional studies of primary and/or revision total hip arthoplasty (THA) reporting intra-operative and/or post-operative periprosthetic fractures as an outcome and fulfilling the following criteria were included. For multi-centre, regional or national registry based cohorts a minimum of 10,000 primary THAs or 1000 for revision THA was required. For single-centre studies, or studies reporting results of primary THA in a specific group (i.e. age-based or single implant based cohorts of consecutive cases) a minimum of 1000 THAs was required (500 for revision THA). Included studies were required to report duration of follow-up and use appropriate survival and regression analysis techniques to quantify risk and associations. Cohort studies that did not include all cases of primary/revision THA within the specified time-frame were excluded. Where studies were

specific to a group of patients/implants used, all cases within the time-frame reported had to be included.

2.2.2 Data Extraction

Two authors independently extracted data relating to study design, data sources, country of conduct, case or cohort selection, exposures and outcomes. Outcomes included probability of intra-operative and/or post-operative fracture. Individual covariates specific to each study were recorded along with the appropriate measure of interest (i.e. Risk Ratio, Hazard ratio, Odds Ratio, Relative Risk). In cases of disagreement on extracted data, a third author independently performed data extraction.

2.2.3 Quality Assessment

Quality assessment was performed independently by two authors using the The Joanna Briggs Institute Critical Appraisal Checklists (see Appendix 11.3). Using the appropriate Joanna Briggs Institute checklists for each study type (cohort, case-control, cross-sectional), each study was scored such that if a component of the checklist was fulfilled by the study, a score of 1 was awarded and if not fulfilled a score if 0 was awarded. The cohort studies were therefore scored out of 11, case series out of 10 and cross-sectional out of 10. Where there was disagreement in scoring between the two authors, a third author scored the study.

2.2.4 Summary Measures and Synthesis of Results

Extracted data was categorised into primary and revision THA and subdivided into intra-operative and post-operative periprosthetic fractures to compare risk and risk factors for each. For intraoperative fractures, comparisons of simple probability were made. For post-operative fractures, appropriate comparisons were made for probability of fracture between studies where the outcome (i.e. any PFF or revision PFF), survival methodology and specified time following THA for risk estimate, were the same. Comparable effect sizes for individual covariates and their 95% confidence intervals were log transformed and pooled using the DerSimonian and Laird random-effects method.[161] Meta-analysis was performed in STATA SE v14.2 (StataCorp, USA).

2.3 Results

2.3.1 Study Selection

Our search strategy yielded 2070 results. After removal of duplicates, 1543 abstracts were reviewed. 1367 abstracts were excluded and 176 full text articles were reviewed independently by two authors for inclusion. Thirty articles fulfilled the inclusion criteria and were included in the data synthesis. Figure 2.1 shows the PRISMA flowchart of identification and inclusion of studies.

The design of the 30 studies included 23 cohorts, 2 case-control and 5 cross-sectional. Table 1 summarises the study population and design. For 20 studies the outcome event of interest was periprosthetic femoral fracture which included 1 study that reported intra-operative calcar fractures. For the other 10

studies, revision for periprosthetic femoral fracture was the extracted outcome of interest.

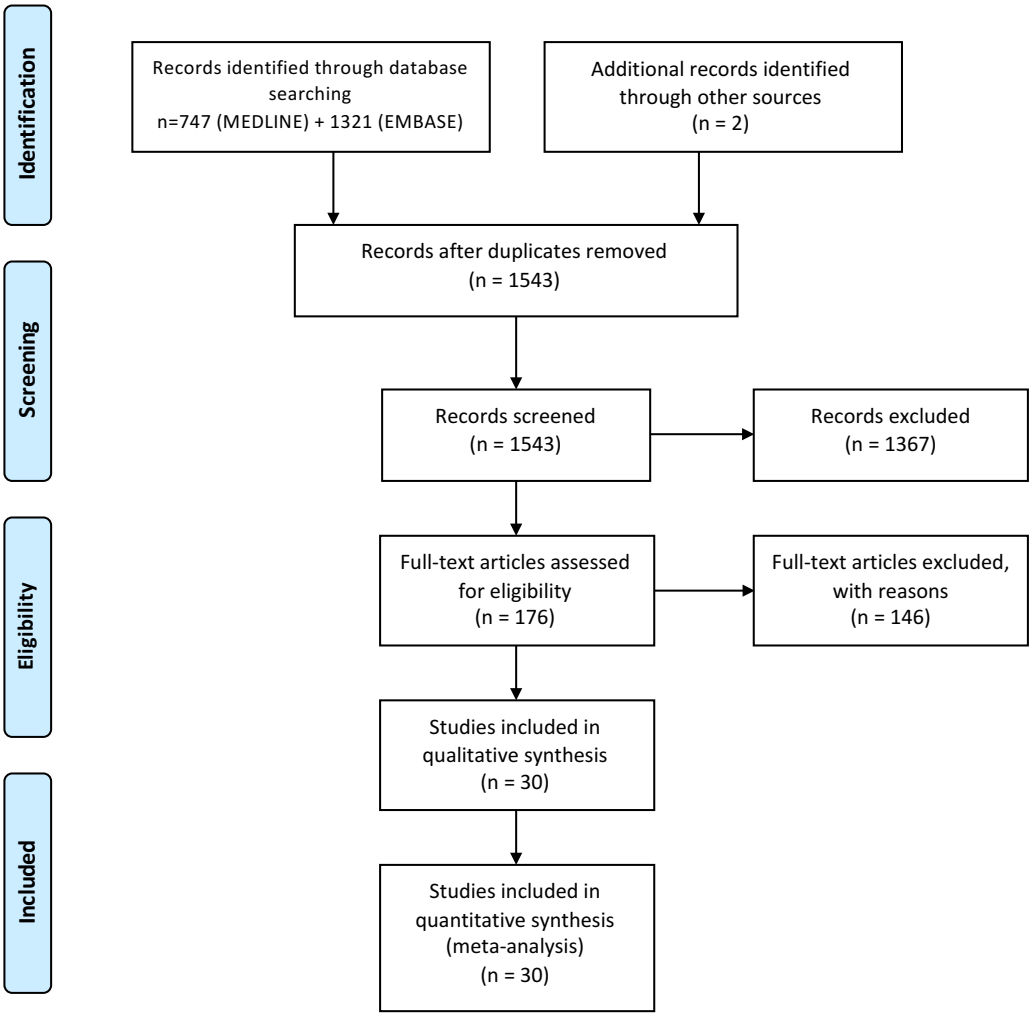


Figure 2-1 PRISMA Flowchart of Identification and Inclusion of Studies

Two studies used data from the Nordic Arthroplasty register.[140,162] Bergh's study was a cross-sectional study comparing the risk of PFF after THA for individuals with and without a history of femoral head necrosis.[162] Thien's cohort study investigates the risk of PFF within 2 years of primary THA based

on all individuals with a recorded THA in the register between the inclusion dates.[140] They did not investigate femoral head necrosis as a covariate in the analysis. Therefore, the study designs, inclusion criteria, reported outcomes and regression analyses were sufficiently different to warrant independent inclusion of the studies. However, as only data from cohort studies were used to investigate the probabilities of PFF after THA, Bergh's study[162] was not included in this.

The Swedish Arthroplasty Register was used in 2 studies.[163 164] Leonardsson's study only included patients who had undergone THA for subcapital femoral neck fracture whereas Hailier's study was a cohort of all THA's in the register with either a fully cemented or fully cementless design. Again, the studies were included independently although Leonardsson's study was cross-sectional in design, was not included in the analysis of probability of fracture after THA.

Five studies used data from the Mayo Clinic institutional database.[129,135,158,165,166] Abdel[167] and Singh[165] report data on post-operative PFF after revision THA. Singh's study[165] does not include time-to-event analysis to conclude overall probability of post-operative PFF after revision THA so was excluded from data synthesis. With respect to the regression analysis, for potential risk factors which were examined in both studies, only effect sizes from Abdel's paper were included in meta-analysis where possible as it was the most recently published and included the largest number of patients from the Mayo Clinic database.[167] For covariates assessed only in Singh's study,[165] the results were included in our data reporting. The three papers[135,158,166] describing PFF risk after primary THA using Mayo Clinic data

all included time-to-event analysis. Therefore, only results from Abdel[158] were included in comparisons of PFF probability. For risk factor analysis if covariates were not examined in Abdel's study but reported in any of the other two studies, these were included in our data synthesis.

2.3.2 Probability of Intra-operative & Early Post-operative Periprosthetic Fracture

2.3.2.1 Primary THA

2.3.2.1.1 Intra-operative

One study reported the overall risk of intra-operative PFF, regardless of stem design or brand [158]. They reported a 1.70% overall risk of intra-operative fracture. For cementless stems, they reported a risk of 3.0% and 0.23% for cemented stems. Solgaard reported a 1.70% risk of intra-operative PFF using the Bimetric cementless stem.[168] For proximal 1/3 HA coated double wedge tapered cementless stems, Capello reported a risk of 3.66% for intraoperative PFF.[169] **Table 2.1** summarises the comparative reported probabilities of intra-operative fractures for cemented and cementless stems. The reported early post-operative fractures are summarised in **Table 2.2**.

Table 2-1 Reported numbers of intraoperative PFF during primary THA for cementless and cemented stems

Study	Total primary THAs	All PFF	Cementless stem	Cemented stem
Abdel et al.	32,644	564	529/17466 (3.0%)	35/15,178 (0.23%)
Solgaard et al.	2408	41	41/2408 (1.70%)	-
Capello et al.	1039	38	38/1039 (3.66%)	-
Miettinen et al	3207	118	118/3207 (3.70%) (calcar fractures only)	-
Lindberg-Larsen	7169	70	58/5482 (1.06%)	12/1687 (0.7%)
Total	46,467	831 (1.79%)	784/29602	47/16865

Table 2-2 Reported numbers of early PFF following primary THA

Study	Total Primary THAs	Early PFF	*%*
Lindberg-Larsen (within 90 days)	7169	80	1.16
Park (during inpatient stay)	1,187,969	1062	0.09
Sheth (within 90 days)	5313	32	0.60
Solgaard (within 60 days)	2408	28	1.16
Total	1,202,859	1202	0.10

2.3.2.2 Revision THA

Only one of the included studies reported the risk of intra-operative PFF during revision THA.[167] They reported 668 fractures in 5417 revision THAs giving an overall risk of 12.33%.

2.3.3 Probability of Post-operative Periprosthetic Femoral Fracture

2.3.3.1 Primary THA

Three studies reported the cumulative probability of PFF using Kaplan-Meier survival analysis for all patient inclusive cohorts. At 1 year, cumulative probability ranged from 0.1% to 0.4%. At 10 years, the range was 1.2% to 3.5%. Table 2.3 and 2.4 summarise the reported probability of post-operative PFF following primary THA in studies using Kaplan-Meier (Table 2.3) and Person-time-incidence-rates (Table 2.4)

Table 2-3 Probability of post-operative PFF from studies using Kaplan-Meier Survivorship

Study	Risk Measure	Probability at 1 year	Probability at 2 years	Probability at 5 years	Probability at 10 years	Probability at 20 years
Abdel 2016	Cumulative probability	0.4% (0.3-0.5)	-	0.8% (0.7-0.9)	1.6% (1.4-1.8)	3.5% (3.2-3.9)
Cook 2008	Cumulative Probability	0.1% (0-0.1)	-	0.8% (0.5-1.0)	3.5% (2.8-4.2)	
Meek 2011	Cumulative Probability	-	-	0.9%	1.2%	

Table 2-4 Probability of post-operative PFF from studies using person-time incident rates

Study	Risk Measure	Cohort	Risk
Palan 2016	PTIR	All primaries with cemented stem	0.38/1000 person years
Palan 2016	PTIR	Exeter	0.33/1000 person years
Palan 2016	PTIR	CPT cemented stem	1.3/1000 person years
Palan 2016	PTIR	C-stem	0.29/1000 person years
Palan 2016	PTIR	Charnley	0.14/1000 person years
Sarvillinna 2003	PTIR	All primaries	0.18/1000 person years
Katz 2014	PTIR	All primary THAs for non-fracture indications	2.6/1000 person years

**PTIR = Person-time-incidence-rates*

2.3.3.2 Revision THA

Two studies reported the risk of post-operative PFF after revision THA. At 10 years, the reported probabilities of PFF were 6.4%[167] and 6.2%.[127] The results for each study are summarised in Table 2.5.

Table 2-5 Risk of post-operative PFF following revision THA

Study	Number of revisions	Number of PFFs	Probability of PFF at 1 year (%)	Probability of PFF at 5 years (%)	Probability of PFF at 10 years (%)	Probability of PFF at 20 years (%)
Abdel 2016	5417	668	1.9	3.8	6.4	11.4
Meek 2011	8726	360	-	4.2	6.2	-

2.3.4 Risk Factors for PFF

2.3.4.1 Primary THA

2.3.4.1.1 Intra-operative and Early Fracture

Five studies investigated the influence of covariates on the risk of intra-operative and early PFF.[170-174]

Cementless Stems

All three studies comparing the risk of intra-operative or early fracture for cemented versus cementless stems demonstrated a higher risk for cementless stems (see **Table 2.6**).

Gender

The three studies comparing risk of intra-operative or early fracture in males versus females found a significantly higher risk in females.

Age

The four studies that investigated the association between increasing age and risk of intra-operative or early PFF, demonstrated an age effect with a higher fracture risk for older individuals.

Other covariates tested for an association with risk of intra-operative or early PFF

Table 2.7 summarises other associations with intra-operative and early PFF tested in included studies.

Table 2-6 Key covariates with significant association with risk of intra-operative or early PFF in primary THA.

Study	Intra-operative/Early post-operative	Cementless Stem	Female Gender	Age
Abdel	Intra-operative	OR 13.5 (9.6-19)	OR 1.4 (1.2-1.7)	>65 OR 2.5 (2.1-3.0)
Miettinen	Intra-operative (calcar fractures)	-	-	Decreasing age: OR 0.94 (0.94-1.00)
Park	Early- during inpatient hospitalisation	-	OR 1.93 (1.67-2.22)	-
Sheth	Early- within 90 days of THA	Flat wedge taper stem: OR 13.56 (5.40-34.04) Metaphyseal filling stem 4.11 (1.68-10.04)	OR 2.74 (1.28-5.89)	1.06 (1.03-1.09)
Lindberg-Larsson	Early- within 90 days of THA	OR 4.1 (2.3-7.2)	RR 1.6 (1.1-2.2)	Per 10-year increase: RR 1.4 (1.2-1.6)

Table 2-7 Other covariates tested for association with risk of intra-operative/early PFF in primary THA.

Covariate	Study	Effect Size (95% CI)
Osteoporosis	Park Lindberg-Larsson	1.49 (1.21-1.84) 2.8 (1.6-4.8)
Developmental Dysplasia of the Hip (DDH)	Sheth	25.25 (6.54-97.51)
Diagnosis other than arthrosis	Lindberg-Larsson	1.4 (0.9-2.3)
BMI 30+	Lindberg-Larsson	0.9 (0.6-1.3)
Lower Household Income (<$40,000)	Park	1.40 (1.18-1.65)
Rheumatological Disease	Park	1.35 (1.02-1.77)
Malnutrition	Park	10.36 (7.41-14.47)
Liver Disease	Park	2.64 (1.67-4.18)
Heart Failure	Park	1.90 (1.40-2.57)
Hemiparesis/hemiplegia	Park	6.24 (4.04-9.65)
Well-controlled Diabetes	Park	0.70 (0.57-0.86)
Non-teaching hospitals	Park	1.15 (1.01-1.32)
Rural areas	Park	1.27 (1.06-1.53)
Ethnicity: Non-black minority	Park	2.12 (1.54-2.91)
Hardinge (Lateral) surgical approach to hip joint versus Posterior Approach	Miettinen	2.4(1.3-4.4)

2.3.4.1.2 Post-operative

2.3.4.1.2.1 Primary

Cementless vs Cemented Femoral Stem

Four studies compared the risk of post-operative PFF for cemented versus cementless femoral stems.[140,158,173,175,176] All four studies demonstrated a significantly higher risk of fracture with use of cementless stems.

Two of the four studies compared the risk of revision for PFF for cemented and cementless stems within the first two years following THA. Pooling the data (**Fig. 2.8**) from each using the random effects model described in the methods, provided a Risk Ratio of 8.66 (95% CI 7.37 – 10.18).

Table 2-8 Risk of post-operative PFF for cemented vs. cementless femoral stems in included studies (baseline=cemented stem)

Study	Cohort details	RR or HR	Effect Size (95% CI)
Abdel et al. [158]	All-inclusive cohort – all fractures	HR	3.3 (2.7-4.0)
Jamsen et al. [176]	Octogenarians – revision for PFF only	HR	13.4 (4.4-40.8)
Hailer et al. [175]	PFF within 2 years of primary THA	RR	8.0 (4.5-14)
Thien et al. [140]	PFF within 2 years of primary THA	RR	8.72 (7.37-10.32)

Gender

Twelve studies compared risk of post-operative PFF after THA in males and females (Table 2.9). Five studies reported a significantly higher risk of PFF in females.[127,172-174,177] Three of these studies referred to early risk of fracture, within 90 days and during inpatient admission for primary THA.[172-174] Two studies conversely reported a significantly higher risk of post-operative PFF in males.[164,178] The remaining six studies found no significant difference in risk of PFF between the two genders.[167,176,179-182]

Table 2-9 Influence of gender on risk of post-operative PFF after primary THA

Study	Baseline gender	OR/HR/ RR	Effect Size (95% CI)	Higher Risk Group
Abdel (2016)	Female	OR	1.0 (0.8-1.2)	No difference
Katz	Male	OR	1.13 (0.85-1.50)	No difference
Park	Female	OR	1.93 (1.67-2.22)	Female
Sheth	Female	OR	2.74 (1.28-5.89)	Female
Broden	Female	HR	0.9 (0.4-1.6)	No difference
Leonnardson	Male	HR	2.7 (1.43-5.10)	Male
Meek	Female	HR	1.5 (1.3-1.7)	Female
Watts	Female	HR	1.5 (0.96-2.5)	No difference
Gromov	Female	HR	2.02 (0.97-4.19)	No difference

Palan	Male	RR	1.96 (1.57-2.43)	Male
Lindberg-Larson	Female	RR	1.6 (1.1-2.2)	Female
Sarvillina	Male	RR	0.86(0.99-3.5)	No difference

Age

Eight studies investigated the influence of age on the risk of post-operative PFF after primary THA (Table 2.10). Seven of the eight studies found that older age categories were associated with a higher risk of post-operative PFF. Three studies demonstrated that age over 80 was associated with a significantly higher risk of post-operative PFF. Due to heterogeneity of regression analysis techniques, pooled meta-analysis was not possible.

Table 2-10 Influence of age on risk of post-operative PFF after primary THA

Study	Age Category	HR/RR	Effect Size (95% CI)
Watts	>60	HR	3.6 (2.0-6.3)
Abdel	>65	HR	1.0 (0.8-1.1)
Gromov	>70	HR	1.25 (0.69-2.24)
***Meek**	>70	HR	1.6 (1.4-1.9)
Broden	>80	HR	2.0 (1.1-4.5)
Palan	75-79	RR	1.81 (1.26-2.61)
Palan	80+	RR	1.51 (1.05-2.19)
Thien	80+	RR	1.17 (0.91-1.49)
Lindberg-Larsson	Per 10-year increasing	RR	1.4 (1.2-1.6)

**Primary and Revision THA amalgamated*

2.4.3.1.2.2 Revision THA

Three included studies investigated risk factors for PFF in revision THA. They were all based on data from the Mayo Clinic database.[165-167] The two earlier studies[165,166] included a number of covariates which were not reported in the most recent study[167] and were therefore reported in this systematic review.

Intra-operative PFF

One included study reported risk factors associated with intra-operative PFF in revision THA.[167] Female gender (OR 1.25, 95% CI 1.06-1.47) and cementless stems (OR 3.72, 95% CI 3.08-4.50) were reported to be significant independent risk factors. Fully coated cementless stems had a higher risk of intra-operative PFF compared to modular taper fluted stems (OR 1.34, 95% CI 1.05-1.71). Age over 70 years was not found to be a significant risk factor for intra-operative PFF in revision THA (OR 1.04, 95% CI 0.88-1.22).

Post-operative PFF

Table 2.11 summarises the effect sizes for covariates tested for association with post-operative PFF in revision THA.

Table 2-11 Covariates tested in included studies for association with risk of post-operative PFF in revision THA

Covariate	Study	Hazard Ratio (95% CI)
Age>70	Abdel	0.74 (0.57-0.96)*
Male gender	Abdel	1.48 (1.16-1.89)*
Cemented stem	Abdel	1.2 (0.9-1.5)
BMI (baseline<25)	Singh	25-29.9: 0.88 (0.67-1.15), 30-39.9: 0.98 (0.53-1.82), 40+: 0.77 (0.59-1.00)
Deyo-Charlson Index	Singh	1: 1.22 (0.91-1.64), 2: 1.52 (1.06-2.18), 3+: 2.08 (1.52-2.86)*
ASA grade (baseline=1)	Singh	2: 0.75(0.45-1.26), 3: 0.64(0.38-1.09), 4: 1.20 (0.48-3.09)
Prior cardiac event	Singh	0.86 (0.58-1.25)
Prior thromboembolic event	Singh	0.50 (0.21-1.23)
Cancer	Singh	1.28 (0.92-1.75)
Diabetes	Singh	1.07 (0.71-1.60)
Connective tissue disease	Singh	1.10 (0.79-1.54)
Chronic Obstructive Pulmonary Disease (COPD)	Singh	1.08 (0.72-1.60)
Cerebrovascular disease	Singh	1.27 (0.82-1.98)
Moderate to severe renal disease	Singh	1.08 (0.67-1.72)
Peptic ulcer disease	Singh	1.61 (1.11-2.33)
Peripheral vascular disease	Singh	1.32 (0.79-2.22)
Heart disease	Singh	1.38 (0.91-2.08)

2.3.5 Quality Analysis

The overall quality scores of included studies were high. For the cohort studies (n=22), the mean quality score was 9.14/11 (SD 1.21). For the case-control studies (n=4), the mean quality score was 7.5/10 (SD 1.00). For the case-series included (n=4), the mean quality score was 9 (SD 1.15).

2.4 Discussion

In this systematic review, we have amalgamated data from large observational studies to estimate the overall probabilities of intra-operative and post-operative PFF in primary and revision THA. We have also investigated the key reported risk factors for PFF in THA and the magnitude of their effect. Intra-operative PFF are relatively common in primary THA, particularly when cementless stems are used, with reported probabilities of between 1.7% to 3.66% for all cementless stem intra-operative fractures and 3.7% for calcar fractures only. For post-operative fractures after primary THA, at 5 years, the cumulative probability ranged from 0.8% to 0.9% and at 10 years, 1.2% to 3.5%. In revision THA, the probability of intra-operative fracture was 12.2% and for post-operative fracture the cumulative probability ranged from 6.2% to 6.4%.

Cementless stems, female gender and increasing age were universally associated with a higher risk of intra-operative PFF. Two studies reported a

higher risk of intraoperative PFF for osteoporotic individuals. Park et al. demonstrated significantly increased risk of intra-operative for other medical conditions as well as lower household income (<$40,000) and non-teaching hospital arthroplasty.[172] For post-operative PFF after primary THA, cementless stems were found to be a significant risk factor, particularly in the first 2 years following arthroplasty. Increasing age was also a significant risk factor in most of the studied but there was opposing findings of the influence of gender on risk of PFF after primary THA. There were fewer studies investigating the covariates associated with fracture during and after revision THA and all studies were based on data from the Mayo Clinic. For intra-operative PFF in revision THA, female gender and cementless stems were risk factors. Interestingly, for post-operative PFF after revision THA, male gender and age less than 70 were associated with a higher risk of PFF.

This is the first systematic review investigating the overall risk of PFF in THA. There were a number of single-centre cohort studies, which did not fulfil the criteria for inclusion in this review, mainly due to a small numbers of patients or lack of necessary survival analysis. While such studies often add useful information to the literature base, estimating an overall risk estimate for a population which can be used in a wider context requires significant numbers and statistical survival analysis which can be compared.

A previous systematic review studied the influence of stem design on risk of PFF.[183] Similar to the present study, the authors demonstrated a higher risk of fracture with cementless stems. Amongst these, single wedge and double

wedge were associated with the highest fracture risk. They also reported a higher risk of PFF with polished taper compared to composite beam stems. Cook's study which was included in this systematic review, reported 96.5% of their primary THA cohort were Exeter (Stryker, USA) and Charnley (DePuy, USA) stems, which are the two most commonly used polished taper and composite beam cemented stems.[134] Similar to Carli et al.[183] they reported a higher 10-year fracture risk for Exeter compared to Charnley stems with a cumulative probability of 3.6% (3.6-4.6) and 2.6% (2.4-4.8) respectively.[134]

The importance of quantifying the risk of complications for orthopaedic interventions is becoming increasingly important. One of the key reasons is for adequately informing patients of the likely risk of intra-operative complications and post-operative outcomes so that they will be able to make a more balanced decision of whether to consent to surgery. Recent UK legislative changes following the landmark case of Montgomery versus Lanarkshire[184] has important implications for surgeons. After the Montgomery case, the so called Bolam test, which questions whether a doctor's conduct is acceptable to a reasonable body of medical opinion, no longer applies to the topic of consent.[185] Informing patients of material risks specific to the procedure and the patient is now imperative from a medicolegal standpoint. For primary and revision THA, as this systematic review demonstrates, intra-operative PFF has a sufficiently high probability to be included within the material risks discussed with patients and providing a synthesised estimated probability during the consent process is a robust way ensuring an evidence-based approach has been used. When discussing long-term outcomes of THA

and common modes of failure, PFF again should be included in the same manner. An evidence based and quantitative approach to risk factors is equally necessary in counselling patients of their comparative risk of PFF, which may be higher or lower than average.

With low overall revision rates for primary THA, it follows that the risk of re-operation or revision for any of the common specific indications is actually relatively low at the 10-year point. However, both at individual and at population level, reducing the risk of failure to the lowest possible level is an important priority and at a national level, initiatives such as the UK "Getting it right first time (GIRFT)" have been introduced to address this.[186] A primary aim of GIRFT is to improve outcomes of orthopaedic interventions by setting a framework in which to do so. It promotes the use of cost-effective implants with a proven track record. Although this systematic review demonstrates a reasonably low overall post-operative PFF risk after primary THA at 10 years, the risk was significantly higher with the use of cementless compared to cemented femoral stems, particularly within 2 years and in older individuals. If taken together with the evidence that age is an independent risk factor for PFF, the results of this study suggest that, at population level, cementless stems in older age groups should be avoided with respect to PFF risk. For revision THA, our study highlights the significantly higher risk of both intra-operative and post-operative PFF as well as the relative lack of longitudinal data available from high volume observational studies.

There are limitations of this study. Heterogeneity in study design and data reporting particularly of time-to-event analysis limited the quantitative comparative analysis that could be performed. Although we tried to reduce the bias associated with heterogeneity in cohorts by including only larger studies and by only synthesising comparable data, it would not be possible to eliminate this bias completely in a systematic review of this nature. Another limitation is national practice differences in terms of arthroplasty, which cannot be easily accounted for. However, this study investigated specific implant and patient factors which could be adjusted for to reduce the innate biases associated with differing national cohorts. The reported failure outcome varied between studies. Some studies reported failure as any PFF while others reported only revision PFF. Although this does have implications in terms of synthesising data, as most all-inclusive cohorts suggest that revision arthroplasty is used for PFF treatment in a large proportion of cases, the data should be comparable. Another potential criticism with regards to the study design are the strict criteria, which required significant volume of arthroplasties for inclusion of a study. As our aim was to investigate risk and risk factors, large studies are required to draw any meaningful quantitative or qualitative conclusions accounting for heterogeneity. Furthermore, the majority of studies which we reviewed from the database searches either easily fulfilled the criteria based on case volume or they were much smaller single-centre case series which the study did not intend to capture.

In conclusion, this is the first systematic review of high volume studies reporting the risk and risk factors for PFF in primary and revision THA. The

risk of both intra-operative PFF is significantly higher in revision THA, with cementless stems in primary THA, and older age groups. Interestingly, data relating to the independent association of gender with PFF is conflicted even amongst the highest volume cohort studies. There is a need for homogeneity of data analysis and reporting to allow quantitative comparisons.

3 Temporal Trends in Revision Arthroplasty for Periprosthetic Fracture in England & Wales

3.1 Introduction

Revision arthroplasty is commonly used in the management of periprosthetic fractures around hip replacements. For fractures around the stem, revision techniques are indicated where there is evidence of loosening in conjunction with the fracture.[156] In terms of the Vancouver classification, type B2 and B3 fractures by definition have a loose stem and would therefore warrant revision arthroplasty.[59,187] According to the Swedish Arthroplasty register, which records all periprosthetic fractures in THA, Vancouver B2 (52%) and B3 (4.1%) fractures combined account for 57.1% of periprosthetic femoral fractures in THA.[126]

It is expected that the number of revisions performed worldwide will increase.[120] This is thought likely due to a combination of rising number of primary THAs and an ageing population. Wider indications for THA with higher numbers performed in younger age groups are also thought to be contributory factors.

The most common indications for revision hip arthroplasty include aseptic loosening, pain, lysis, infection, dislocation and periprosthetic fracture. Aseptic loosening is overall the commonest indication for revision arthroplasty, which is supported by worldwide arthroplasty registry data.

However, data from the Swedish Arthroplasty Register indicates that from 4 years following primary arthroplasty, periprosthetic fracture is the second most common indication for revision.[121]

As revision arthroplasty is the treatment method of choice for periprosthetic fractures in the presence of stem loosening, it follows that both these indications for revision are intertwined. In terms of primary indication, revision for aseptic loosening precludes revision for PFF from occurring and vice-versa. The higher overall numbers of revisions performed for aseptic loosening compared to PFF and the rising numbers of revisions for PFF with increasing time from surgery, would therefore suggest that the ratio of PFF revisions to aseptic loosening revisions is growing with time. However, this has not previously been investigated.

There are 41 national arthroplasty registries, which are members of the International Society of Arthroplasty Registries (ISAR). Membership of ISAR is granted to national registries that receive data from more than 80% of hospitals, which each report over 90% of procedures performed and have appropriate validation procedures in place. Lacny and colleagues assessed the comparability of hip arthroplasty registries that publish annual reports in English.[188] Of the six registries included, they demonstrated limited consistency in outcome reporting between individual registries, particularly with regards to survivorship analysis and reporting of revision

arthroplasties.[188] For incidence of revision, different metrics were used including revision burden, cumulative incidence and person-time incidence rates.

Revision burden, a term introduced by Malchau, is defined as the ratio of revision procedures to the total number of arthroplasties within a specific time period.[189] It was introduced to aid comparison of outcomes between national arthoplasty registries. However, only 2 of the 6 registries included in Lacny's study report revision burden of THA specifically (The Australian Orthopaedic Association National Joint Replacement Registry and the Slovak Arthroplasty Register).[188] There is some evidence that overall revision burden for THA has decreased over the last 2 decades[190] but there are no previous studies which have reported temporal changes in revision burden by indication for revision.

In order to allow comparison of incidence of revision with different follow-up times and across registries, person-time incidence rates (PTIR) were introduced but thus far have not been widely used in registry annual reports. PTIR is an epidemiological representation used classically in Doll's study of British doctors which investigated the association between smoking and lung cancer.[191] Doll analysed the occurrences of lung cancer in individuals with different exposures to smoking, comparing the event rate (lung cancer) with the individual exposures to the risk factor (smoking). It allows direct comparisons of datasets with varying follow-up periods and numbers of cases.

When applied to arthroplasty data, the calculation assumes that the risk of revision is present from the time of implantation of the prosthesis to the patient's death or revision surgery. The total follow-up time is calculated as the sum of each individual's 'time at risk of revision' within the period in question. This figure is then used as the denominator to allow a standardised comparison of the number of observed revisions within the same time frame (numerator). This can then be presented as 'revisions per 100 observed component years' or 'revisions per 1000 observed component years'.

The aim of this study was to investigate the temporal trends in revision surgery for periprosthetic femoral fracture in England and Wales based on data from the National Joint Registry (NJR).

3.2 Methods

3.2.1 Study Design & Data Source

The study was a cohort investigation of THAs in England and Wales and entered into the National Joint Registry (NJR). Hip resurfacings were not included. Two NJR datasets were used in this study:

1) 'Primary THA' – All primary THAs performed from January 2003 onwards.

2) 'Revision THA' – All revision hip arthroplasties performed from January 2003 onwards.

In order to include all eligible entries for each complete year, primary and revision hip arthroplasties performed in 2015 were excluded from analysis. The NJR primary THA dataset was linked to the NJR revision dataset to determine which primary THAs recorded in the NJR had undergone revision surgery. Information relating to date of death was provided by the Office of National Statistics (ONS) via matching with patient NHS numbers. Each primary THA therefore had one of three outcomes: death without revision, revised or unrevised.

The 'Revision THA' dataset was used to assess the numbers of revision THAs performed each year and for calculation of Revision Burden.

3.2.2 Data Management

All raw data was provided by the NJR. String variables were transformed into coded numerical variables in Stata SE Version 14.2 (StataCorp, USA).

Bilateral Observations

The NJR records each primary implantation as an individual observation, some of which are the second operated side in the same patient. The presence and outcome of an earlier THA on one side can potentially influence surgical decision making about the second side and influence outcome. Furthermore, bilateral hip replacements are often performed on the same day, in stages with the second side being performed weeks or months after the first, or at a later time when the second side becomes symptomatic. This leads to issues surrounding the assumption of independence of each observation.

The two key ways of dealing with this are either to include only the first of bilateral THAs or to include them both and assume the revision risk for each side is independent of one another. However, there is convincing evidence that including both sides as independent observations does not significantly influence the overall analysis and hence including both is a reasonable option.[192,193] In the studies in this chapter, both sides have been included as independent observations.

3.2.3 Indications for Revision

The NJR Minimum Dataset for revision THA (Appendix 11.1) allows the entry of multiple indications for revision. Due to the acute nature of periprosthetic femoral fractures, it is a reasonable assumption that if it is selected as an indication for revision, it is likely to be the main indication necessitating revision surgery. This assumption was used to classify revised primary THAs into two groups – 'revised for periprosthetic femoral fracture' and 'revised for all other indications. In order to compare differences in revision incidence by individual indications, assumptions were made as to which was the primary indication where multiple indications had been selected according to the following ranking system:

1) Periprosthetic femoral fracture
2) Infection
3) Dislocation
4) Aseptic loosening (stem or socket)

5) Pain
6) Other indications

Where two or more of the above indications had been selected as reasons for revision THA, the indication with the lower numerical rank was taken as the primary indication.

Intraoperative fractures were recorded on the NJR form as an intraoperative complication, so for each patient, a fracture either occurred or it did not.

3.2.4 Statistical Analysis

Statistical Analyses were performed using Stata SE Version 14.2 (StataCorp LLC, USA).

Number of primary THAs performed since 2003 were stratified into chronological year, as were subsequent revision procedures.

For intraoperative PFF, annual incidence was recorded as a percentage of THAs performed in that year. Linear regression, using the year of primary THA as a primary continuous independent factor, was used to assess the overall linear trends in proportion of intra-operative PFF between January 1st 2006 and December 31st 2014. This period was selected as NJR data capture in terms of primaries recorded in the NJR as a proportion of those actually performed were >99% from 2006[119].

Primary indications for revision were tabulated by year. Annual incidence rate of first revisions was calculated for each indication for revision by dividing the number of revisions during a year by the number of implant-years-at-risk estimated for that specific year. The implant-years-at-risk was calculated by

multiplying the number of individuals in the risk set by the sum of the follow-up periods during that year. For each specific year the entry date was the latest of 1st January or date of primary THA. The exit date was the earliest date of revision date, death, or 31st December of the specified year.

Incidence rates of first revision were presented for periprosthetic fracture, infection, dislocation, aseptic loosening, pain, by age and gender and expressed as per 10,000 implant-years-at-risk. Age was stratified into groups: less than 65, 65-69, 70-74, 75-80, over 80. The Stata "strate" command was used to estimate IRs with 95% confidence intervals (CI) which assumes a Poisson distribution. As the incidence of revision is relatively low comparative to the number of primary THAs, the Poisson distribution is appropriate for incidence calculations. Linear regression was used to assess the linear trend in incidence with chronological year as the independent continuous factor.

Overall revision burden was calculated for each year by dividing the total number of revisions (using the dataset containing all revisions recorded on the NJR) by the total number of revisions and primaries within the specific year. Revision burden for each of the indications was calculated by year by diving the total number of revisions for the individual indication by the total number of arthroplasties (primary and revision).

3.3 Results

3.3.1 Demographics

There were 675,078 primary THAs performed at 466 centres included in the cohort. This consisted of 414,130 females and 260,945 males. Gender information was missing for three cases. Overall mean age at time of primary THA was 69.14 (SD 11.06). When stratified by gender, mean age at time of primary THA was 69.94 (SD 10.94) for females and 67.87 (SD 11.13) for males. There were a total of 16,174 matched revisions within the observed time period.

The number of primary THAs increased from 13,093 in 2003 to 84,056 in 2014. Figure 3.1 demonstrates the total number of primary and revision THAs performed between 2003 and 2014.

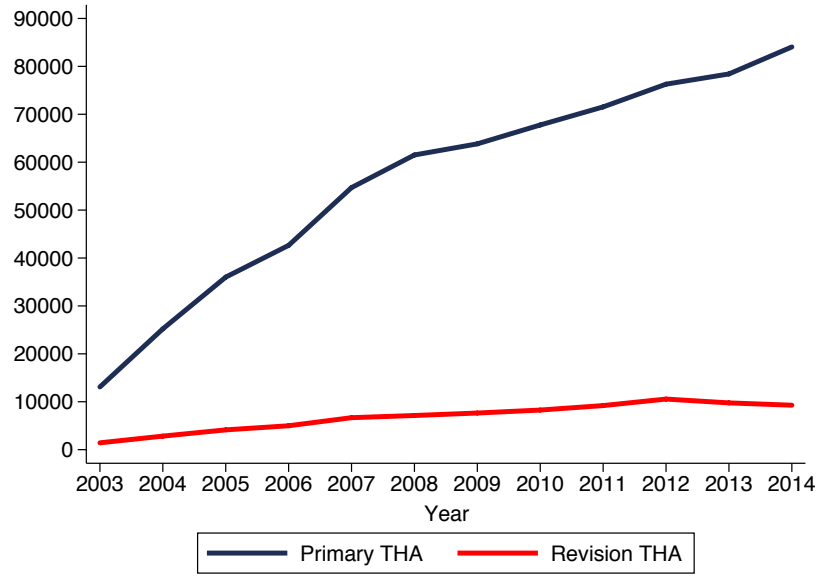


Figure 3-1 Total numbers of primary and revision THA performed in England & Wales by year.

3.3.2 Intraoperative Fractures

There were 4,585 intra-operative PFFs reported (0.68%). The number of primary THAs and intra-operative PFF by year of primary THA are shown in Table 3.1. There was no significant correlation between proportion of fracture and year between 2006 and 2014 (p=0.47).

Table 3-1 intra-operative fractures during primary THA reported to the registry 2003-2014.

Year	Primary THA	Intra-operative Fracture	% Intra-operative Fracture
2003	13,093	0	0
2004	25,218	175	0.69
2005	36,014	272	0.76
2006	42,641	293	0.69
2007	54,704	362	0.66
2008	61,507	449	0.73
2009	63,828	496	0.78
2010	67,771	445	0.66
2011	71,541	498	0.70
2012	76,288	533	0.70
2013	78,417	526	0.67
2014	84,056	536	0.63

3.3.3 Revision THA: Revision Burden and Incidence of Revision for Periprosthetic Fracture and other Common Indications

3.3.3.1 Number of Revisions

The commonest five indications for revision THA in order of descending frequency were aseptic loosening, dislocation, infection, periprosthetic fracture and unexplained pain. Figure 3.2 demonstrates the total numbers of revision THAs by primary indication between 2003- 2014.

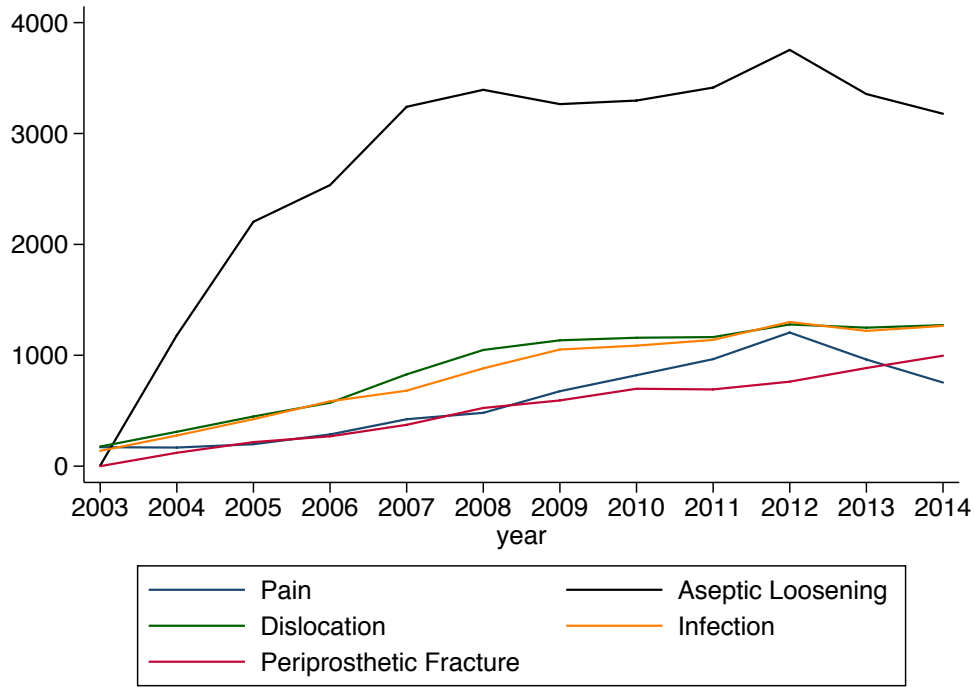


Figure 3-2 Total numbers of Revision THAs by Primary Indication and Year (2003-2014).

3.3.3.2 Revision Burden

Total revision burden was 10.10 in 2004 and 9.95 in 2014. For periprosthetic fracture there was an increase in revision burden from 0.43 in 2004 to 1.07 in 2014. Table 3.2 demonstrates the change in overall revision burden and revision burden by indication between 2004 and 2014.

Table 3-2 Total Revision Burden and Revision Burden by Primary Indication 2003-2014

Year	Total Revision Burden	PFF	Aseptic Loosening	Infection	Dislocation	Pain
2003	9.85	0	0.03	0.95	1.22	1.18
2004	10.10	0.43	4.21	0.99	1.11	0.60
2005	10.30	0.54	5.49	1.06	1.12	0.49
2006	10.48	0.56	5.32	1.23	1.20	0.60
2007	10.88	0.61	5.28	1.11	1.35	0.69
2008	10.40	0.76	4.94	1.28	1.53	0.70
2009	10.80	0.83	4.57	1.47	1.59	0.95
2010	10.88	0.92	4.34	1.43	1.52	1.08
2011	11.40	0.86	4.23	1.41	1.44	1.20
2012	12.17	0.88	4.32	1.50	1.47	1.39
2013	11.07	1.00	3.81	1.38	1.42	1.09
2014	9.95	1.07	3.40	1.36	1.36	0.81

3.3.4 Incidence of First Revision THA for Periprosthetic Femoral Fracture (PFF)

The overall incidence of first revision was 0.490 per 100 observed component years (95% CI 0.482-0.498). Figure 3.3 shows the incidence of first revision for the commonest five indications between 2004 and 2014.

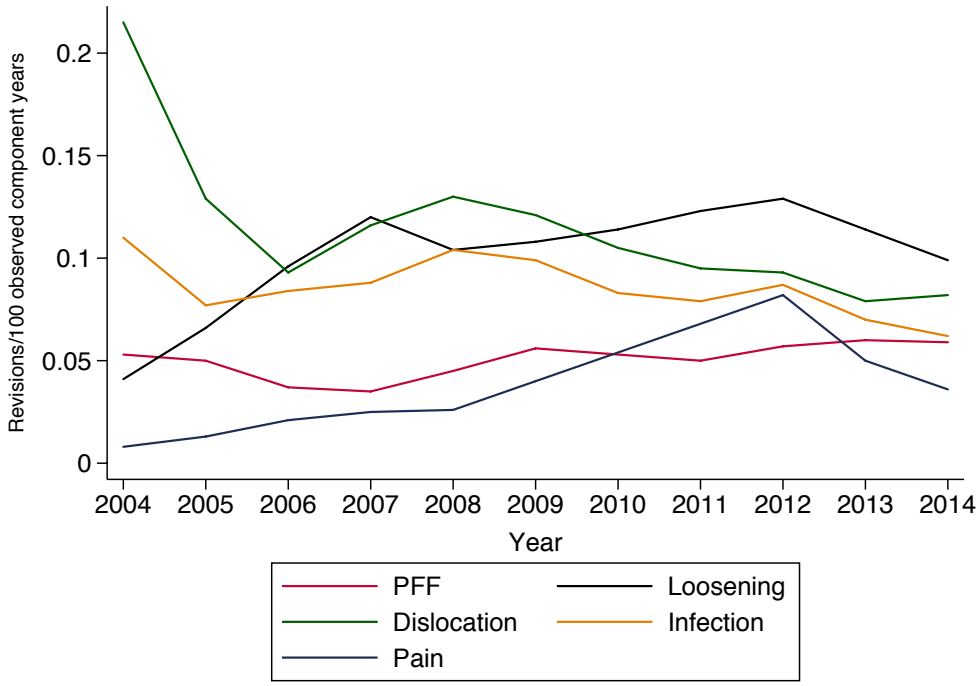


Figure 3-3 Incidence of First Revisions (per 100 observed component years) by Primary Indication 2003-2014.

For PFF, the overall incidence of first revision was 0.052 per 100 observed component years (95% CI 0.050-0.055). Incidence of first revisions per 100 observed component years between 2003 and 2014 for all revisions are shown in Table 3.3.

Table 3-3 Overall Annual Incidence of First Revision (per 100 observed component years)

Year	Total Revisions	Observed component years	Revisions per 100 observed component years	95% CI
2003	35	4,617	0.76	0.54-1.06
2004	124	24,677	0.50	0.42-0.60
2005	238	54,322	0.44	0.39-0.50
2006	353	92,566	0.38	0.34-0.42
2007	637	138,457	0.46	0.43-0.50
2008	901	192,934	0.47	0.44-0.50
2009	1240	249,490	0.50	0.47-0.53
2010	1560	307,743	0.51	0.48-0.53
2011	2129	367,575	0.58	0.56-0.60
2012	2690	430,355	0.63	0.60-0.65
2013	2543	492,264	0.52	0.50-0.54
2014	3724	946,174	0.39	0.38-0.41

Tables 3.4 and 3.5 demonstrate the incidence of first revision for PFF (per 100 observed component years) by year from 2003 and 2014 (Table 3.4) and by age group (Table 3.5).

Table 3-4 Incidence of First Revision for PFF 2004-2014 (per 100 observed component years).

Year	Observed Component Years	Revisions for PFF	Incidence of Revisions for PFF per 100 observed component years (95%CI)
2003	-	0	-
2004	24,677	13	0.053 (0.031-0.091)
2005	54,322	27	0.050 (0.034-0.072)
2006	92,566	34	0.037 (0.026-0.051)
2007	138,457	48	0.035 (0.026-0.046)
2008	192,934	86	0.045 (0.036-0.055)
2009	249,490	140	0.056 (0.048-0.066)
2010	307,743	162	0.053 (0.045-0.061)
2011	367,575	185	0.050 (0.044-0.058)
2012	430,355	245	0.057 (0.050-0.065)
2013	492,264	300	0.060 (0.054-0.068)
2014	946,174	486	0.051 (0.047-0.056)
Overall	3,301,174	1726	0.053 (0.050-0.055)

Table 3-5 Annual Incidence of First Revision for PFF by Age Category (per 100 observed component years).

Age Category	Revisions for PFF	Observed Component Years	Revisions per 100 observed component years	95% CI
<60	201	417654	0.048	0.042-0.055
60-64	168	338219	0.050	0.043-0.058
65-69	217	512668	0.042	0.037-0.048
70-74	288	610956	0.047	0.042-0.053
75-80	349	630761	0.055	0.050-0.061
80-84	300	471786	0.064	0.057-0.071
85+	246	336584	0.073	0.065-0.083

For PFF revision, when modelling year as a continuous variable, there was a rising trend in incidence of first revision increased by advancing year, which was statistically significant ($p=0.005$, $r^2=0.61$)). The positive trend remained when adjusted for age at primary THA and gender ($p=0.002$). For aseptic loosening, there was no significant increasing trend in incidence of first revision ($p=0.53$, $r^2=0.06$). Figure 3.4 demonstrates the comparative trends in incidence of first revision for PFF and aseptic loosening between 2006 and 2014.

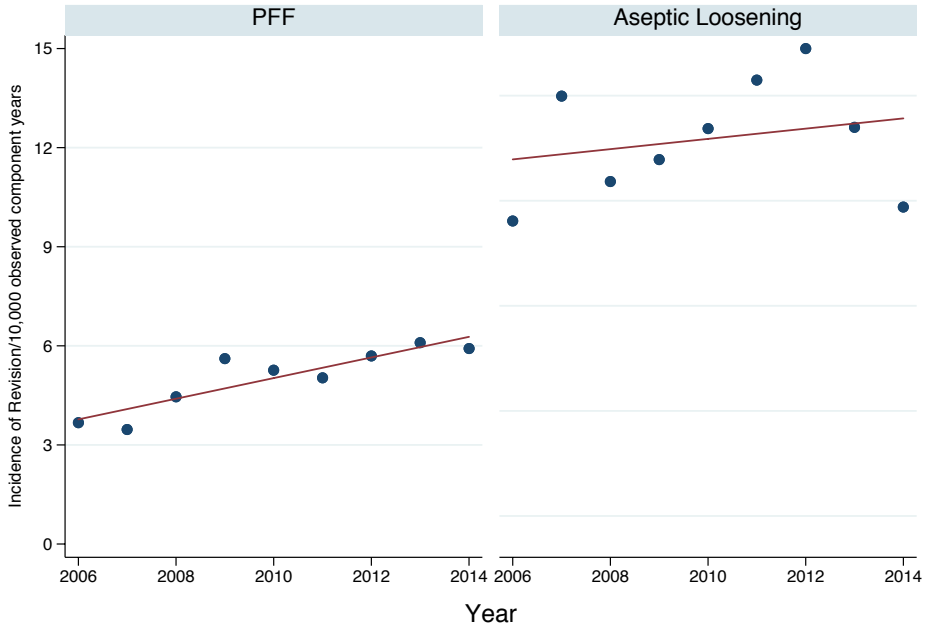


Figure 3-4 Trends in Incidence of first revision for PFF and Aseptic Loosening between 2006 and 2014.

3.4Discussion

This study aimed to describe the temporal trends of revision surgery for periprosthetic femoral fracture in England & Wales. Analysis of NJR data demonstrates an increasing number of revisions for periprosthetic femoral fractures being performed since 2003. Although, overall all-indication revision burden was largely unchanged, revision burden in relation to PFF specifically, gradually increased from 0.43 in 2004 to 1.07 in 2014. Incidence of first revision for PFF presented in terms of implant years at risk also showed an increase between 2006 and 2014.

The overall all-indication incidence of first revision based on NJR data was low compared to data from other countries [194]. Interestingly the incidence of revision THA based on the Swedish and Australian joint registries which are the second and third largest, were similar, with a reported incidence of 0.72 (2007) and 0.81 (2008) revisions per 100 observed component years respectively.[194]

It has been suggested based on an amalgamation of registry data that overall revision burden for THA is decreasing.[190] However, amalgamation of registry data is challenging and problematic and conclusions are more accurate when based on individual registries, which consider a specific population. The largely unchanged overall revision burden demonstrated in this study highlights the problem related to an increasing periprosthetic fracture revision burden.

This study is the largest-to-date investigating the incidence of revision surgery for periprosthetic femoral fracture. A robust investigation of incidence typically requires population level data. The Swedish Arthroplasty Register study of periprosthetic fractures in Sweden between 1979 and 2000, demonstrated a tendency for incidence to increase with advancing chronological year.[121] In the present analysis, where incidence is presented in terms of implant years at risk thereby taking into account individual follow-up times, the incidence showed a rising trend between 2003 and 2014. This trend

was also present when age and gender were adjusted for. Based on the Finnish Arthroplasty Registry data from 1990-1999, Sarvilinna et al. demonstrated a lower overall incidence of revision for PFF of 0.018 per 100 observed component years (95% CI 0.013-0.025).[182] The same paper also demonstrated a reduction in incidence for primaries performed between 1995 and 1999, compared with primaries performed between 1990 and 1994.[182] The cohort in the present study is much larger with 722,013 primaries included compared to 33,154 in Sarvilinna's study which suggests the estimate from the present study is likely to be more accurate. Secondly, the Finish cohort refers to arthroplasties performed between 1990 and 1999 whereas the NJR started recording THAs in 2003, which makes direct comparison between the incidence estimates problematic.

There are a number of potential reasons for the increasing revision burden and incidence of revision for PFF. Firstly, with regards to periprosthetic revision burden it could be related to a cumulative influence of increasing risk of PFF with time from primary THA which would lead to significantly large number of primary THAs within the NJR at risk of fracture. The increase in incidence of revision for PFF, it could be a representation of wider indications for primary THA which include those at higher risk. Risk factors and Risk of revision for PFF based on NJR data will be explored in Chapter 4.

A key limitation of this study is that only PFF's treated with revision are entered onto the NJR and those treated with internal fixation and non-operatively are not included. According to Swedish Registry data, approximately 50% of PFF are treated with revision.[125,126] While this is a significant limitation when trying to estimate the incidence of PFF after THA as a whole, knowledge of the incidence of revision for PFF at national level is an important consideration. The strength of the cohort is the size and despite not being able to speculate on the incidence of PFF treated with internal fixation, the pattern of temporal change is likely to be comparable, although this cannot be assumed without reasonable doubt.

In summary, both revision burden and incidence of revision for PFF are increasing in England and Wales, based on NJR data.

4 Risk Factors for Periprosthetic Femoral Fracture Revision after Primary THA in England & Wales for Osteoarthritis

4.1 Introduction

As demonstrated in the systematic review (Chapter 2), there are a number of observational studies that have explored the risk and risk factors for periprosthetic femoral fractures in THA. The studies included in the systematic review were based on either national-level registry data or institutional databases. For post-operative fractures, which account for the vast majority, cementless stems and increasing age were reported to be significant risk factors for PFF. However, a detailed exploration of implant design and patient factors and their association with PFF is lacking.

Within cemented and cementless stems, there are differences in stem design. For cemented stems, the commonly used stems are based on either polished taper or composite beam philosophies, which demonstrate different properties. Therefore, it follows that PFF risk could differ within these cemented stem groups. Cementless stems can be classified as collared and collarless stems, with the collared design aimed to protect against early subsidence. The influence of collared stem design on revision for PFF has not previously been investigated.

Khanuja's classification of cementless stems identifies Types I-VI, with type III being subdivided into IIIa, IIIb and IIIc (Figure 4.1). The influence of stem design on PFF risk was explored in a systematic review by Carli et al.[195] The authors reported that polished taper cemented stems showed higher PFF risk

than composite beam stems and for cementless stems Type I and II designs were associated with higher PFF risk than other cementless stem designs used in primary THA. However, they indicated that overall reporting was poor and suggested that registry level studies were needed to investigate stem design and PFF risk.

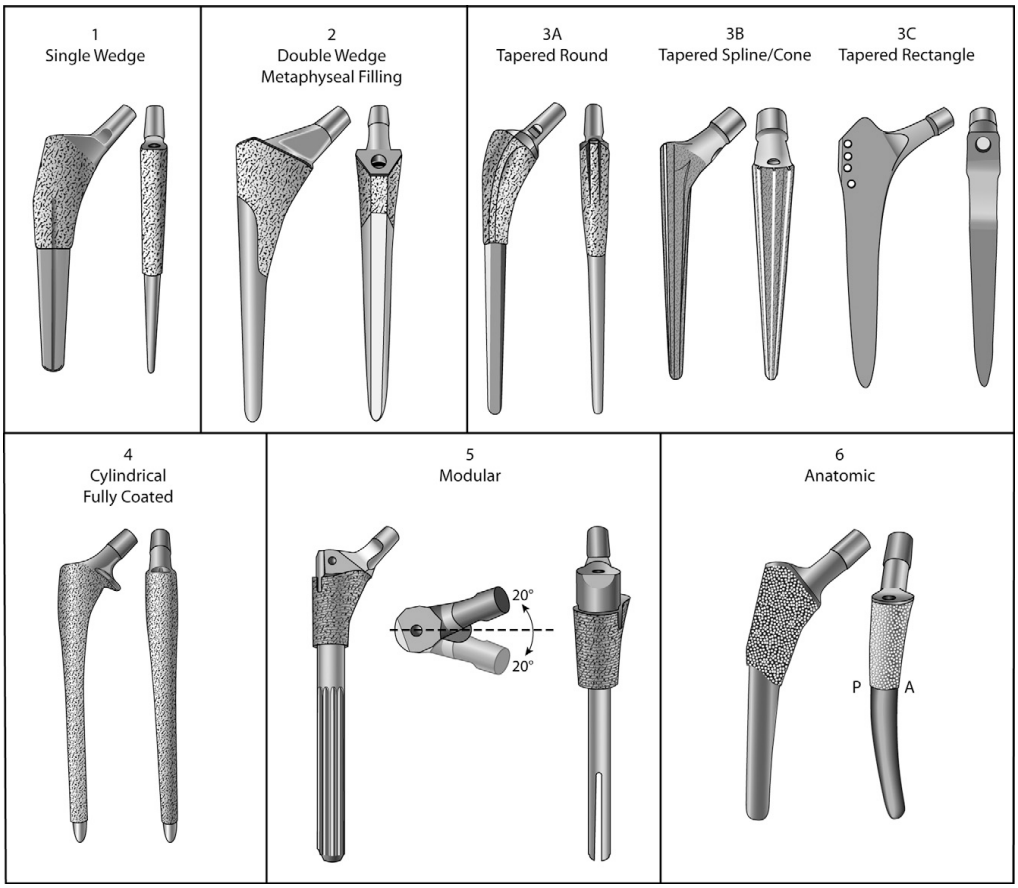


Figure 4-1 Classification of Cementless Stems[31]

With regards to patient factors, there are mixed results with respect to the influence of gender with some studies suggesting a higher PFF risk in females compared to males and other studies demonstrating the converse. Despite interest, there is little evidence of the independent effect of comorbidities and surgical fitness on PFF risk.

The aim of this study was to investigate the risk factors and probability or PFF revision after Primary THA using the NJR.

4.2 Methods

4.2.1 Study Design and Data Source

This study was a cohort investigation of primary THAs for osteoarthritis performed in England and Wales and entered into the National Joint Registry (NJR). Hip Resurfacings were not included. The same cohort of primary THAs used in Chapter 3 ('Primary THA' dataset) was used except that THAs performed in 2015 were included. Only THAs for osteoarthritis were included (except when comparing risk of PFF revision after primary THA for femoral neck fracture for which the data used included these cases). The primary THA dataset was linked to the NJR revision dataset to determine which cases had undergone revision surgery. Information relating to dates of death was provided by the Office of National Statistics (ONS) via matching with patient NHS numbers. Each primary THA therefore had one of three outcomes: death without revision, revised or unrevised.

4.2.2 Data Management

All raw data was provided by the NJR. String variables were transformed into coded numerical variables in Stata SE Version 14.2 (StataCorp, USA).

4.2.3 Indications for Revision

The NJR Minimum Dataset for revision THA (Appendix 11.1) allows the entry of multiple indications for revision. Due to the acute nature of

periprosthetic femoral fractures it is a reasonable assumption that is that if it is selected as an indication for revision, it is likely to be the main indication necessitating revision surgery. This assumption was used to classify revised primary THAs into two groups – 'revised for periprosthetic femoral fracture' and 'revised for all other indications. In order to compare differences in revision incidence by individual indications, assumptions were made as to which was the primary indication where multiple had been selected according to the following ranking system:

1) Periprosthetic femoral fracture
2) Infection
3) Dislocation
4) Aseptic loosening (stem or socket)
5) Pain
6) Other indications

Where two or more of the above indications had been selected as reasons for revision THA, the indication with the lower numerical rank was taken as the primary indication.

4.2.4 Statistical Analysis

4.2.4.1 Intraoperative Fracture

Logistic regression was used to compare odds of intraoperative fracture for covariates of interest: Stem fixation (cemented/cementless), age group (<70, ≥70), gender and ASA grade (≤2, ≥3) and primary surgeon grade

(consultant/non-consultant). Adjusted odds ratios were presented accounting for all the listed covariates of interest.

4.2.4.2 Competing Risks Analysis

In survival analysis, competing risks are present when individuals are at risk of more than one mutually exclusive event. For example, in cancer studies, the outcome of interest might be death from a specific cancer, but individuals are also at risk of death from other causes. A graphical representation of competing risks is shown in Figure 4.2. The figure shows three patients who have cancer, followed up for a 10-year period. All three patients are at risk of dying from cancer and other causes. Patient one is at risk of dying from cancer and other causes for the whole 10-year period but does not suffer either of these outcomes in the follow-up period and is therefore censored. Patient two died from other causes at the 3-year follow up point. However, in this hypothetical scenario, had they not died from other causes, they would have died from cancer at the 7-year follow-up point. Patient three died from cancer at four years and had they not been revised would have died from other causes at the 8-year follow-up point.

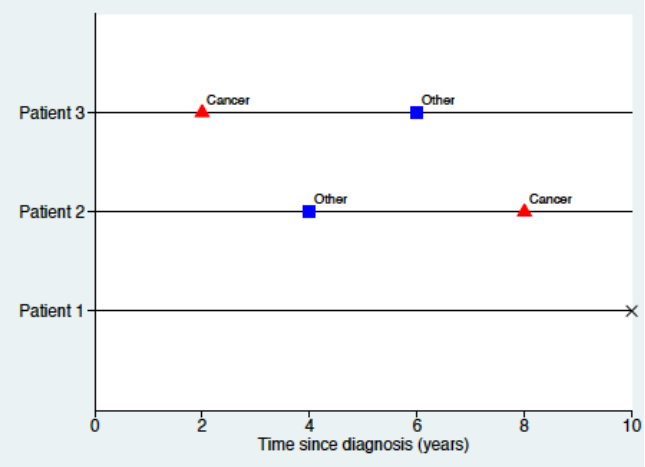


Figure 4-2 Graphical Representation of Competing Risks

In arthroplasty studies investigating all-cause revision as the outcome of interest, death is the competing risk. This hypothetical information in real life would not be known. Standard cause-specific survival analysis techniques in arthroplasty estimate the probability of not undergoing revision surgery in a world where it is not possible to die. Competing risks survival methods allow "real-world" estimates for probability of revision to be calculated where the individual is not only at risk of revision but also of death.

4.2.4.2.1 Cause-Specific Hazards

Where an individual is at risk of K events which are mutually exclusive, then the cause-specific hazard $h_k(t)$ is defined as the rate of failure from cause k at any specific timepoint (t), given that the individual has not already experienced failure from any cause. In arthroplasty survival analysis, when investigating a single cause of failure, for an individual to be at risk of failure from that specific cause, they cannot have experienced failure due to that, any other cause, or have died. After estimating the cause-specific hazards, the

cumulative incidence function can be calculated by transforming all K cause-specific hazards.

4.2.4.2.2 Cumulative Incidence Function

The cumulative incidence function can be defined as the proportion of individuals that have experienced a specific event by a particular time in follow-up. It can be derived as a product of all cause-specific survival functions. Therefore, any method used to estimate the cause-specific hazards can be used to obtain the cumulative incidence function. The cumulative incidence function incorporates the cause-specific hazards for both the event of interest and the competing events. This means there is not a one-to-one association between the cause-specific hazard for an event of interest and the probability of that event occurring.

4.2.4.2.3 Approaches to modelling competing risks

The two key approaches to modelling competing risks to obtain the cumulative incidence function are:

1) To model the cause-specific hazards and transform these to the cumulative incidence function
2) To model the cumulative incidence function directly by transforming the subdistribution hazards.

One of the advantages of the cause-specific hazards approach is that it gives a comparative measure (cause-specific hazard ratio) in addition to providing

estimates of the cumulative incidence. However, the cumulative incidence function encompasses the cause-specific hazards not only for the event of interest but the cause-specific hazards for the competing events. It follows that it is not a 1:1 relationship between the cause-specific hazard and probability of a particular outcome (e.g. revision arthroplasty) so the cause-specific hazard ratios do not summarise the differences in cumulative incidence function between covariate groups and cannot be used for this purpose. In the subdistribution hazard approach, the cumulative incidence function is only a function of the subdistribution hazard for the outcome of interest (e.g. revision) and therefore maintains the 1:1 ratio when transforming to the cumulative incidence function for quantifying the magnitude of difference between covariate groups. However, the subdistribution hazard ratio is not useful as an epidemiological measure as patients that suffer a competing event (e.g. death) remain in the risk set.

As the methodology used in this study focusses on using cause-specific hazards and transforming these to obtain the cumulative incidence function, the rest of this section relates to techniques for achieving this.

4.2.4.2.4 Non-parametric Approach

A common misconception regarding competing risks is to assume that the cumulative incidence function can be calculated using the complement of the Kaplan-Meier estimate (1-KM), which for revision after arthroplasty would mean the cumulative incidence is represented by 1-survival. However, the

competing events would be censored and the probability of the revision would follow the independence assumption, meaning it would represent an estimate in a hypothetical world where there are no competing risks.

4.2.4.2.5 Cox Proportional Hazards Approach

Cause-specific hazards can be modelled using Cox regression but the baseline hazard function cannot be directly estimated using the Cox model. Therefore, in order to obtain cause-specific hazards rates, the baseline hazard needs to be estimated via post-estimation using a method called kernel smoothing.[196] The key assumption with the Cox model is proportional hazards, which means the effects of the covariates remain constant over time. If this is a reasonable assumption, then the cumulative incidence functions obtained will be similar to the non-parametric approach. Incorporation of time-dependent effects is possible within the Cox model but standard statistical software restricts this to either piecewise or linear functions of (log) time.

4.2.4.2.6 Flexible Parametric Model Approach

As opposed to estimating the cause-specific hazard functions for each failure event using separate proportional hazards models, a joint flexible parametric model can be used. Flexible parametric models allow time-dependent effects to be incorporated with relative ease, which is one of its primary benefits. In addition, flexible parametric models directly estimate the baseline hazard

function and also allow flexibility in the shape of the baseline hazard function to differ over the follow-up time. Interaction effects also allow the effect of covariates to differ for each failure event.

Flexible parametric survival models were originally proposed by Royston and Parmar[197]. Restricted cubic splines are piecewise polynomial functions used to summarise non-linear associations in regression models. "Knots" are used to split the independent variable into segments on the x-axis, with separate curves to fit each segment. The splines are defined such that the overall fitted curve is smooth. A restriction of the restricted cubic splines is that the splines must be linear before the first knot and following the final knot. The location and number of knots are specified for the model and evidence indicates that the number of knots is more important than their location and therefore as long as an appropriate number of knots is selected, the location has little influence on the overall model.[198-200] Time dependent effects are incorporated in the flexible parametric models is by forming interactions between the derived variables and restricted cubic splines.

The present study uses flexible parametric competing risks models to obtain both the cause specifics hazards and the cumulative incidence function for revision surgery for periprosthetic femoral fracture, in the presence of competing risks of death and revision for all other indications.

4.2.4.2.7 Application of Flexible Parametric Competing Risk Model to the NJR Dataset

A flexible parametric model, which jointly modelled the outcome of interest (revision for PFF) and the competing events (death and revision for indications other than PFF) was used for this study. In order to apply a joint model for each of the three outcomes, the data was stacked such that each individual in the dataset had three rows of data, one for each outcome. Table 4.1 is an illustrative example of how the NJR dataset looked for two individuals after stacking.

Table 4-1 Example of NJR dataset for two patients with selected variables after 'stacking'

Patient ID	Age	Time (Years)	Cause	Status
1	65	10	Revision for PFF	0
1	65	10	Revision for other indications	0
1	65	10	Death	0
2	76	5	Revision for PFF	1
2	76	5	Revision for other indications	0
2	76	5	Death	0

Each individual with a primary THA in the NJR is at risk of three outcomes. Patient 1 remains unrevised and alive at 10 years following primary THA. Patient 2 is at risk of all three outcomes until 5 years when they require revision for PFF so are no longer at risk of any of the three outcomes. The inclusion of the three competing outcomes (death, revision for PFF and

revision for other indications) as both main effects and time-dependent effects, allowed a stratified model with three separate baselines, one for each outcome. The knot locations were for the splines were selected using the default settings for both the outcome of interest and the competing events using three degrees of freedom for both the baseline effects and time-dependent effects.

Management of Covariates

Age was analysed primarily as a continuous variable but to make meaningful comparisons between groups of patients it was used as a categorical variable. Covariates of interest were included in the flexible parametric model. Table 4.2 demonstrates the covariates used in the analysis.

Table 4-2 Variables used in survival models

Variable	Categorical/Continuous
Age at primary THA	Continuous & Categorical
Gender	Categorical
ASA grade	Categorical
Body Mass Index (BMI)	Categorical
Stem Fixation	Categorical
Stem Design	Categorical
Stem Brand	Categorical
Bearing Surface	Categorical
Surgeon Factors	Categorical
Primary Surgeon Grade	Categorical

Using the full dataset, the covariates included in the flexible parametric model were gender, age, stem fixation (cemented/cementless) and ASA grade.

When examining the risk of PFF for cemented stems, stem design (polished taper/composite beam), gender, age and ASA grade were included in the model. For cementless stems, stem design (Type I-VI and short stems), presence of a collar, gender, age and ASA grade were included.

Interactions between the outcomes (revision for PFF, death, revision for other indications) and each covariate was included in the model to account for varying effects of the covariates on each outcome.

When analysing the association between bearing surfaces and revision for PFF as well as surgeon grade and revision for PFF, the covariates included in the model were age, gender and ASA grade. For comparison of risk of revision for PFF after primary THA for femoral neck fracture compared with osteoarthritis, the dataset exclusion was relaxed such that primary THAs for both osteoarthritis and femoral neck fracture were included in the analysis. Age, gender and ASA grade were also included in the model.

4.3 Results

4.3.1 Demographics

There were 649,479 primary THAs included in the analysis with a total of 1,517 matched revisions for PFF. The overall mean age at time of primary THA was 69.6 (SD 10.4). There were 396,177 female patients (mean age 70.3,

SD 10.3) and 253,299 males (mean age 68.5, SD 10.4). Gender data was missing for three patients.

4.3.2 Intra-operative Fracture

There were 3,859 intra-operative PFF of the 649,479 primary THAs included in the analysis, which equates to an overall risk of 0.59%. Of the 3,859 cases complicated by intra-operative PFF, 29 required revision for PFF. Cementless stems were strongly associated with higher odds of intra-operative PFF, with an adjusted odds ratio of 2.50 (95% CI 2.34-2.68, $p<0.001$) when compared to cemented stems. Age≥70, female gender, ASA≥3 and non-consultant primary surgeon were all also associated with higher odds of intra-operative PFF. Table 4.3 summarises the covariates assessed for association with intra-operative PFF and individual odds ratios for each.

Table 4-3 Adjusted Odds Ratios for intraoperative PFF for each covariate

Covariate	Intra-operative PFF/Total Primary THA (%)	Adjusted Odds Ratio (95% CI)	p value
Cement Status			
Cemented Stems	1418/365077 (0.39%)	2.50 (2.34-2.68)	<0.001
Cementless Stems	2441/284402 (0.86%)		
Age			
Age<70	1816/300798 (0.60%)	1.12 (1.05-1.19)	0.001
Age ≥70	2043/348681 (0.59%)		
Gender			
Female	2831/396177 (0.71%)	0.52 (0.49-0.56)	<0.001
Male	1028/253299 (0.41%)		
ASA			
ASA 1/2	3091/554105 (0.56%)	1.26 (1.21-1.31)	<0.001
ASA ≥ 3	768/95374 (0.81%)		
Primary Surgeon			
Consultant	3146/532525 (0.59%)	1.12 (1.03-1.21)	0.007
Non-Consultant	713/116954 (0.61%)		

4.3.3 Revision for Post-Operative Fracture

4.3.3.1 Stem Design

4.3.3.1.1 Cementless vs Cemented Stems

Cause-Specific Hazard Ratios

The unadjusted hazard ratio (HR) for PFF revision for cementless compared to cemented stems was 1.43 (95%CI 1.29-1.58). After adjustment for age, gender

and ASA grade, the HR was 1.68 (95% CI 1.51-1.87, p<0.001). Comparing the rate of PFF revision within and beyond the first 3 months following primary THA in cementless versus cemented stems, the covariate-adjusted HRs were 8.82 (6.89-11.30, p<0.001) and 0.84 (95% CI 0.49-1.41) respectively.

Probability of Fracture (Cumulative Incidence)

The cumulative incidence of PFF for cementless and cemented stems in gender groups aged<70, 70-79 and ≥80 in the presence of the competing risks of death and non-PFF revision at 1-years, 5-years and 10-years following primary THA shown Table 4.4. Figures 4.3-4.5 show the flexible parametric cumulative incidence curves. Despite an overall higher risk of revision for PFF for cementless stems suggested by the cause-specific hazards, looking at the cumulative incidence function, the difference is age dependent and most pronounced for patients aged ≥80 at primary THA. The wide 95% confidence intervals for cementless stems suggests wide variation in the probability estimates.

Table 4-4 Cumulative Incidence (Probability) of Revision for PFF at 1-year, 5-years and 10 years (with 95% CIs) following Primary THA for cemented and cementless stems by age group and gender.

	1 year (%)		5 years (%)		10 years (%)	
	Cemented	Cementless	Cemented	Cementless	Cemented	Cementless
Males Aged ≤ 69	0.06 (0.05-0.07)	0.08 (0.02-0.13)	0.21 (0.17-0.25)	0.27 (0.07-0.46)	0.45 (0.37-0.52)	0.55 (0.16-0.95)
Females Aged ≤69	0.04 (0.03-0.05)	0.05 (0.01-0.09)	0.14 (0.12-0.17)	0.18 (0.05-0.31)	0.30 (0.25-0.35)	0.38 (0.11-0.64)
Males Aged 70-79	0.08 (0.06-0.09)	0.12 (0.03-0.20)	0.27 (0.23-0.31)	0.40 (0.11-0.68)	0.53 (0.45-0.61)	0.76 (0.21-1.30)
Females Aged 70-79	0.05 (0.04-0.06)	0.08 (0.02-0.13)	0.18 (0.16-0.21)	0.26 (0.07-0.46)	0.37 (0.32-0.42)	0.53 (0.15-0.91)
Males Aged ≥80	0.10 (0.08-0.12)	0.25 (0.06-0.43)	0.33 (0.26-0.40)	0.79 (0.20-1.37	0.55 (0.44-0.67)	1.25 (0.32-2.17)
Females Aged ≥80	0.07 (0.05-0.08)	0.16 (0.04-0.29)	0.22 (0.18-0.27)	0.54 (0.14-0.94)	0.41 (0.33-0.49)	0.94 (0.25-1.63)

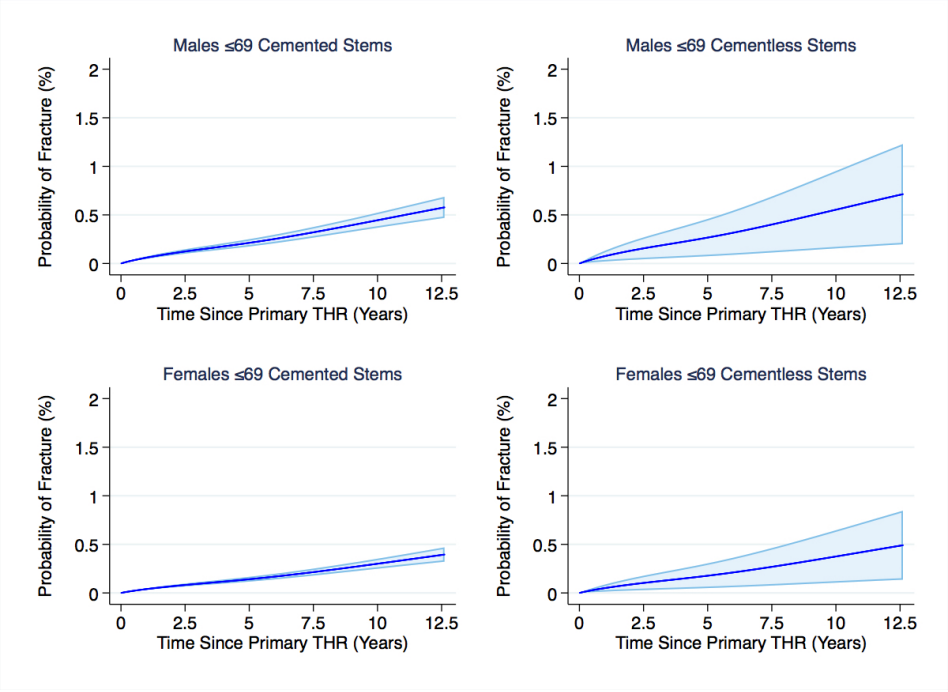


Figure 4-3

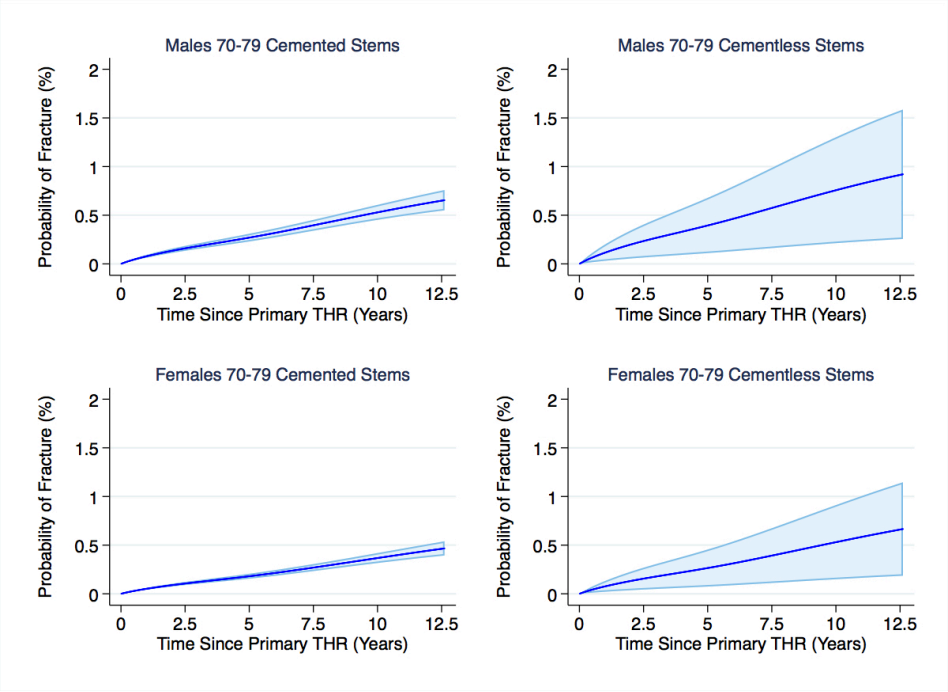


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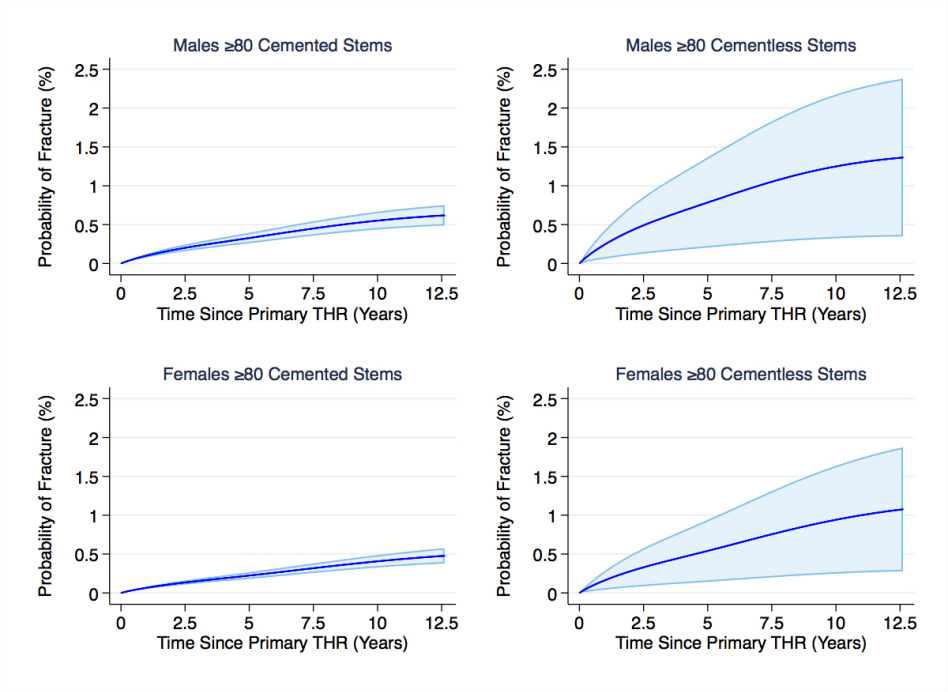


Figure 4-5 Cumulative Incidence of revision for PFF in cemented and cementless stems for patients aged ≤69 (4.3), 70-79 (4.4), and ≥80 (4.5).

4.3.3.1.2 Cemented Stem Design

A total of 309,970 implanted polished tapered and 44,838 composite beam stems were included in the analysis. The Stem Brands included and numbers implanted are shown in Table 4.5.

Table 4-5 Cemented Polished Taper and Composite Beam Stems in the NJR

Stem Brand	Polished Taper/Composite Beam	Number Implanted
C-Stem AMT	Polished Taper	14,827
C-Stem	Polished Taper	19,711
CCA	Composite Beam	1,645
CPCS	Polished Taper	3,558
CPS Plus	Polished Taper	2,099
CPT	Polished Taper	39,893
Charnley	Composite Beam	21,905
Charnley Modular	Composite Beam	1,096
Elite Plus	Composite Beam	1,653
Exeter v40	Polished Taper	217,994
Furlong Cemented	Polished Taper	1,877
MS-30	Polished Taper	5,042
Muller Straight Stem	Composite Beam	3,134
Muller-Biomet	Composite Beam	3,221
Olympia	Polished Taper	1,098
Omnifit	Composite Beam	1,565
SPII	Composite Beam	2,565
Stanmore	Composite Beam	8,054
Taperfit	Polished Taper	2,402
Taperloc	Polished Taper	1,469
Total	**-**	**354,808**

Cause-Specific Hazards

The unadjusted and covariate-adjusted (age, gender, ASA grade) HR for PFF revision in polished taper cemented stems compared to composite beam cemented stems were 4.03 (95% CI 2.88-5.64) and 4.09 (95% CI 2.92-5.72) respectively. This suggests a higher risk of PFF revision for polished-taper cemented stems. When cementless stems were compared with cemented polished taper stems, the unadjusted and adjusted HRs (age, gender, ASA grade) for PFF revision were 1.20 (95% CI 1.08-1.34) and 1.41 (95% CI 1.26-1.57), suggesting a higher risk of PFF for cementless stems.

Cumulative Incidence of PFF

The 5-year and 10-year cumulative incidences of PFF revision for polished taper and composite beam cemented stems for each age-gender group are demonstrated in Table 4.6 and Figures 4.6-4.7 show the corresponding flexible parametric curves.

Table 4-6 Cumulative Incidence (Probability) of PFF revision at 5 and 10 years for polished taper and composite beam cemented stems by gender and age.

	Females ≥70		Males ≥70		Females<70		Males <70	
	PT	**CB**	**PT**	**CB**	**PT**	**CB**	**PT**	**CB**
5 years (%)	0.17 (0.15-0.19)	0.03 (0.01-0.04)	0.37 (0.34-0.40)	0.06 (0.04-0.08)	0.12 (0.10-0.14)	0.06 (0.04-0.08)	0.26 (0.23-0.29)	0.13 (0.10-0.16)
10 years (%)	0.34 (0.31-0.38)	0.05 (0.03-0.07)	0.72 (0.70-0.74)	0.11 (0.08-0.14)	0.26 (0.22-0.30)	0.13 (0.10-0.16)	0.58 (0.55-0.61)	0.29 (0.26-0.32)

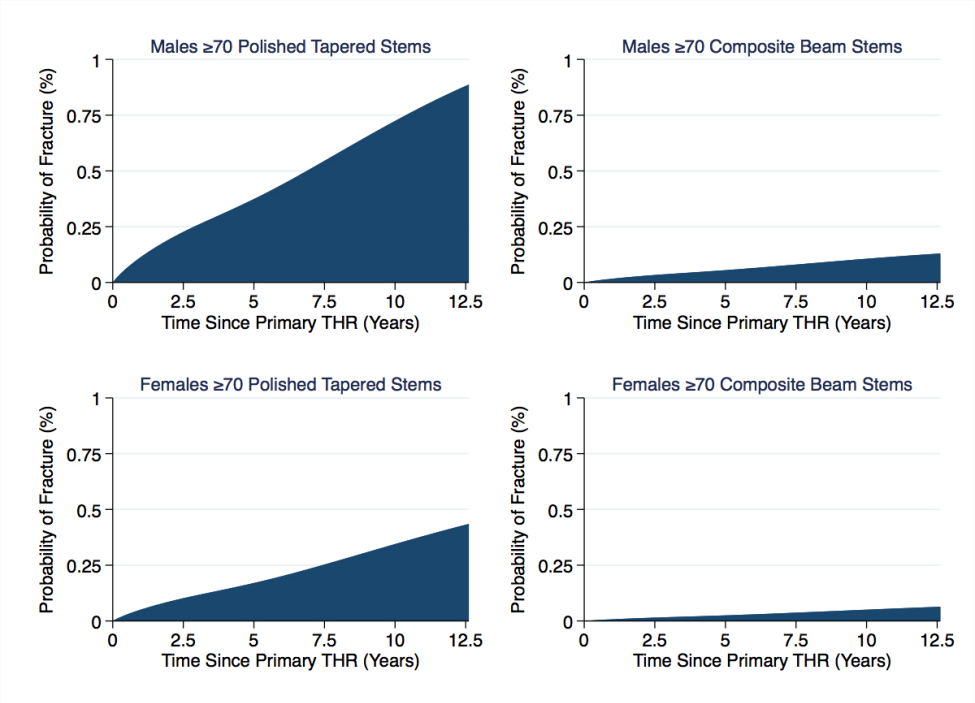


Figure 4-6

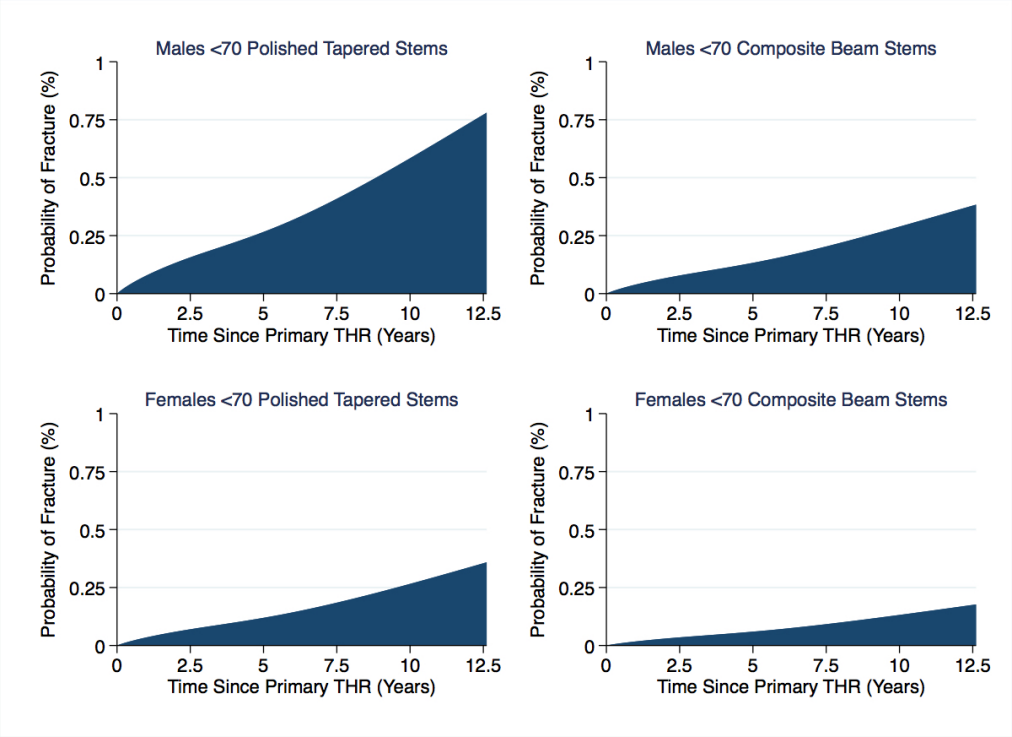


Figure 4-7 Cumulative Incidence (Probability) of PFF Revision for Polished Taper vs. Composite Beam cemented stems for patients aged <70 (4.6) and aged ≥70 (4.7) at time of primary THA (95% CI removed).

4.3.3.1.3 Cementless Stem Design

Collared vs. Collarless Cementless Stems

There were 214, 430 collarless and 69, 972 collared cementless stems included in the analysis. The covariate adjusted Hazard Ratio for PFF revision in collared cementless compared to collarless cementless stems was 0.41 (95% CI 0.31-0.54), suggesting a lower risk for collared stems.

The 5-year and 10-year risk of PFF revision for collared and collarless cementless stems grouped by gender and age group in the presence of the competing risks of death and revision for other indications is demonstrated in Table 4.7.

Table 4-7 Cumulative Incidence (with 95% CI) of revision for PFF for collared and collarless cementless stems.

	Females ≥70		Males ≥70		Females<70		Males <70	
	Collared	**Collarless**	**Collared**	**Collarless**	**Collared**	**Collarless**	**Collared**	**Collarless**
5 years (%)	0.43 (0.38-0.48)	0.43 (0.38-0.48)	0.34 (0.29-0.39)	0.43 (0.38-0.48)	0.19 (0.11-0.28)	0.20 (0.17-0.22)	0.15 (0.09-0.22)	0.20 (0.17-0.22)
10 years (%)	0.77 (0.67-0.87)	0.80 (0.70-0.9)	0.61 (0.52-0.70)	0.80 (0.70-0.91)	0.38 (0.21-0.55)	0.39 (0.34-0.45)	0.30 (0.17-0.43)	0.39 (0.34-0.45)

Cementless Stem Type

There were 24 cementless stems included in the analysis. Stem classification (Khanuja et al[31]) with stem brands and numbers implanted in primary THA are shown in Table 4.8. Table 4.9 shows the cause-specific hazards for PFF revision for each cementless stem type. Type II stems had the lowest overall revision risk. Type VI and Short femoral stems were associated with the highest risk of PFF revision in those aged ≥70 at time of primary THA. Figures 4.8-4.11 demonstrate the flexible parametric cumulative incidence of PFF revision for each of the stem types, stratified by age and gender.

Table 4-8 Cementless stems by design classification and numbers implanted

Stem Classification (Khanuja)	Stem Brands	Number of Implantations
I	Accolade, Accolade II, ML Taper Cementless, ML Taper Kinectiv, Taperloc, Trilock	53901
II	Bimetric, Corail, Evolution, Excia, Furlong HAC, Metafix, Omnifit, Polarstem, Profemur L, Summit, Synergy,	191542
III	Anthology, CLS, SL-Plus, Versys	18367
VI	ABG II Monolithic	3197
Short Stems	AMIStem, MiniHip	2620
Total	-	269627

Table 4-9 Unadjusted and adjusted cause-specific hazard ratios (HR) for PFF revision by cementless stem design classification (95% CI)

Cementless Stem Type	HR (unadjusted)	HR (Adjusted)
Type I	1.17 (0.97-1.42)	1.22 (1.01-1.49)
Type II	1	1
Type III	1.33 (1.02-1.72)	1.48 (1.14-1.92)
Type VI	3.24 (2.29-4.59)	4.04 (2.85-5.74)
Short Stems	2.27 (1.25-4.13)	2.89 (1.59-5.27)

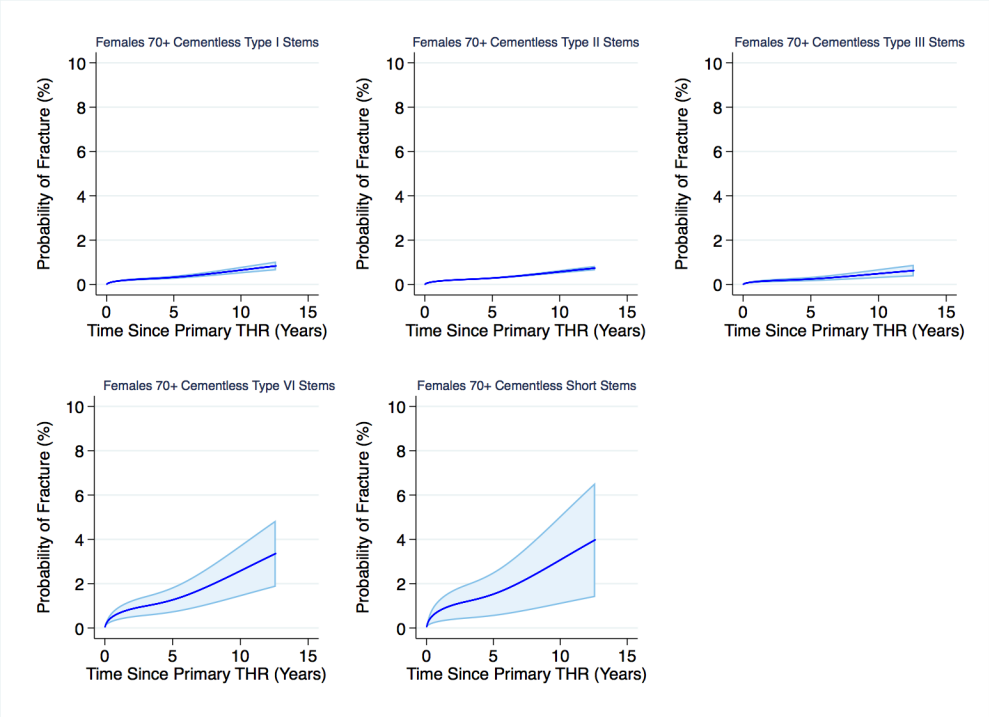


Figure 4-8

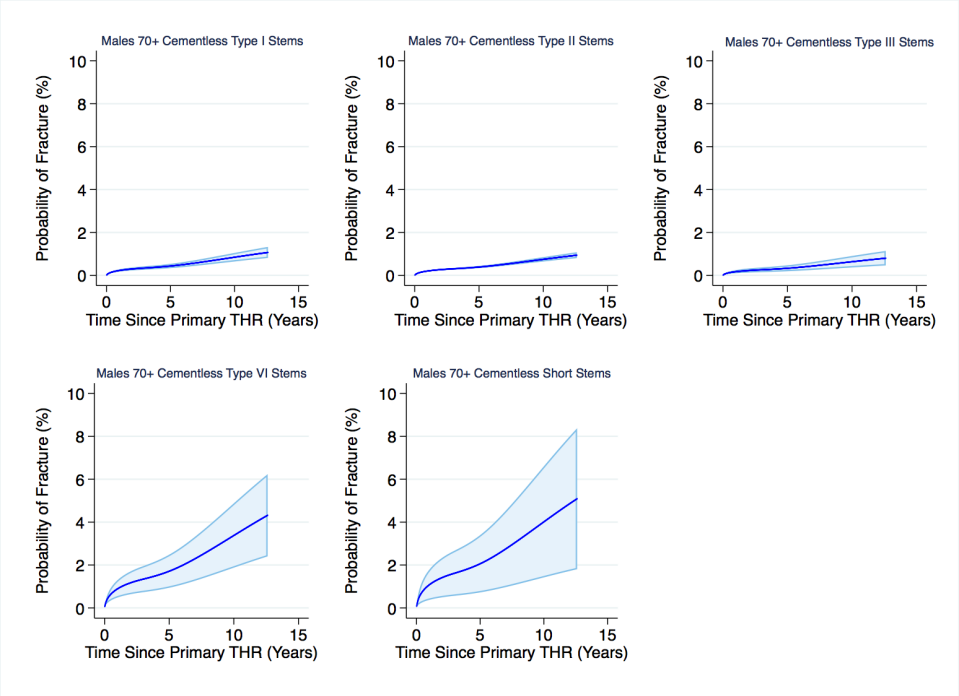


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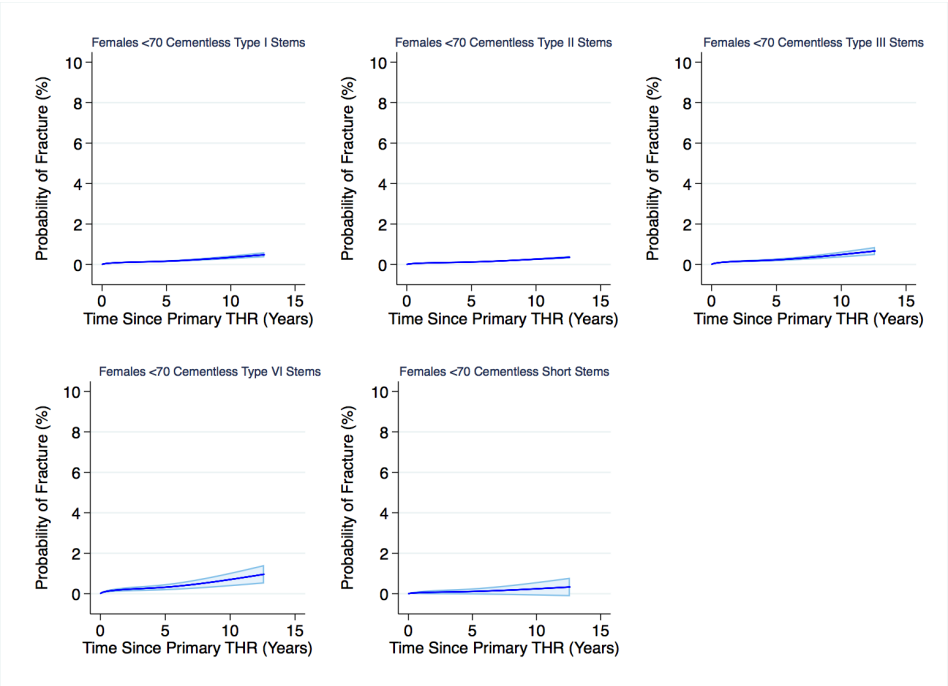


Figure 4-10

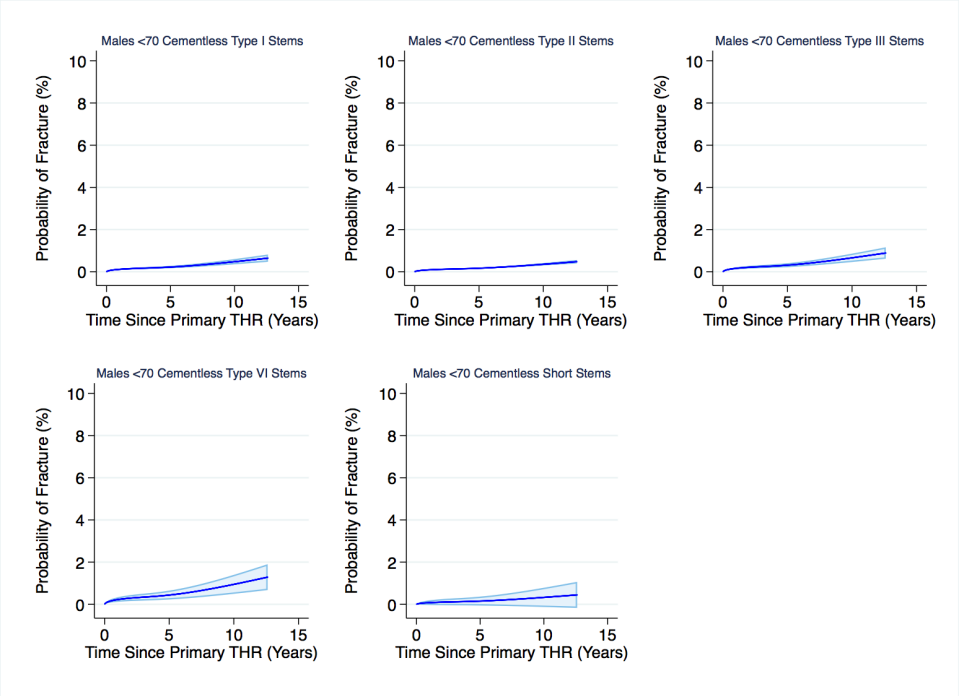


Figure 4-11 (4.8-4.11) Cumulative Incidence (Probability) of PFF revision for cementless stem by classification and age/gender group.

4.3.3.1.4 Popular Stems

The four most commonly used stems accounted for 424177/649709 (65.3%) of all primary THAs included in the dataset. These included: The Exeter v40 (Stryker, cemented polished taper, n=218,314), Corail (DePuy, cementless, n=130,094), CPT (Zimmer-Biomet, cemented polished taper, n=39,936) and Furlong HAC (JRI Orthopaedics, cementless, n=35,833). The CPT stem showed the highest risk of revision for PFF, which was significantly greater than the other commonly used stems. This was the case in all 4 age-gender categories as reflected in the cumulative incidence function. The age gender and ASA grade adjusted cause-specific hazard ratios of PFF revision are presented in Table 4.10. The 10-year probabilities of PFF revision (cumulative incidence), accounting for the competing risks of death and revision for other

indications are shown in Table 4.11 and the flexible parametric cumulative incidence curves in Fig 4.12-4.15.

Table 4-10 Causes-specific hazard ratios for PFF revision for commonest implanted stems

Stem	Cause-Specific Hazard Ratio	95% CI
Exeter V40	1	-
Corail	1.89	1.62-2.22
CPT	4.28	3.64-5.04
Furlong HAC	1.34	1.04-1.71

Table 4-11 Probability (Cumulative Incidence) of revision PFF for commonest implanted stems

	CPT	Corail	Exeter	Furlong HAC
Males aged ≥70	1.44 (1.18-1.70)	0.89 (0.74-1.04)	0.43 (0.36-0.49)	0.62 (0.44-0.79)
Females aged ≥70	0.99 (0.82-1.15)	0.60 (0.50-0.71)	0.29 (0.25-0.33)	0.42 (0.30-0.54)
Males aged <70	1.92 (1.50-2.30)	0.42 (0.33-0.50)	0.26 (0.20-0.31)	0.30 (0.18-0.41)

Females aged < 70	1.26 (0.99-1.53)	0.27 (0.22-0.33)	0.17 (0.13-0.21)	0.19 (0.12-0.27)

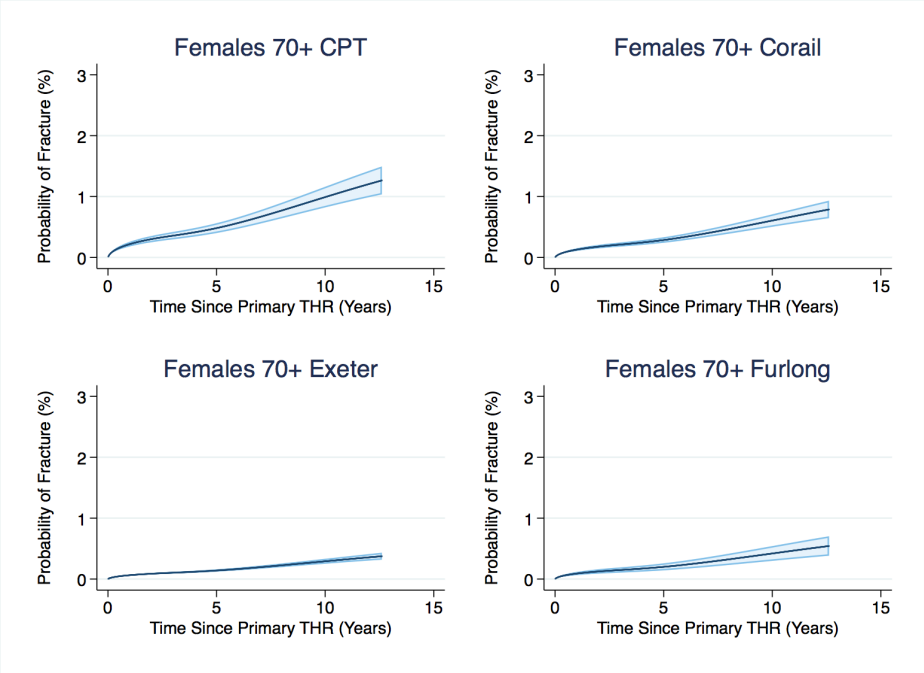


Figure 4-12

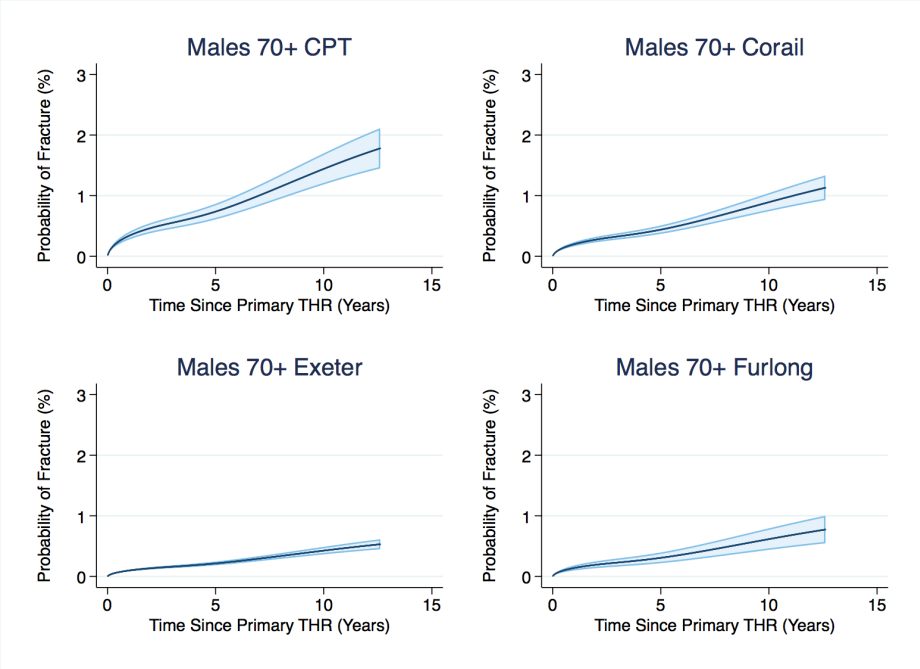


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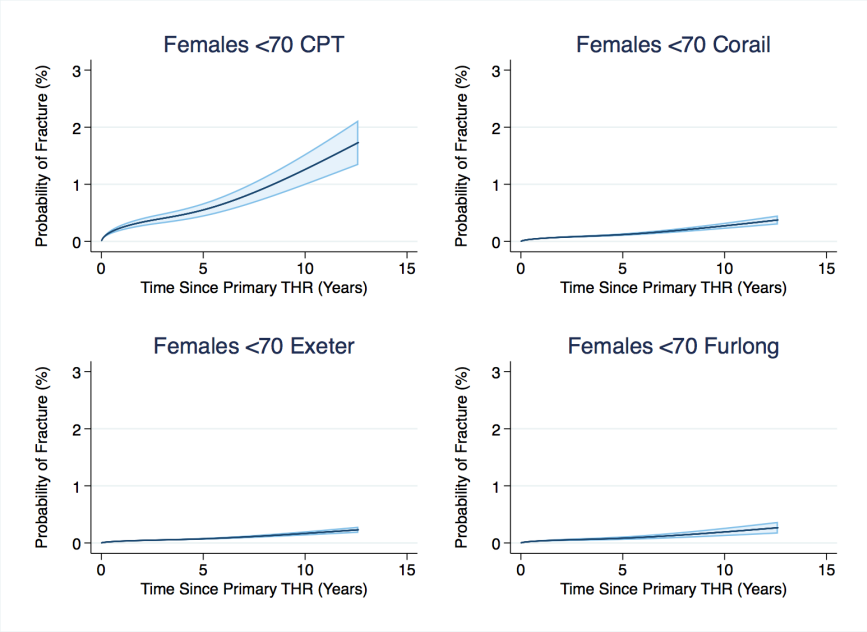


Figure 4-14

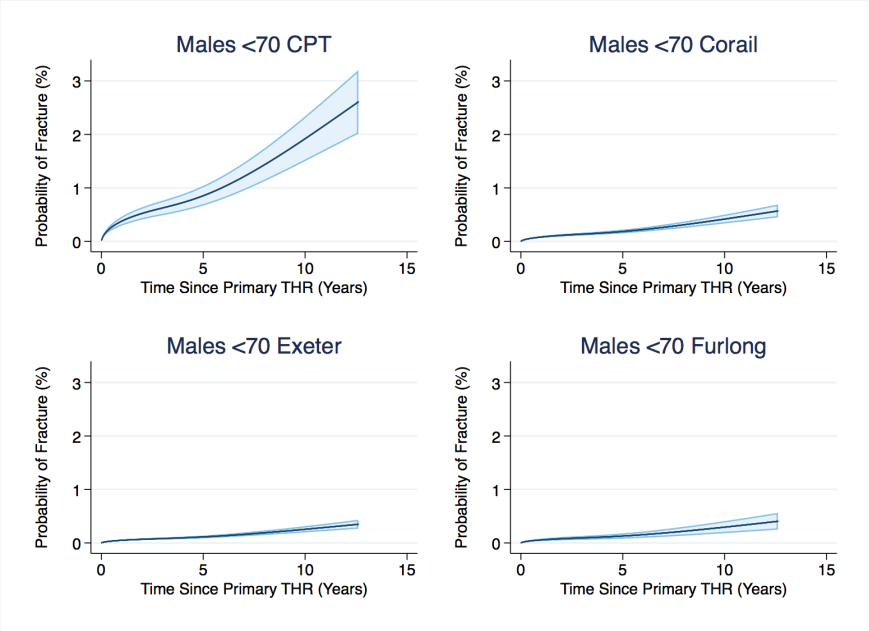


Figure 4-15 (Figures 4.12-4.15) Cumulative Incidence of PFF revision for commonest stems in the NJR for age/gender groups.

4.3.3.2 Age

Increasing age at time of primary THA was a significant independent risk factor for PFF revision surgery. When analysed as a continuous variable, the unadjusted hazard ratio was 1.023 (1.018-1.029). After adjustment for gender, ASA grade and stem fixation (cemented/cementless), the hazard ratio was 1.030 (1.024-1.036).

When analysed as a categorical variable, age at primary THA was grouped into five age groups:

age<65, age 65-69, age 70-74, age 75-79 and age 80+. The adjusted and unadjusted hazard ratios are shown in Table 4.12, with the hazard for age<65 taken as the denominator.

Table 4-12 Unadjusted and Adjusted HRs (<65=baseline) for PFF revision by age group

Age Category	Number of THAs	Hazard Ratio (unadjusted)	Hazard Ratio (adjusted)
<65	185,827	1	1
65-69	114,971	1.00 (0.85-1.18)	1.06 (0.89-1.26)
70-74	125,560	1.24 (1.06-1.44)	1.37 (1.17-1.60)
75-79	113,626	1.36 (1.16-1.59)	1.56 (1.33-1.83)
80+	109,494	1.92 (1.66-2.23)	2.29 (1.96-2.68)

4.3.3.3 Gender

Male gender was associated with a higher risk of revision for PFF with an unadjusted hazard ratio of 1.35 (1.22-1.49). After adjustment for age, ASA grade and stem fixation (cemented/cementless stem), the hazard ratio was 1.36 (1.23-1.51).

4.3.3.4 ASA Grade

Higher ASA grades were associated with an increased risk of revision for PFF. The unadjusted and adjusted hazard ratios (age, gender and stem fixation) of PFF revision are shown in Table 4.13. The adjusted hazard ratio included an interaction term to account for an interaction between age and ASA grade.

Table 4-13 Adjusted and unadjusted HRs for PFF revision by ASA grade (ASA 1=baseline).

ASA Grade	Number of THAs	Unadjusted HR	Adjusted HR
1	102,705	1	1
2	450,400	1.33 (1.14-1.55)	1.20 (1.03-1.40)
3	92,357	1.77 (1.47-2.13)	1.48 (1.23-1.79)
4	3017	1.96 (1.00-3.82)	1.56 (0.80-3.04)

4.3.3.5 THA for Femoral Neck Fracture

There were 18, 547 primary THAs performed for fractured neck of femur. The mean age was 72.4 (SD 10.2) and included 13,587 females and 4,960 males. The unadjusted hazard ratio for PFF revision for primary THAs performed for fractured neck of femur compared to those performed for osteoarthritis was 2.35 (1.86-2.96). After adjustment for age, gender, ASA grade and stem fixation (cemented/cementless) the hazard ratio was 2.38 (1.39-3.00), suggesting a higher risk of PFF revision in THAs performed for fractured neck of femur.

4.3.3.6 Bearing Surfaces

The four commonest bearing surfaces were included in the analysis and accounted for 612,528/649,479 (94.3%) of primary THAs in the dataset. Table

4.14 summarises the unadjusted and adjusted (age, gender, ASA grade and stem fixation) hazard ratios of revision for PFF in comparison to the most popular bearing surface for primary THA in the NJR (metal-on-polyethylene). The results indicated that the lowest risk of revision for PFF was for the ceramic-on-polyethylene. Metal-on-metal bearing surfaces showed a significantly higher risk of revision for PFF compared to metal-on-polyethylene.

Table 4-14 Unadjusted and adjusted HRs for PFF revision by bearing surface

Bearing Surface	Number of THAs	Unadjusted HR	Adjusted HR	P value
Metal-on-Polyethylene	382,477	1	1	-
Ceramic-on-Ceramic	106,687	0.92 (0.79-1.06)	1.01 (0.85-1.19)	0.933
Ceramic-on-Polyethylene	95,006	0.65 (0.54-0.78)	0.72 (0.60-0.87)	0.001
Metal-on-Metal	28,358	1.31 (1.09-1.58)	1.23 (1.01-1.52)	0.040

4.3.3.7 Surgeon Grade

532,525 of the primary THAs included in the analysis were performed with a consultant surgeon as the primary surgeon. 116,954 of the cases were performed with the primary surgeon as a non-consultant grade surgeon. Comparing consultant with other surgeon grade, there was no significant association with risk of PFF revision, with an unadjusted and adjusted (age,

gender, ASA grade and stem fixation type) hazard ratios of 0.96 (0.84-1.10, p=0.56) and 0.95 (0.84-1.09, p=0.49) respectively.

4.4 Discussion

This study has analysed the risk factors for intra-operative PFF and post-operative PFF revision surgery in THA, based on the largest arthroplasty registry in the world. Figure 4-16 summarises the risk factors identified and effect sizes. For intra-operative PFF, the identified risk factors were: Cementless stem fixation, female gender, age ≥ 70, ASA ≥ 3 and non-consultant grade primary surgeon. For post-operative PFF, male gender, increasing age, increasing ASA grade, cementless stem fixation, THA for femoral neck fracture and metal-on-metal bearing surface were independently associated with a higher risk of PFF revision surgery. For cemented stems, polished taper stems were associated with a higher risk of PFF revision compared to composite beam designs. For cementless stems, collared design was protective against revision for PFF. Type VI and short cementless stems demonstrated a higher risk of revision for PFF. There were significant differences in PFF revision risk between the 4 commonest stems with the CPT demonstrating the highest overall risk in all age-gender categories reported.

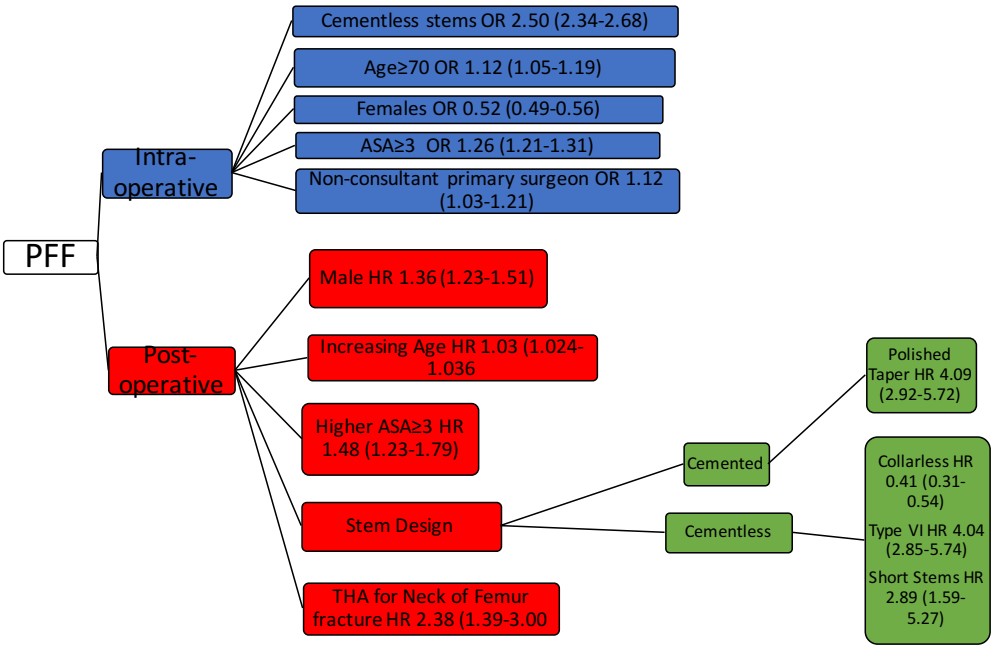


Figure 4-16 Risk Factors for PFF

Applying flexible parametric competing risk models, which have not previously been used to assess indication-specific revision risk, this study has also estimated the risk of intraoperative PFF and the comparative risk of PFF revision over time for age-gender groups based on stem design factors and patient factors.

A systematic review in Chapter 2 assessed the evidence for risk factors for PFF based on high volume studies. With respect to gender the evidence is conflicted with a number of studies suggesting higher risk of PFF in females compared to males and others demonstrating the converse. The present study shows a strong association between male gender and a higher risk of revision for PFF. Increasing age has been demonstrated to be significant risk factor and

this study supports that. A detailed comprehensive comparative analysis of stem design and PFF revision risk has not previously been performed, despite previous studies comparing cementless stems with cemented stems. Abdel reported a hazard ratio for post-operative PFF of 3.3 (95% CI, 2.7-4.0) for cementless compared to cemented stems.[158] The present study, with respect to PFF revision surgery, demonstrated an adjusted HR of 1.7 (95% CI, 1.5-1.9). It is difficult to speculate on the reason for the difference in effect size, particularly as Abdel's study is an institutional cohort study and the present study is a registry based study. However, the observation of a higher risk of PFF and PFF revision in both studies is significant.

Although some previous registry-based studies have investigated PFF in THA, the magnitude of primary THAs recorded in the NJR is significantly greater. The most recent publication relating to PFF based on data from The Swedish Arthroplasty Register, the second largest arthroplasty registry, analysed 246,679 primary THAs (before exclusions) which is less than a third of the pre-exclusion cases in the NJR primary THA dataset within a similar time frame.[122] Although the aim of this study was to assess the incidence of PFF by linking to the National Patient Register (NPR), the statistical methodology has significant flaws in attempting to achieve this aim. The primary flaw is that the study does not take into account the fact that registry data is 'time-to-event' data so any analysis must consider the time since implantation. The estimated incidence is therefore not comparable to those in Chapter 3. Despite a lack of regression analysis to assess the effect size, the authors reported a high proportion of PFF for polished tapered cemented stems. In particular, the

CPT stem, which only accounted for only 1.2% of all THAs in the Swedish Arthroplasty Register between 1992 and 2011, represented 4.1% of all PFFs between 2001 and 2011, which is similar to the findings of the present study. The reason for this is very difficult to speculate on, without a detailed biomechanical analysis of the CPT comparative to other polished tapered stems. However, the magnitude of the difference in PFF revision risk and the fact a similar finding has been noted in the Swedish Arthroplasty Registry, is indicative that the association is strong and needs to be explored. The use of cementless stems is relatively low in Sweden (12.4%) compared to the NJR (43.7%), but Chatziagorou's study did not show a disproportionate number of PFF in cementless stems.[122]

An important finding, not previously reported, was the reduced risk of PFF revision for collared cementless stems. Collars are designed to prevent stem subsidence and in the case of cementless stem fixation, which relies on bony ingrowth to confer stem stability, stem subsidence could compromise the stability of the stem. Therefore, a potential explanation is that in preventing the subsidence of cementless stems, the collar reduces micro-motion of the stem in the femoral canal and in doing so decreases the risk of PFF. This is another area that biomechanical studies are necessary to explore the association in more detail.

A key limitation of investigating PFF from NJR data is that PFF's treated without revision (i.e. internal fixation and non-operative treatment) are not reported to the registry. Therefore, any conclusions relating to risk factors are restricted to PFF requiring revision surgery. Despite this, large cohorts have

indicated that a large proportion of PFF in THA are treated with revision and these are the most challenging to treat operatively so despite this limitation the clinical conclusions drawn from this study and very relevant to clinicians, healthcare providers and policy makers.

5 A Systematic Review of Vancouver B2 and B3 Periprosthetic Femoral Fractures

5.1 Introduction

With a rising number of total hip arthroplasties (THA) being performed worldwide,[118,120] periprosthetic femoral fractures are an increasing problem. Based of predictive modelling of National Joint Registry (NJR) data, projected numbers of primary and revision THAs in England and Wales have been estimated to reach 186,893 and 137,056 respectively by 2030.[120] A higher risk of periprosthetic femoral fracture has been shown in revision THR[129] but also following uncemented femoral fixation,[129] which is increasing in incidence.[118,120,201] This suggests that the incidence of periprosthetic femoral fractures is likely to rise. The Swedish National Hip Arthroplasty Register, which contains data from 1979 onwards, show periprosthetic fracture as the second commonest reason for revision from four years after primary arthroplasty.[121]

The management algorithm surrounding the treatment of periprosthetic femoral fractures is complex. There a number of factors involved in determining the correct treatment path. The major influences are the location of the fracture relative to the implant, the state of fixation of that implant and the influence of the surrounding bone quality. These three important variables are identified in the Vancouver classification and form the basis of the established management algorithm.[58] There are however challenges in identifying B2 fractures when implant loosening is not obvious and the

determination of B3 status can be subjective. In this study, one of the objectives was to demonstrate supportive evidence of the importance of attributing an accurate Vancouver classification.

A number of studies have indicated a poorer outcome and higher mortality after revision for periprosthetic fracture compared with other indications for revision.[102,130,141] Drew calculated the combined risk of either death or re-operation in the first year after periprosthetic femoral fracture to be as high as 24%.[144] Furthermore, the costs associated with periprosthetic femoral fracture treatment are significant.[143,154] In todays' challenging healthcare environment, only successful clinical outcome will provide cost effective management.

A large proportion of periprosthetic femoral fractures in Total Hip Arthroplasty (THA) are Vancouver Type B2 or B3.[58,59] Published data from the Swedish Arthroplasty Register, reported that 555 of 1049 (53%) periprosthetic femoral fractures were classified Vancouver B2 and 43 (4.1%) were B3 fractures[126] Due to the presence of a loose femoral stem with either good bone stock (Type B2) or with poor surrounding bone (Type B3), it is generally recommended that treatment revision arthroplasty be performed.

Joint registries can provide an analysis of revision surgery for periprosthetic femoral fractures, but the breadth of data collected is limited. Much of this is related to the challenges associated with data collection at the time of an emergency admission for fracture. Similarly, registry data will not identify the entire cohort, specifically will often not identify those treated with fixation alone. With the exception of publications based on the Swedish registry,[125,126] most other reported registry studies do not describe details of fracture

classification and internal fixation techniques used alongside revision arthroplasty.[127,138,140,182]

Results from observational studies have the potential to provide detailed information, which can be used collectively to assess outcomes of different fracture treatment strategies for Vancouver B2 and B3 fractures. Although, systematic reviews have assessed the outcomes of B1[82,202] and C[202] fractures, there are no previous formal systematic reviews assessing the outcomes or comparative outcomes of B2 & B3 fractures.

The primary aim of this study was to perform a systematic review of the surgical treatment methods and outcomes of Vancouver B2 and B3 fractures. The secondary aim was to compare the reported outcomes in fractures treated with stem revision versus those treated with internal fixation without stem revision. We hypothesised that appropriate classification of periprosthetic fractures is critical in avoiding unnecessary further re-operation and ensuring cost effective and clinically successful outcomes.

5.2 Methods

We followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist for systematic reviews.[160] The review was registered on PROSPERO, an international prospective register of systematic reviews.

5.2.1 Data Sources

A comprehensive electronic search of Ovid MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials and Database of Systematic Reviews from the earliest available year of indexing up until August 2016 was conducted. As an example, the key terms utilised in the Ovid Medline search are shown in Appendix 11.4. The electronic search was supplemented with a manual search of the reference lists of all retrieved review articles for any other relevant citations. Abstracts of all citations were screened and full texts of articles were obtained to decide on inclusion of relevant studies. The attrition flow chart is shown in Figure 5.1.

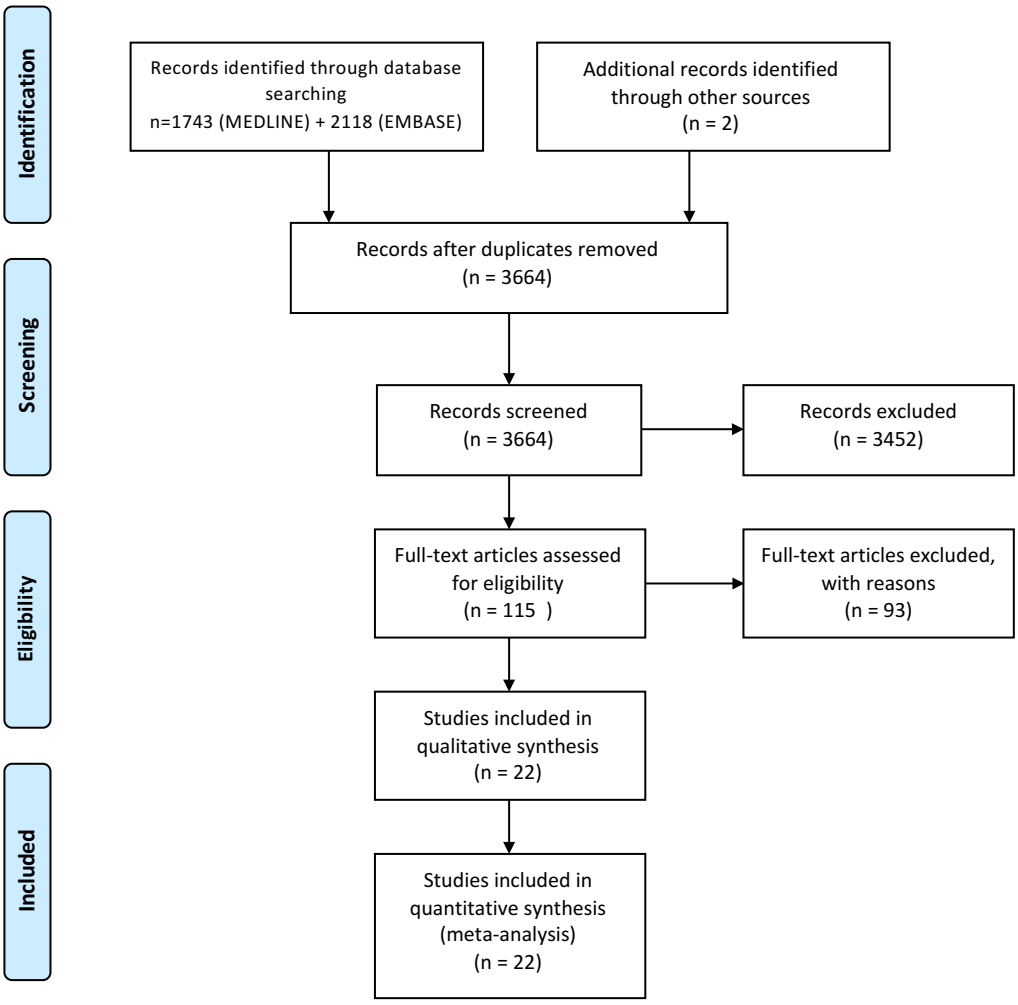


Figure 5-1 PRISMA flowchart for Systematic Review Process

5.2.2 Study Selection

Observational studies reporting the outcomes of surgical treatment of periprosthetic femoral fractures after THA, which fulfilled the following criteria were included. Periprosthetic femoral fractures were classified according to the Vancouver system,[59] included at least 10 patients with a Vancouver B2 fracture and/or 10 patients with a Vancouver B3 fracture. A

minimum of 2 years mean follow-up was required and studies had to report reoperation (including revision arthroplasty) as an outcome measure.

Studies were excluded if fractures were not classified according to the Vancouver system, if treatment methods and outcomes of Vancouver B2 fractures and B3 fractures were not reported separately by fracture classification.

5.2.3 Data Extraction & Quality Assessment

Two authors independently extracted data relating to study design, country of conduct, study period, case selection, exposure and outcomes assessment and patient characteristics. In cases of disagreement on extracted data, a third author independently performed data extraction. Quality assessment was performed independently by two authors using the validated tool specifically designed by Guo and colleagues to assess quality of case series,[203] and a minimum dataset was designed to improve data reporting specific to periprosthetic femoral fractures.

5.2.4 Data Analysis

Extracted data from included studies were entered onto RevMan Version 5.3. Treatment was categorised by fracture type (Vancouver B2 or B3) and treatment type (Revision +/- ORIF, ORIF alone). Specifics of prosthesis used

for stem revision was also recorded. Reoperation demographics were also reported according to fracture type and treatment. Risk Ratios (with 95% confidence intervals) for re-operation were calculated using the Mantel-Haenszel random effects model to make comparisons between treatment type and fracture type. Data was represented as Forest plots and two-tailed z tests were used with a significance level of 5%. Studies which reported treating both fracture types or similarly used both revision +/- ORIF and ORIF alone could be included for calculating risk ratios.

5.3 Results

Twenty-two studies fulfilled the inclusion criteria and were included in the review. All were case series[89,92,204-223]. Two studies involved the same patients [205,223] and data were extracted from both separately and then combined for analysis.

Five hundred and ten B2 or B3 fractures treated between 1984 and 2012 were included for analysis. The mean follow-up ranged from 32 to 74 months.

5.3.1 Vancouver B2 Fractures

There were 343 B2 fractures reported in 14 case series. Gender information was available for 125 cases (64 females: 61 males). Treatment involved stem revision with or without internal fixation techniques in 298 (87.6%) cases. 45 B2 fractures were treated with internal fixation without stem revision. For

those treated with revision arthroplasty, cemented stems were used in 82 (27.6%) cases and uncemented in 153 (51.3%) cases. Stem type was not specified in 63 (21.1%) cases, which involved stem revision.

There were 43 (12.8%) cases that required re-operation following treatment for B2 fractures. Overall 6/45 (13.3%) B2 fractures treated with internal fixation without stem revision and 37/258 (12.4%) treated with revision with or without internal fixation underwent reoperation. Table 5.1 demonstrates the re-operations by periprosthetic fracture treatment type.

Table 5-1 Total numbers and reoperations n (%) of Vancouver B2 & B3 fractures by fracture treatment type.

Fracture Type	Revision +/- ORIF			ORIF without Revision	Total
	Cemented	Uncemented	Unspecified		
Total Type B2 Fractures	82	153	63	45	343
Reoperations Type B2 fractures n (%)	11(13.4)	19 (12.4)	7 (11.1)	6 (13.3)	43 (12.5)
Total Type B3 Fractures	49	90	21	7	167
Reoperations Type B3 Fractures n (%)	8 (16.3)	12 (13.3)	3 (14.3)	2 (28.6)	25 (15.0)

Four studies reported results of treating B2 fractures with either ORIF alone or stem revision with or without ORIF. The calculated risk ratio of re-operation

was 1.74 (95%CI 0.61-4.97, p=0.30) in favour of revision arthroplasty with or without ORIF (Figure 5.2). Table 5.2 summarises indications for re-operation by fracture type.

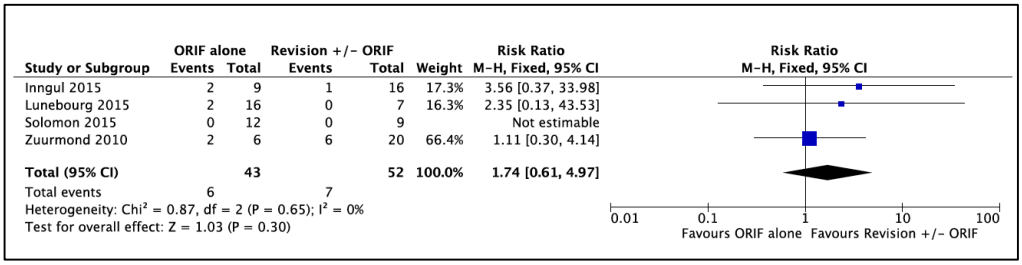


Figure 5-2 Forest plot comparing the risk of re-operation for Vancouver B2 fractures treated with revision arthroplasty with or without open reduction and internal fixation (ORIF) versus ORIF alone (M-H, Mantel-Haenszel method; CI, confidence intervals; df, degrees of freedom).

Table 5-2 Indications for re-operation by fracture type

Indication for Re-operation	B2 Fractures	B3 Fractures
Refracture	9	2
Infection	3	3
Subsidence	6	3
Stem loosening (aseptic)	4	1
Non-union	4	0
Dislocation	4	2
Wound infection/superficial haematoma	4	3
Implant breakage	1	1
Not specified	8	10
Total	43	25

5.3.2 Vancouver B3 fractures

There were 167 Vancouver B3 fractures in the included studies. Gender information was available for 99 patients (59 females, 40 males). In the vast majority of cases, 160 (95.2%), treatment involved stem revision with or without internal fixation. Eight (4.8%) cases were treated with internal fixation without stem revision. Of the 160 cases involving revision arthroplasty, 90 (53.9%) used uncemented femoral components, 28 (16.8) used a cemented revision stem and 21 (12.6%) fractures were treated with cemented proximal femoral replacement. Revision prostheses were not specified for 21 (12.6%) cases. Table 5.3 demonstrates the reported femoral components used for revision in B2 and B3 cases in included studies.

Table 5-3 Revision femoral stems used for B2 & B3 fractures by implant design.

Stem Design	Type B2 Fractures	Type B3 Fractures	Total
Tapered, collarless polished (cemented)	24	3	27
Tapered, polished, Collared (cemented)	7	0	7
Non-tapered, collared, rough finish (cemented)	23	0	23
Matte finish (Cemented)	0	25	25
Tapered fluted (uncemented)	114	58	172
Distal locking (uncemented)	15	24	39
Proximal Femoral Replacement	0	21	21

(cemented)			
Unspecified cemented	28	0	28
Unspecified Uncemented	46	8	54
Unspecified	41	21	62
Total	298	160	458

There were 25 (15.0%) reoperations (Table 5.1), 23 of those that were treated with stem revision +/- ORIF (14.4%) which included two re-operations (for wound infection) in B3 fractures treated with proximal femoral replacements. There were two (28.6%) reoperations for cases treated with ORIF alone (1 for further periprosthetic fracture and 1 for aseptic loosening of the stem). In two studies, results of both ORIF alone and stem revision with or without ORIF were reported. The calculated risk ratio based on these two studies was 1.38 (95% CI 0.38-5.01, p=0.63) in favour of stem revision +/- ORIF (Figure 5.3).

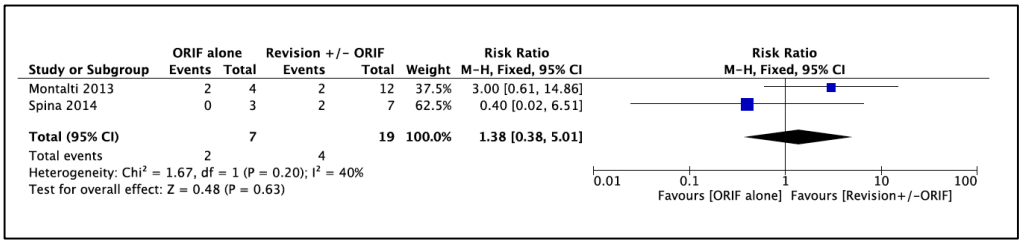


Figure 5-3 Forest plot comparing the risk of re-operation for Vancouver B3 fractures treated with revision arthroplasty with or without open reduction and internal fixation (ORIF)versus ORIF alone (M-H, Mantel-Haenszel method; CI, confidence intervals; df, degrees of freedom).

5.3.3 Vancouver B2 vs B3 fractures

Four studies reported outcomes of sufficient numbers (>10) of both B2 and B3 fractures for a total of 180 periprosthetic fracture cases. The risk ratio of re-operation regardless of treatment type was 0.49 (95%CI 0.24-0.99, p=0.31) in favour of B2 fractures (Figure 5.4). The risk ratio when excluding cases treated with ORIF alone was 0.52 (95%CI 0.28-0.98, p=0.23) in favour of B2 fractures.

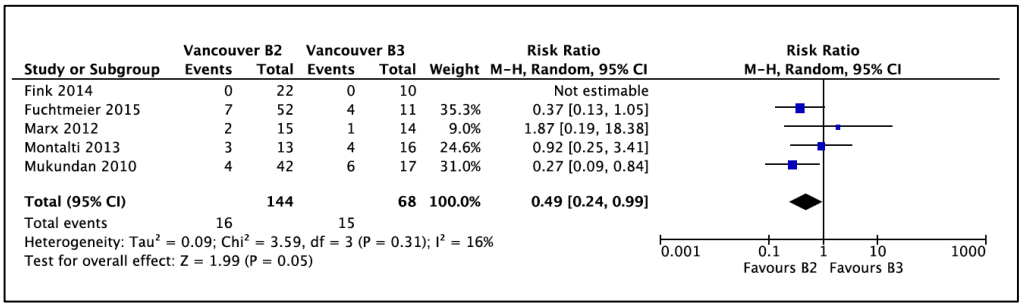


Figure 5-4 Forest plot comparing the risk of re-operation for Vancouver B2 and B3 fractures (M-H, Mantel-Haenszel method; CI, confidence intervals; df, degrees of freedom).

5.3.4 Cementless Tapered Fluted Stems

Cementless tapered fluted stems were used for stem revision in 114 (33.2%) B2 fractures and 58 (34.7%) B3 fractures. The reported overall percentage re-operation was 14/114 (12.3%) for B2 and 9/58 (15.5%) for B3 fractures. Indications for re-operation included refracture (3), dislocation (3), aseptic loosening (3), wound complications (3), stem breakage (1). Stem subsidence was reported in 9/172 (5.2%) cases, although only three (1.7%) of which required revision. The indication for re-operation was unspecified for seven cases.

5.3.5 Quality Assessment

The mean quality score was 11.5/18 (SD 2.39). Only two studies reported detailed individual case-by-case demographic, diagnosis, treatment and outcomes data, both adopting a table format with a row per patient.[207,222] Only five of the included studies had a mean follow-up time of 5 years or more.[208,213,214,218,220] Fourteen studies reported either the names of the specific prostheses or design details of the femoral components used for stem revision. None of the included studies reported time to event data for survival analysis.

5.4 Discussion

This systematic review demonstrates that as per consensus, the majority of B2 and B3 fractures reported in the literature are treated with revision arthroplasty with or without internal fixation. However, for B2 fractures particularly, a significant proportion (13.1% of cases analysed in this review) were treated with internal fixation alone. This could demonstrate the difficulties in determining whether the implant was loose prior to injury from the available imaging. However, this determination is important. Often the differentiation between a B1and B2 fracture is straightforward. However, there are fractures, initially felt to be around solid femoral implants, in which only a careful review of previous radiographs or a thorough history identifying pre-existing thigh pain, will raise the suspicion of associated stem loosening. Similarly, there are specific fracture patterns and locations, such as a relatively transverse fracture through an area of lysis below an apparently well-fixed stem, which should alert the surgeon to the likelihood that the stem was

actually failing and should be revised. Our study has shown that for both fracture types, treatment with internal fixation alone was associated with a higher percentage of re-operations, but the difference in relative risk did not reach statistical significance. For B3 fractures treated with internal fixation without stem revision, almost a third of cases required re-operation. This trend is supported by national level data from the Swedish Joint Registry which indicates a higher percentage of re-operations for B2 fractures treated with ORIF without stem revision (32%), compared with those treated with revision alone (10%) or revision combined with internal fixation (23%).[125]The overall proportion of cases re-operated upon were higher than reported in this systematic review which is potentially a reflection of the longer follow-up period of registry data as opposed to published observational series. Another potential explanation is that there is bias in the selection of cases, which surgeons/centres treat with internal fixation alone. This is perhaps related to patient fitness for a longer more physiologically demanding revision procedure, non-ambulatory patients, or where the patient life expectancy is extremely limited. Furthermore, some authors have reported good results at 5-year follow up of treating selected B2 fractures around polished, tapered, collarless stems in which anatomical reduction can be achieved, with internal fixation alone.[218] The data available for this systematic review limits our ability to address the question of which, if any, patients sustaining B2 or B3 injuries, would be suitable for treatment with internal fixation alone.

The analysis of included studies with sufficient data available for comparison, indicates a higher relative risk of reoperation for B3 fractures compared to B2

fractures, even when comparing fractures treated with stem revision +/- internal fixation. Anecdotally, this has been appreciated by surgeons experienced in the management of these injuries, but there is little previous data, to quantify this difference in risk of failure. It is important to remember, that compromise in the surrounding bone stock, that determines differentiation of B2 and B3 fractures, is potentially representative of other factors, which may contribute to a higher risk of failure. These include factors such as multiple previous hip arthroplasty procedures, previous infection or fracture, severe lysis or osteopenia and poor overall patient physiology, which have not been accounted for as confounders in this analysis.

For the management of both B2 and B3 fractures, uncemented stems were found to be more commonly used in the included studies. Among those treated with uncemented stems, a significant proportion reported the use of taper fluted titanium stems. Of these, the non-modular Wagner SL was used in almost a quarter of all cases involving stem revision. Tapered fluted titanium stems provide reliable and versatile distal diaphyseal fixation, which overcomes concerns over proximal stress shielding and the difficulties associated with advanced proximal bone loss. These systems facilitate an accurate restoration of hip biomechanics with options to re-establish length and version independently, with modular proximal components. Good results have been reported in the literature after femoral revision for aseptic loosening.[224-229] Encouraging results with these technologies have been reported in the management of periprosthetic fractures.[230-233] However, in

many studies, the results are reported as part of larger observational cohorts, with their use in B2 and B3 fractures as only one of a number of other indications for femoral revision. This is likely under reported in this review as the papers did not satisfy the formal criteria for inclusion set out in our systemic review.

In this systematic review, the percentage re-operation using tapered fluted stems for both B2 (12.3%) and B3 (16.7%) was comparable to the Swedish registry overall re-operation rates for B2 (18.5%) and B3 (15.5%) fractures treated with stem revision +/- ORIF. One of the complications of tapered fluted stems reported in the literature is stem subsidence. This can be a particular concern in the presence of poor bone quality. The rates and magnitude of subsidence differs in different systems. While significant rates of subsidence have been reported with the 2-degree taper angle of the Wagner SL,[106,234] more aggressive taper angles available in some systems have shown lower rates of clinically significant subsidence.[235] The overall proportion of subsidence in the stems used for Vancouver B2 and B3 fractures appears relatively low in this review. Despite, the majority of studies reporting less than 5-year follow-up, it is likely that any clinically significant subsidence would have occurred prior to that time. It is also important to appreciate that there was variation in the threshold for what could be deemed ‘clinically significant’ subsidence.

There are limitations of this systematic review. There is a lack of large prospective cohort studies relating to this field of study, hence, the studies included are all retrospective case series. There were 115 articles, which were assessed for inclusion based on the full-text of which only 22 were included in the review. Many of the studies were excluded either due to small numbers of periprosthetic fracture cases or lack of matched outcomes by fracture classification. Only two of the included studies reported individual case-by-case details.[207,222] Specifics such as original implant details, whether the fracture occurred after primary of revision arthroplasty, implants/fixation strategies used for each patient would have allowed a more detailed analysis. Furthermore, time to event (re-operation or death) was not reported in any of the included studies, therefore comparative survival analysis was not possible.

Similar to the Swedish registry data, Cook reported 52% B2 and 10% B3 fractures in their cohort study of periprosthetic fractures following 6458 primary THRs.[134] Recent results from the Mayo clinic, Minnesota, USA, reported 557 post-operative periprosthetic femoral fractures from their institutional registry of 32644 primary THAs, of which 24.5% were B2 and 9.2% were B3 fractures.[129] It is likely that Vancouver B2 and B3 femoral fractures will continue to increase in incidence. As a consequence of their requirement for complex reconstructive surgery, their high potential morbidity and resulting high cost in financial and clinical resources, these injuries contribute with increasing significance to the overall burden of periprosthetic fractures.

It is important to appreciate that a significant number of Vancouver B2 fractures are potentially misclassified as B1 and treated with internal fixation without stem revision. These B2 fractures would not be captured in this review. Therefore, the true re-operation rate of B2 fractures is likely to be higher than that demonstrated in this review.

The Vancouver classification has good intra- and inter-observer reliability[59,60,156,236] and is a useful tool in guiding clinical decision making. Despite this, it can sometimes be difficult to classify injuries accurately. Previous authors have suggested algorithms based on the host of strategies available which often depend on the design of the existing femoral stem, fracture location and precise fracture configuration.[237] This systematic review highlights both the variability in the reported treatment of B2 and B3 fractures, but also the significance of choosing the correct management strategy to avoid an increased risk or re operation. Our study also demonstrates that although there are established guidelines surrounding the principles of management, there is a need for high quality reporting of the outcomes of the various treatment options. Comparison of these studies will then allow further refinement in an algorithmic approach to management.

Currently, the National Joint Registry, the largest arthroplasty register in the world, records all primaries performed in England and Wales with matched

revision arthroplasty procedures by indication. However, as a large population-based database, the breadth of data on each specific indication for revision is limited. For periprosthetic fractures, only those undergoing revision arthroplasty are entered, therefore, those treated by internal fixation, although a relatively small number in the case of B2 and B3 fractures, are not recorded. Fracture classification and details of any use of additional internal fixation strategies are also not recorded. There is therefore a necessary reliance on detailed observational studies to bridge this gap in information. There are reporting recommendations for case series in colorectal[238] and more recently plastic surgery.[239] On this basis, we have designed a suggested minimum dataset to aid reporting of case series relating to outcomes of periprosthetic fractures (Fig 5.2).

In conclusion, this study is the only systematic review of Vancouver B2 and B3 femoral fractures. There are a proportion of both fracture types treated with internal fixation alone, which were associated with higher re-operation rate. Despite a large number of case series relating to treatment of B2 and B3 fractures, the breadth and detail of data reporting limited the quantitative comparisons of specific treatment strategies. We have designed a minimum dataset for case series relating to periprosthetic fracture.

Age at primary	Sex	Fracture: post-primary THA, revision, hemiarthroplasty	Year of Primary	Primary Implants	Time to fracture (months)	Fracture Type (Vancouver)	ASA grade + comorbidities	Treatment: Stem Revision only, Stem Revision + ORIF, ORIF only, Stem Revision + Socket Revision, cement-in-cement revision	Revision Implants	ORIF Implants (including strut allograft if used)	Time to Union (weeks)	Reoperation/died/ No reoperation (R/D/NR) If reoperation, give indication: E.g. Infection, dislocation, fracture, stem failure, subsidence, aseptic loosening	Reoperation details e.g. Washout, stem revision,	Time to re-operation/ death	Date of latest follow-up/death	Other outcomes: PROMS Subsidence Complications

Figure 5-5 Suggested minimum dataset for case series reporting results of periprosthetic fractures

This study has been published in the Bone & Joint Journal[240] (see Appendix 11.7).

6 The Outcomes of Revision Surgery for Periprosthetic Femoral Fracture

6.1 Introduction

It was demonstrated in Chapter 5 that PFF in the presence of a loose femoral stem (Vancouver B2 and B3 fractures) have poorer outcomes if treated without stem revision. As the number of PFF cases in individual series is relatively low, it is difficult to quantify the success of revision for PFF specifically without using registry level data. However, registry data on the outcomes of PFF treatment is limited. Lindahl et al, reported the results of PFF treatment and demonstrated that 25/135 revised type B2 fractures, 5/43 revised type B3 fractures and 5/31 revised type C fractures required re-operation.[125] Although the study did not include a time-to-event analysis, the results suggest a high failure risk of revision for PFF. Other authors have reported similar poor outcomes based on New Zealand and French joint registry data.[141,241] Despite this, there are no high volume studies comparing outcomes of PFF revision with other indications for revision hip arthroplasty using time-to-event survivorship analysis. Several authors have also reported a high risk of mortality after PFF treatment.[123,141,155] The only study to investigate the comparative mortality of revision for PFF with aseptic loosening reported a higher 6-month mortality for PFF revision but this was based on only 232 revisions for PFF.[141]

Given the high reported revision risk following revision for PFF, it is important to determine which patient, implant and surgeon-related factors contribute to this. There are no previous studies that have addressed this. Furthermore, there has been a recent drive within the UK to centralise revision arthroplasty surgery to specialist centres with the intention to improve outcomes. The difficulty for PFF treatment is the acute and emergency nature of the problem. Patients with PFF are admitted acutely and require urgent surgery to allow mobilisation and pain relief. Revision arthroplasty for some other common indications such as aseptic loosening (the most common indication for revision), typically present in the outpatient setting and can be managed electively. With regards to revision for PFF, key questions include whether surgeon and centre volume influences failure (further revision) or mortality.

The aim of this study was to assess, using NJR data, the risk and risk factors for further revision following first revision for PFF, to investigate the mortality following first revision for PFF and compare these outcomes with the results of first revision for other common indications.

6.2 Methods

6.2.1 Study Design

The study was a cohort investigation using data from the NJR. A dataset of all first revisions recorded in the NJR was linked using two unique identifiers

(NJR ID and Procedure ID) and laterality of THA with a second dataset of all second revisions. Second revision THAs performed up to and including 28th September 2015 were included in the analysis. Outcome data for each first revision was available on the dataset and was recorded as either unrevised, death without revision or revision.

In a separate analysis, the dataset used in Chapter 3 and 4 which included all Primary THAs performed in England and Wales was merged with the dataset including all first revisions. This provided a dataset to analyse the outcomes after first revision of all primary THAs recorded in the NJR.

6.2.2 Data Management

Data linkage was performed in STATA SE v15 using the 'joinby' and '_merge' commands. Variables were managed in the same manner as Chapter 4.

6.2.3 Statistical Analysis

6.2.3.1 Survivorship Model

A flexible parametric competing risks model (see Chapter 4 for detail) was used to estimate the cause-specific hazards and risk of further revision at time (t) following first revision for PFF in the presence of the competing risk of death (see Chapter 4 for detail on flexible parametric competing risks model).

To compare probability of death after PFF revision with that following primary THA, a separate flexible parametric competing risk model using the same covariates (Age group, ASA grade and gender) was fitted with the primary THA database

To compare the outcomes (further revision and death) of PFF revision with revision for aseptic loosening, dislocation and infection, the model was fitted by indication.

6.2.3.2 Management of Covariates

For assessment of risk factors for further revision following PFF revision, covariates of interest included age at first revision, gender, ASA grade, first revision stem fixation, surgeon volume and unit volume. Table 6.1 shows the covariates examined for association with further revision after PFF revision.

Table 6-1 Covariates of Interest in assessing outcomes of first revision

Covariate	Categories
Age	<75/≥75
Gender	M/F
First revision stem fixation	Cemented/Cementless
First revision stem design	Distally Fixed Modular Standard Stems
Surgeon volume	≤9 10-19 20-49 ≥50
Unit Volume	≤19 20-49 50-99 100-149 ≥150

Cause-specific hazards were calculated to assess the association of each covariate with regards to risk of further revision after PFF revision. Cumulative Incidence (CI) of further revision and death at time (t) following first revision for PFF was tabulated and demonstrated as CI curves.

For comparison of risk of further revision and death between patients who underwent first revision for periprosthetic fracture, aseptic loosening, dislocation and infection, covariates of interest were included in the model. These included age at first revision (categorical), gender (categorical) and ASA grade (categorical). Age was included as a categorical variable to compare the outcomes in older (≥75) and younger (<75) age groups. ASA grade was categorised into low ASA (ASA 1 or 2) and high ASA (≥3).

6.3 Results

6.3.1 Demographics

There were 74,223 first revision THAs included in the analysis. Table 6.2 summarises the frequency and gender distributions of first revision THAs by indication. The overall mean age at revision was 70.65 (SD 11.94). Outcome data was available for 74219/74223 (9.99%) of cases: 11,607 had died without revision, 6,391 underwent further revision and 56,221 remained alive without further revision.

Table 6-2 First Revision THA: Frequency by Indication and Gender

Indication for first revision	Frequency	F:M
PFF	6131	3400:2731
Aseptic Loosening	33637	18524:15113
Dislocation	9515	6504:3011
Infection	5400	2561:2839
Lysis	2497	1402:1095
Unexplained Pain	5865	3744:2121
Other indications	11178	6735:4443
Total	**74223**	**42870:31,353**

6.3.2 First Revision for PFF: Risk of Further Revision and Mortality

Further Revision

Of the 6131 first revisions for PFF included in the analysis, there were 3,400 females and 2731 males. The overall mean age at time of first revision was 74.8 (SD11.86). 1487 had died without revision, 516 underwent further revision, and 4128 remained alive without revision.

The cause-specific hazard ratios of the covariates tested for association with risk of further revision after first revision for PFF are summarised in Table 6.3. Age≥75 at first revision was independently associated with a lower risk of

further revision with an adjusted hazard ratio of 0.61 (95% CI 0.51-0.74, $p<0.001$). This is likely due to a higher risk of mortality in older patients (see Mortality sub-section). Unit volume of ≥150 first revisions for PFF was independently associated with a lower risk of further revision when compared to units performing ≤19 revisions for PFF (HR 0.60, 95% CI 0.39-0.94), $p=0.02$. Gender, high/low ASA grade, and cemented vs. uncemented first revision stem fixation and individual surgeon volume were not independently associated with risk of further revision.

When comparing distally fixed modular cementless stems with all other stems used in PFF revision, there was no difference in risk of further revision with an adjusted HR of 0.95 (95% CI 0.66-1.37).

Table 6-3 Covariates tested for association with further revision after first revision for PFF with unadjusted and adjusted hazard ratios. (95% CI in brackets)

Covariate	HR (Unadjusted)	HR (Adjusted)	P value
Age (1st Revision)			
<75	1	1	0.001
≥75	0.59 (0.49-0.70)	0.61 (0.51-0.74)	
Gender			
F	1	1	0.32
M	1.16 (0.97-1.38)	1.09 (0.92-1.30)	
ASA			
≤2	1	1	0.13
≥3	0.76 (0.63-0.91)	0.86 (0.71-1.05)	
Stem Fixation			
Cementless	1	1	0.86
Cemented	1.02 (0.82-1.27)	1.02 (0.82-1.27)	
Unit Volume			
≤19	1	1	
20-49	0.91 (0.74-1.13)	0.96 (0.77-1.18)	0.68
50-99	0.81 (0.62-1.05)	0.87 (0.67-1.12)	0.28
100-149	1.07 (0.75-1.52)	1.12 (0.79-1.60)	0.53
≥150	0.60 (0.38-0.92)	0.60 (0.39-0.94)	0.02
Surgeon Volume			
≤9	1	1	
10-19	0.84 (0.69-1.03)	0.85 (0.69-1.04)	0.12
20-49	0.94 (0.75-1.17)	0.96 (0.77-1.20)	0.72
≥50	0.68 (0.41-1.14)	0.69 (0.42-1.18)	0.15

Stem Type			
Standard Stems	1	1	0.79
Distally Fixed Modular Cementless Stems	0.97 (0.67-1.39)	0.95 (0.66-1.37)	

The probability of further revision at 1 year ranged from 2.56% (1.83%-3.28%) in females ≥75 with high ASA at time of first revision to 6.30% (3.01%-9.59%) in males<75 with low ASA at time of first revision. At 10 years, the probability of further revision ranged from 6.64% (4.81%-8.46%) in females≥75 with high ASA at time of first revision to 22.72% (12.12%-33.33%) in males<75 and low ASA at time of first revision. Table 6.4 demonstrates the cumulative incidence (probability) of revision at 1 year, 5 years and 10 years following first revision for PFF by Age and ASA category.

Table 6-4 Cumulative Incidence (Probability) of further revision after revision for PFF a 1, 5 and 10 years with 95% CI

	Revision 1 year	Revision 5 years	Revision 10 years
Females <75 Low ASA	6.15 (5.00-7.29)	14.50 (12.21-16.78)	22.00 (18.48-25.51)
Males <75 Low ASA	5.70 (4.61-6.80)	13.48 (11.29-15.67)	20.48 (17.13-23.82)
Females <75 High ASA	4.56 (3.04-6.08)	10.46 (7.18-13.73)	15.04 (10.38-19.71)
Males <75 High ASA	4.09 (2.55-5.63)	9.22 (5.91-12.53)	12.87 (8.29-17.45)
Females ≥75 Low ASA	2.83 (2.04-3.62)	6.37 (4.69-8.04)	8.80 (6.47-11.13)
Males ≥75 Low ASA	3.66 (2.57-4.74)	7.97 (5.74-10.20)	10.59 (7.62-13.56)
Females ≥75 High ASA	2.56 (1.83-3.28)	5.31 (3.87-6.76)	6.64 (4.81-8.46)
Males ≥75 High ASA	3.89 (2.79-4.99)	7.49 (5.45-9.53)	8.70 (6.32-11.08)

Mortality

Increasing age at first revision, ASA grade and male gender were strongly associated with a higher overall risk of death after revision for PFF. When taken as a continuous variable, the unadjusted HR for increasing age was 1.10 (95% CI 1.09-1.13). After adjustment for ASA and gender, the HR was 1.09 (95% CI 1.08-1.10). As a categorical variable, comparing those aged ≥75 at

time of revision for PFF with those <75, the unadjusted and adjusted HRs were 5.28 (95% CI 4.61-6.05) and 4.49 (95% CI 3.90-5.16) respectively. For ASA, the unadjusted and adjusted HRs comparing ASA≥3 with ASA≤2 were 3.15 (95% CI 2.82-3.50) and 2.07 (95% CI 1.86-2.31) respectively. Male gender was associated with a higher risk of mortality with an unadjusted HR of 1.11 (95% CI 1.00-1.23). After adjustment for age at first revision and ASA grade, the HR increased to 1.51 (1.36-1.67).

Table 6.5 shows the cumulative incidence (probability) of death at 90 days, 1 year and 5 years following revision for PFF compared with Primary THA categorised by age, gender and High/Low ASA groups. There is a clear trend for a higher probability of death at each time period and for each age/gender/ASA grade category after PFF revision compared with primary THA. This difference was most marked at 90 days and 1 year but remained at 5 years in higher risk groups which included males<75 with high ASA, females ≥75 with lows ASA, males ≥75 with low ASA, females ≥75 with high ASA and males ≥75 with high ASA.

Table 6-5 Cumulative Incidence (Probability) of death after revision for PFF (PFF) and after Primary THA (THA) at 90 days, 1 year and 5 years with 95% CI.

	Death 90 days		Death 1 years		Death 5 years	
	PFF	THA	PFF	THA	PFF	THA
Females <75 Low ASA	0.55 (0.39-0.71)	0.17 (0.13-0.21)	1.40 (1.02-1.79)	0.73 (0.60-0.87)	5.48 (4.07-6.89)	4.04 (3.42-4.66)
Males <75 Low ASA	0.60 (0.44-0.76)	0.29 (0.22-0.36)	1.52 (1.13-1.91)	1.23 (1.02-1.43)	5.96 (4.52-7.39)	6.70 (5.81-7.60)
Females <75 High ASA	1.92 (1.41-2.43)	0.58 (0.39-0.76)	4.84 (3.63-6.05)	2.43 (1.78-3.08)	18.15 (14.10-22.19)	12.75 (9.76-15.74)
Males <75 High ASA	2.67 (2.01-3.33)	0.54 (0.34-0.74)	6.71 (5.17-8.25)	2.28 (1.56-3.01)	24.48 (19.66-29.31)	12.08 (8.61-15.54)
Females ≥75 Low ASA	3.11 (2.60-3.62)	0.85 (0.65-1.05)	7.82 (6.74-8.90)	3.58 (3.00-4.17)	28.41 (25.28-31.44)	18.68 (16.46-20.90
Males ≥75 Low ASA	4.00 (3.31-4.68)	1.16 (0.87-1.44)	9.94 (8.50-11.39)	4.86 (4.02-5.70)	34.55 (30.70-38.40)	24.31 (21.20-27.42)
Females ≥75 High ASA	6.07 (5.26-6.88)	1.63 (1.12-2.08)	14.90 (13.38-16.42)	6.78 (5.30-8.25)	48.23 (45.01-51.45)	32.18 (26.83-37.53)
Males ≥75 High ASA	8.69 (7.53-9.84)	1.92 (1.36-2.50)	20.75 (18.64-22.86)	8.00 (6.14-9.87)	59.92 (56.15-63.70)	37.43 (30.88-44.00)

The Cumulative Incidence Function for further revision and death using the flexible parametric competing risks model are shown in Figures 6.1.

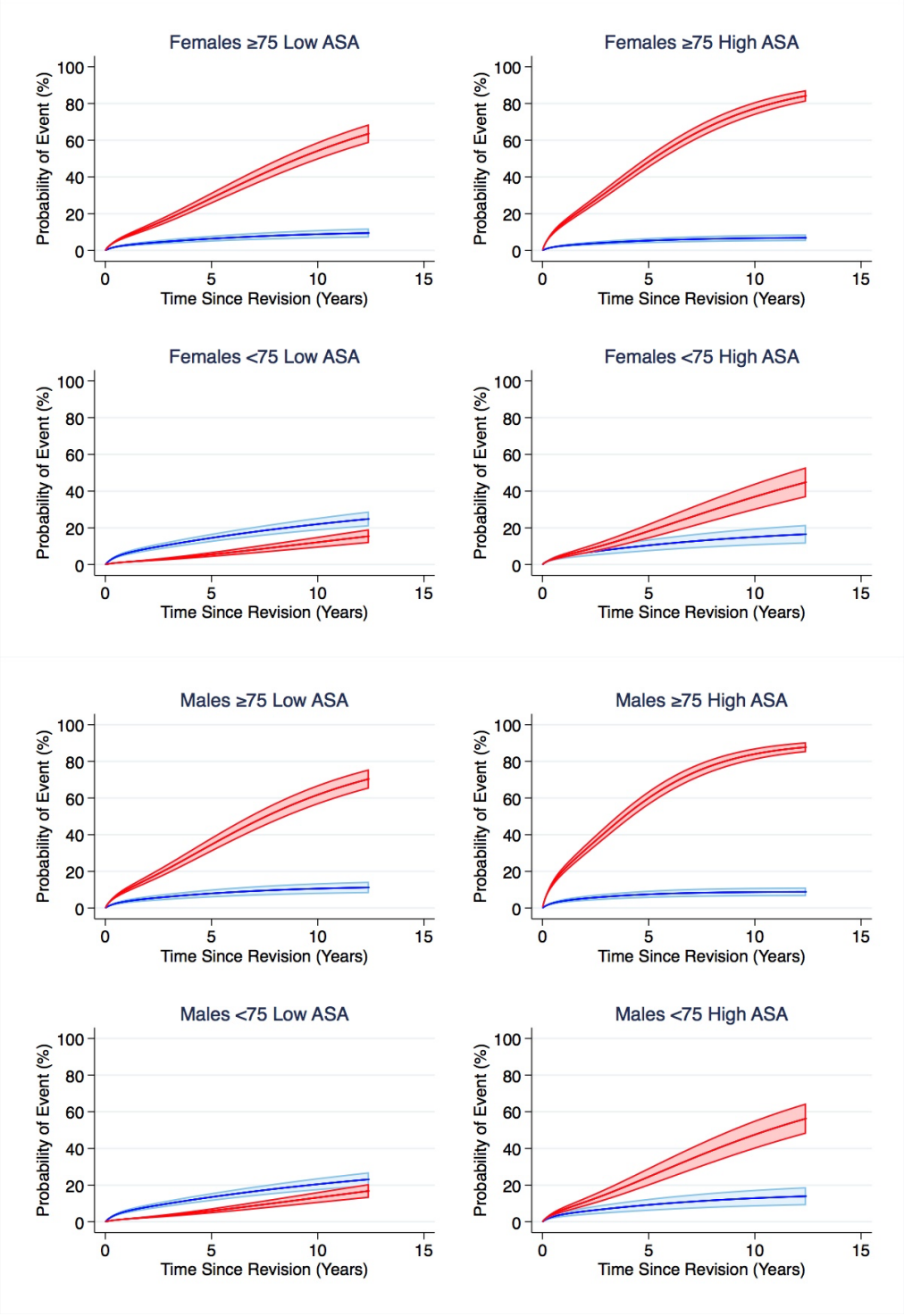


Figure 6-1 Cumulative Incidence Function showing probability of death (Red curve) and further revision (blue) for age/gender/ASA groups. 95% CIs are shaded.

6.3.3 Outcome of PFF Revision compared with Revision for other Indications

6.3.3.1 Further Revision

Table 6.6 shows the comparative probabilities of further revision at 5 years after first revision for each of the most common indications for revision by gender and age group. When compared to revision for aseptic loosening, revision for PFF demonstrated significantly higher probability of further revision at 5 years for males aged ≥ 75 and < 75 with low ASA grade. For females aged both ≥ 75 and < 75 with low ASA grade, despite a higher overall probability of further revision after revision for PFF, overlapping 95% confidence intervals suggested the difference was not significant. For males and females with high ASA grade, the risk of further revision was similar for PFF and aseptic loosening.

Compared to first revision for infection, overall probability of revision at 5 years after PFF revision was lower in all age/ASA grade groups but the difference was significant for females aged ≥75 with low ASA grade.

Probabilities of further revision at 5 years after first revision for dislocation were similar in all age/ASA groups.

Table 6-6 5-year probability of revision by indication and gender/age/ASA category

	PFF	Aseptic Loosening	Infection	Dislocation
Males ≥ 75 Low ASA	7.97 (5.74-10.20)	5.15 (4.47-5.83)	12.55 (9.58-15.51)	8.45 (6.44-10.46)
Females ≥ 75 Low ASA	6.37 (4.69-8.04)	5.77 (5.18-6.36)	10.83 (8.15-13.51)	7.38 (6.21-8.54)
Males < 75 Low ASA	13.48 (11.29-15.67)	9.32 (8.66-9.98)	14.72 (12.88-16.56)	12.44 (10.60-14.27)
Females < 75 Low ASA	14.50 (12.21-16.78)	8.93 (8.32-9.53)	15.98 (13.84-18.12)	12.18 (10.82-13.53)
Males ≥75 High ASA	7.97 (5.74-10.20)	5.46 (4.49-6.42)	8.12 (5.29-10.95)	6.60 (4.46-8.74)
Females ≥75 High ASA	5.31 (3.87-6.76)	5.34 (4.49-6.19)	7.52 (4.93-10.11)	7.50 (6.08-8.92)
Males <75 High ASA	9.22 (5.91-12.53)	9.33 (7.92-10.73)	14.74 (11.53-17.95)	11.27 (8.10-14.43)
Females <75 High ASA	10.46 (7.18-13.73)	10.77 (9.30-12.25)	15.95 (12.45-19.44)	12.92 (10.31-15.52)

6.3.3.2 Mortality

The overall 5-year probability of death following first revision for PFF was higher when compared to first revisions for aseptic loosening, infection and dislocation in all age/ASA groups except males <75 with low ASA grade where first revision for dislocation and infection demonstrated a higher risk of mortality (Table 6.7).

Table 6-7 5-year probability of death after revision hip arthroplasty by indication and gender/age/ASA category

	PFF	Aseptic Loosening	Infection	Dislocation
Males ≥ 75 Low ASA	34.55 (30.70-38.40)	20.85 (19.69-22.02)	18.38 (15.09-21.66)	30.64 (27.45-33.84)
Females ≥ 75 Low ASA	28.41 (25.28-31.44)	16.30 (15.42-17.17)	19.33 (16.18-22.49)	22.93 (21.11-24.75)
Males < 75 Low ASA	5.96 (4.52-7.39)	4.84 (4.42-5.27)	6.41 (5.24-7.58)	8.29 (6.89-9.70)
Females < 75 Low ASA	5.48 (4.07-6.89)	3.72 (3.37-4.07)	4.68 (3.57-5.79)	5.19 (4.35-6.03)
Males ≥75 High ASA	59.92 (56.15-63.70)	31.65 (29.76-33.53)	33.12 (28.32-37.92)	47.08 (42.80-51.37)
Females ≥75 High ASA	48.23 (45.01-51.45)	29.20 (27.56-30.83)	32.10 (27.70-36.50)	46.07 (43.39-48.75)
Males <75 High ASA	24.48 (19.66-29.31)	11.59 (10.20-12.98)	15.96 (12.79-19.13)	20.23 (16.43-24.04)
Females <75 High ASA	18.15 (14.10-22.19)	8.69 (7.50-9.88)	13.02 (9.95-16.08)	16.94 (14.18-19.69)

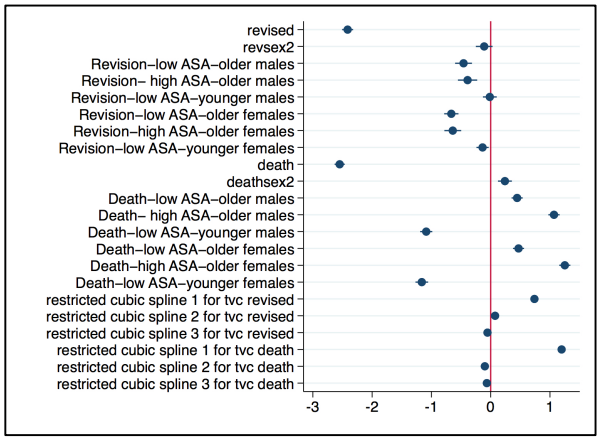


Figure 6-2

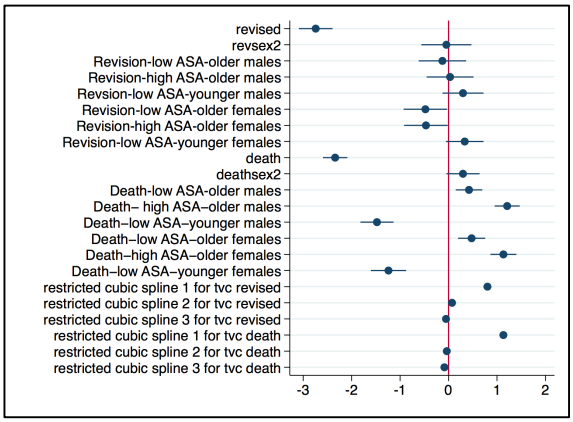


Figure 6-3

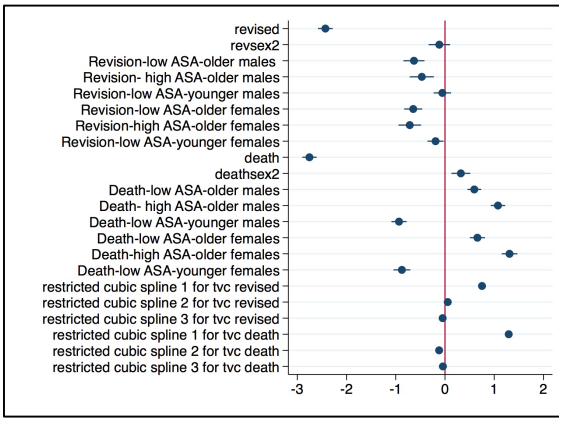


Figure 6-4



Figure 6-5

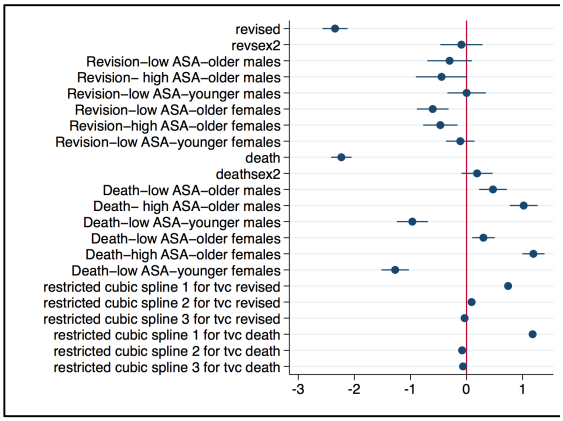


Figure 6-6

Figures 6-2 to 6-6. Forest Plots of coefficients for further revision and mortality for patient age/gender/ASA groups after first revision for all indications (6-2), PFF (6-3), aseptic loosening (6-4), infection (6-5), and dislocation (6-6). *tvc (time varying coefficients).

6.4 Discussion

In this study, the outcomes of revision surgery (first revision) for PFF were explored in terms of further revision and mortality. Older age at first revision (≥75) and higher ASA grade (≥3) were associated with a lower risk of further revision and a higher risk of mortality. Units that had performed ≥150 first revisions for PFF, had a lower risk of further revision compared to those that had performed ≤19. Male gender was independently associated with a higher risk of mortality following revision for PFF. Probability of further revision following first revision for PFF was high at over 20% at 10 years for highest risk groups. These high risk groups were younger with low ASA grade, therefore representing individuals more surgically fit for revision surgery. Probability of death was also high with an almost 9% risk of death at 90 days and 60% at 5 years for the highest risk group (males aged ≥75 with ASA≥3). At 90 days, 1 year and 5 years following PFF revision, the overall probability of death was higher compared to mortality after primary THA. In comparison with the other commonest indications for first revision, PFF revision demonstrated the overall highest risk of mortality at 5 years. Probability of further revision was significantly higher after PFF when compared with aseptic loosening in groups with the highest risk of further revision (males and females aged <75 with ASA≤2). Further revision risk was similar when compared with first revision for infection and pain.

Previous studies have investigated outcomes after treatment for PFF. As demonstrated in Chapter 5, the majority of existing evidence particularly relating to re-operation/further revision is based on single institution small cohort data. Based on included studies, for B2 and B3 fractures, which were treated with revision surgery, re-operation occurred in 12.4% and 14.4% respectively. These figures despite allowing a general comparison of treatment modalities, do not provide accurate risk of further intervention estimates due to the lack of time-to-event data. The Swedish Registry reported the outcomes of 1,049 PFFs.[124,126] Of these, 720 were treated with revision hip arthroplasty. The overall survival rate was 69% at 10 years (with re-operation as the outcome of interest) which also included PFFs treated using internal fixation without revision arthroplasty as well as PFFs occurring after revision arthroplasty. Although, the cohort is significantly smaller than the present study and more heterogeneous (included internally fixed cases and PFFs after first revision), the 10-year survival after treatment suggests the failure rate is even higher than what the NJR data indicates. The Kaplan-Meier survivorship methods tend to overestimate the failure risk estimates as they don't account for the risk of death, which as this study demonstrates is a significant competing risk. Similar to the present study, the authors demonstrated that younger age at time of PFF as a significant risk factor for reoperation and also as in this study gender was not found to be associated with reoperation. In concordance with our findings for further revision after PFF, another study using competing risk methodology accounting for the competing risk of death demonstrated that younger age at time of revision THA was independently associated with a higher risk of all-indication revision.[242]

There are few studies reporting the risk of mortality after PFF. Bhattacharyya and colleagues reported that 11% (12/106 patients) had died within the first year following PFF[142] and Lindahl et al. showed that despite an initially higher risk of death post fracture, for individuals 70 years or older, the mortality risk was the same as the general population.[123] For individuals aged 50-70, the risk of death remained higher than the general population. The present study compared mortality after PFF revision with that after primary THA and demonstrated an overall higher risk of death even at 5 years following revision. Despite conflicting evidence regarding the difference in risk of mortality after primary THA compared to that of the general population, the majority of studies suggest a lower probability of death after primary THA.[243-250]. Therefore, a comparison of mortality after PFF revision with primary THA is likely to be more clinically and epidemiologically relevant in understanding disease processes and analysing the success and failure of treatment.

Despite interest, this is the first study to compare the probability of further revision after first revision for PFF with other indications for revision. The data suggests that PFF revision has a higher probability of further revision compared to aseptic loosening but similar risk compared to infection, and dislocation. There are several possible explanations for this. Firstly, many of the PFFs that are typically treated with revision are Vancouver B2 and B3 fractures which by definition involve a loose femoral stem which results in the potentially larger technical challenge of intraoperatively managing both

loosening and an unstable fracture compared with loosening alone. This may lead to inherently more unstable femoral biology post-operatively and a higher risk of failure. In addition, revisions performed for what the surgeon classifies as aseptic loosening can refer to a wide range of severities and the required operations vary in complexity. By comparison, although revision arthroplasties for PFF are by no means identical procedures they are likely to be more homogenous. Another explanation is that it is likely that PFF patients differ in terms of bone quality compared to those individuals revised for aseptic loosening, which could result in poorer fixation of implant to bone or cement to bone.

Young and colleagues demonstrated a significantly higher mortality at 6-months after PFF compared with revisions for aseptic loosening.[141] The present study demonstrates a higher risk of mortality after PFF revision at 5 years. We also demonstrated a higher risk of mortality for high-risk groups compared with revision for infection.

It was hypothesised before undertaking this study that modular distally fixed cementless stems, by bypassing the proximal component of the femur and achieving fixation beyond the periprosthetic fracture may produce a lower revision risk compared to other stems. Although, this study does not support the hypothesis, the analysis was restricted to the outcomes of first revisions of primary THAs recorded on the NJR, which were far fewer, and therefore may

have influenced the ability of the data to show an association even if there is one present.

The only other high volume study that reported on risk factors for failure after periprosthetic femoral fracture treatment was from the Swedish Arthroplasty Registry.[124] As the study was based on all PFFs and not only the ones that were treated with revision arthoplasty, the covariates explored were primarily to compare treatment modalities. They reported a higher risk of failure with fractures treated without revision. Amongst revised cases, cementless stems showed a reduction in risk of failure. Our data does not support this and while our case volume was much higher, we also accounted for surgical fitness (ASA grade), age category and the competing risk of death which would all potentially influence failure risk. A proportion of the cemented revisions are likely to be cement-on-cement revisions, which in clinical practice are often performed for less surgically fit patients.

Due to the complex technical challenges of revision surgery for PFF, it was important to examine whether unit and individual surgeon case volume influenced risk of revision as this could provide some evidence for centralising the workload to high volume centres/surgeons. While there was trend for lower risk of further revision after PFF revision in centres that had more recoded cases in the NJR, this only reached significance when comparing centres performing ≥150 cases with ≤19 recorded cases. With regards to

surgeon volume, the data does not support any association between recorded cases and risk of further revision. A potential explanation for this is that the majority of surgeons performing revision surgery for PFF have a general revision hip surgery practice and despite not treating many PFFs, they are able to manage the technical challenges associated with PFF surgery.

Several studies have compared the mean financial costs associated with the various indications for revision hip arthroplasty in the UK.[154,251] Revision for PFF has been universally reported to lead to one of the highest costs, second only to revision for infection. The mean costs for PFF revision based on single institutional analyses were reported as £23,834[252], £23,469[251] and £18,185[154]. Revision for aseptic loosening was associated with mean costs of £13,110 and £10,893[252]. The authors indicated that much of the increased costs were related to length of stay which is typically significantly greater after revision for PFF.

This study has some limitations. The recording of implants brands used for first revision was poor in the NJR database of all first revisions hence we used a restricted to a smaller dataset to assess the influence of stem type on revision risk. The study focused on the outcomes of revision for PFF which although more homogenous than a study of all treatments types, does include patients treated with a combination of revision and internal fixation. However, as it was not possible to identify which patients had undergone internal fixation with revision, this could not be accounted for in the analysis. Patient Reported Outcome Measures (PROMS) would be very useful to assess functional outcome after PFF revision but this data was not available. However, the use

of PROMS such as the Oxford Hip Score to compare outcomes of revision surgery would require the scores prior to revision, which would not have been collected on a large proportion of the patients. This would limit the value of PROMS. Another limitation is lack of data collected by the NJR on the time from PFF to surgical treatment which could be a potential confounding factor in terms of outcomes. There is some evidence from institutional level data that a higher risk of 30-day mortality is observed in patients waiting more than 72 hours for surgical treatment for PFF.[253] However, other studies have not shown any association between delay to surgery and morbidity/mortality.[254,255] Although there are no specific studies looking at delay to surgery for PFF treated with revision surgery, for which delays are more likely due to the requirement for specialist surgeons and implants, there is currently no strong evidence for worse outcomes with increased time to the operating theatre.

In conclusion, this study has explored the risk factors for failure after revision hip arthroplasty for PFF and the covariate-adjusted probabilities of further revision and death using flexible parametric competing risks model. The overall outcomes of revision for PFF are poor, particular mortality risk, which is higher than the other common indications for revision. Risk of further revision was higher after PFF revision compared to aseptic loosening, but comparable to revision for dislocation and infection. Individuals with higher surgical fitness (Age <75 and ASA ≤2) demonstrated a greater risk of further revision after PFF revision. Potential explanations for this are that older patients die before revision becomes necessary and some of those with a high

ASA grade despite requiring surgery are not treated with further revision due to the greater risks. The estimates provided will be helpful to counsel patients prior to PFF revision surgery and are useful in the surgical decision process particularly if used in conjunction with results of studies reporting outcomes of internal fixation.

7 Discussion

7.1 Summary of Main Findings

The aim of this thesis was to perform a detailed analysis of periprosthetic femoral fractures (PFF) in THA by combining systematic review of the best existing evidence alongside robust analysis of data from the largest arthroplasty database in the world (NJR).

The introductory chapter demonstrated that PFF in THA is an area of significant interest within arthroplasty and orthopaedics as a whole, which is largely related to the challenges of treatment and the suggestions that the number of patients presenting with PFF is increasing. However, much of the published work thus far is based on single institutional experiences. Since the advent of hip arthroplasty, changes to implant design has been a continual phenomenon and the options have widened vastly but data concerning the influence of implant design on risk of PFF prior to this thesis has been limited.

The results derived from this investigation suggest that PFF in THA are a growing problem in England and Wales with increasing numbers of revision for PFF being performed, rising PFF-specific revision burden and increasing incidence of first revision for PFF. Likely contributory factors include the growing numbers of primary THAs being performed, increasing probability of PFF with time from THA in combination with population factors such as improving life expectancy.

An assessment of risk factors for intraoperative periprosthetic fractures based on a systematic review of high volume studies and analysis of NJR data indicated that increasing age, female gender and cementless stems were strongly associated with a higher risk of fracture.

For post-operative fracture, the findings of this thesis suggest that increasing age, higher ASA grade, male gender and THA for fractured neck of femur are independently associated with higher PFF risk. Implant factors are more complex. Although the results suggest that cementless stems are associated with a higher overall risk of PFF compared to cemented stems, the difference is more apparent for patients older at time of primary THA. Polished taper cemented stems show a higher risk of revision for PFF compared to composite beam cemented stems and among cementless stems, collars appear protective. Anatomic (Type VI) and short cementless stems also demonstrate a higher PFF revision risk. However, one of the key findings from the investigation was that there were implant brand specific differences so there are problems associated with attempting to rationalise risk based on design classification systems.

Figure 7-1 demonstrate the key highest at lowest risk groups for PFF revision at 10 years from primary THA based on patient and implant factors.

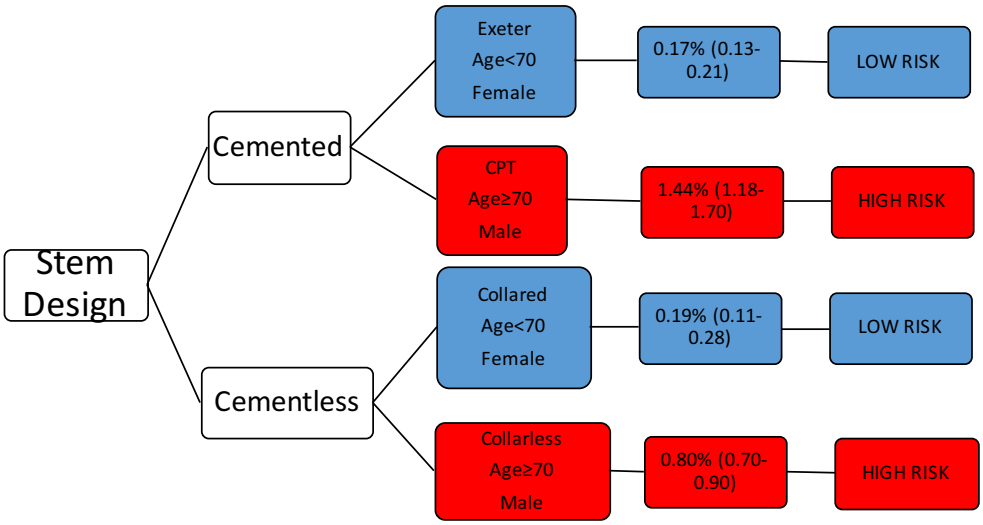


Figure 7-1 Patient-Implant groups at highest and lowest risk of revision for PFF at 10 years from primary THA

A systematic review of outcomes of PFF around loose femoral stems (Vancouver B2 and B3 fractures) indicated poorer outcomes without revision surgery for these cases. Overall, the majority of outcome studies were based on small institutional case series without time-to-event analysis. The review indicated a need for improved data reporting to allow robust conclusions to be drawn.

Analysis of outcomes of first revisions for PFF using NJR data suggest that male gender, better surgical fitness (ASA≤2) and lower age at first revision are risk factors for further revision after first revision for PFF. The data also suggests that units performing very high numbers of PFF revisions have significantly better outcomes in terms of further revision risk. The overall 5-year mortality and further revision risk after PFF revision surgery are high with considerable variability amongst patient groups (Figure 7-2).

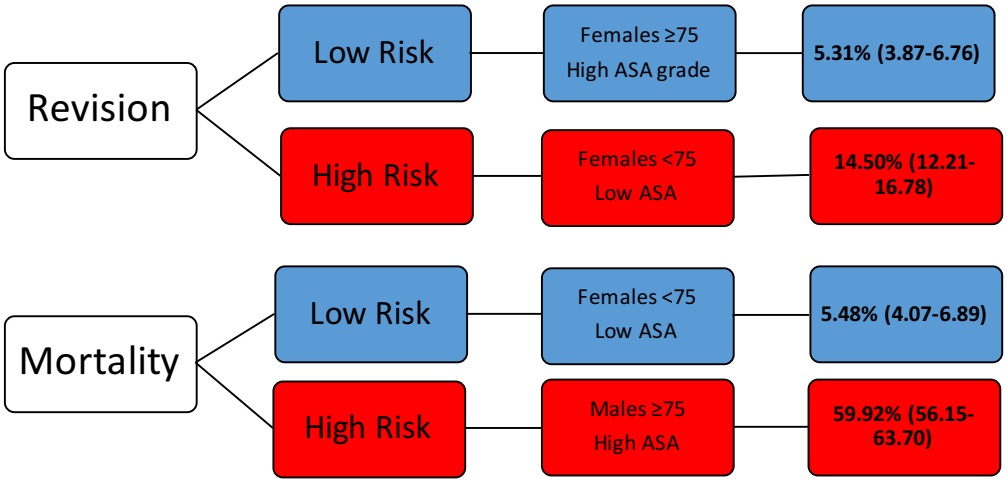


Figure 7-2 Summary of lowest and highest risk patient groups of further revision and mortality following first revision for PFF.

When compared to other commonest indications for first revision, the overall picture is suggestive of higher 5-year mortality after first revision for PFF. Compared to aseptic loosening, the data suggests a higher risk of further revision after first revision for PFF, particularly in younger, more surgically fit patient groups. The risk of further revision was found to be similar to dislocation and infection.

7.2 Contributions to the Field of Study

The findings of this thesis have made significant contributions to the knowledge base and understanding of PFF in THA from both clinical and epidemiological perspectives.

A strong, evidence based approach to understanding risk and risk factors for intra-operative and post-operative PFF using an amalgamation of the best existing studies and an arthroplasty register have allowed useful estimates for both effect sizes and magnitude of risk for different patient groups. These "real-world" estimates in the presence of competing risks are beneficial at all levels from surgeon and unit to national and international. The competing risk models used in this thesis are transferrable to other arthroplasty investigations particularly when assessing indication-specific revision risk as the models take into account not only the competing risk of death but also all other indications for revision other than the one being investigated. This approach to analysing arthroplasty data was not previously used before this thesis.

The increasing volume, revision burden and incidence of first revision (in terms of implant years at risk) associated with PFF in England and Wales, is a significant finding. Certainly, from a national perspective, although understanding the reasons for these observations is important, developing strategies to manage the problem are equally necessary.

Due to financial benefits and good outcomes of cemented THA, the use of cemented as opposed to cementless stems for primary THA in patients 70 years of age and older has been strongly advocated by the UK "Getting in Right First Time (GIIRFT)" report.[186] With regards to revision for PFF, the findings of this thesis may be seen to support this in terms of risk of

intraoperative fractures and revision for post-operative fractures. However, there are more complex implant-brand specific associations with for example the CPT cemented stem (Zimmer-Biomet, USA) showing a significantly higher risk of first revision for PFF compared to the other three most commonly used stems nationally, two of which are cementless.

This thesis is the first large-scale investigation of PFF revision surgery to quantify the risk of further revision and mortality. In the highest risk groups, 90-day and 1-year mortality are roughly 10% and 20% respectively. These estimates are useful to guide clinical decision making when patients present with failure after revision surgery and for counselling patients. With the increasing volume of PFF revision, the development of guidelines and best practice tariffs to reduce mortality are likely to be necessary and the findings of this thesis will be a useful guide to inform healthcare providers of the current state of affairs. Moreover, the findings indicate the need for optimising outcomes similar to the improvements seen in survival of fractured neck of femur patients. This will potentially require networks to facilitate reduction in time to surgery and ensure appropriate surgical expertise. Creation of best practice tariffs would incentivise early surgery and other interventions which have been shown to improve outcomes for patients with fragility fractures.

7.3 Recommendations for Further Work

It is hoped that the findings of this thesis will be used by healthcare providers and policy makers to guide decision-making and future work. There are areas where further investigation is necessary. Although, the NJR allows a detailed

investigation of revision surgery for PFF which, it does not capture those fractures treated with fixation strategies alone and indeed those treated non-operatively. This is a limitation of the majority of worldwide arthroplasty registries, so there is a need to capture the patients treated with fixation which will likely require hospital admissions data. The estimates of risk provided can then be adjusted to include all PFF, not only those requiring revision surgery. Patient Reported Outcome Measures (PROMs) were not available for this thesis, but future work should include comparison of PROMS in terms of outcomes after revision arthroplasty.

Future work should include a health economic analysis of PFF from the UK perspective, which should be based on risk estimates, implant use and the outcomes of treatment investigated in this thesis. Health economic data will provide the necessary information for future healthcare budgeting and forecasting, which is particularly important within the National Health Service.

In the UK, centralisation of complex revision surgery to specialist centres is thought to be the direction of travel with the development of regional revision networks as suggested in the British Orthopaedic Association "Getting it Right First Time (GIRFT)" report.[186] Further work with multilevel analysis techniques will allow a comparison of outcomes of PFF treatment between units to determine the number of PFFs an individual institution should be required to treat for the best outcomes.

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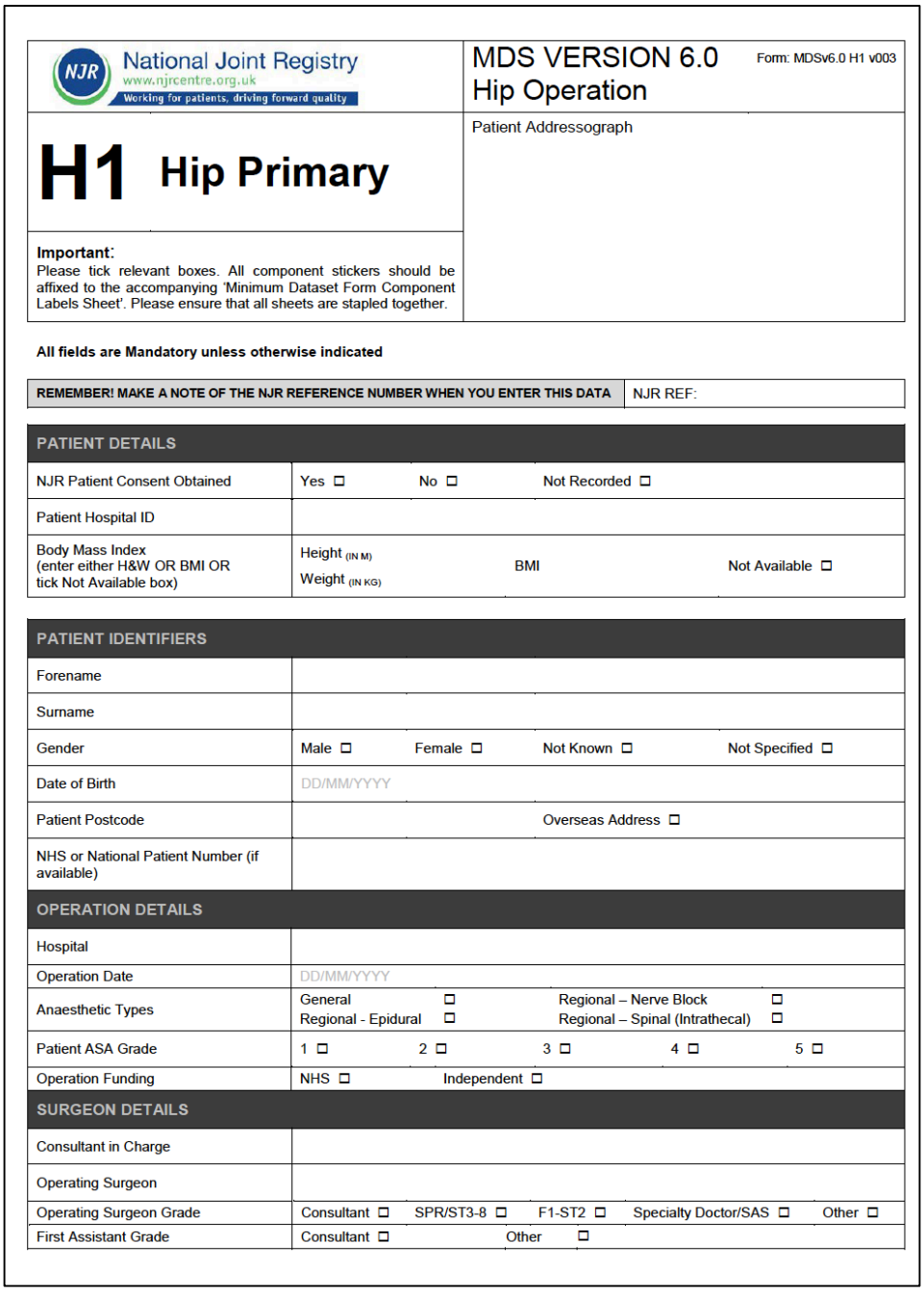
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11 Appendices

11.1 NJR Minimum Datasets (November 2014 versions)



National Joint Registry
www.njrcentre.org.uk
Working for patients, driving forward quality

MDS VERSION 6.0 Form: MDSv6.0 H1 v003
Hip Operation

H1 Hip Primary

Patient Addressograph

Important:
Please tick relevant boxes. All component stickers should be affixed to the accompanying 'Minimum Dataset Form Component Labels Sheet'. Please ensure that all sheets are stapled together.

All fields are Mandatory unless otherwise indicated

REMEMBER! MAKE A NOTE OF THE NJR REFERENCE NUMBER WHEN YOU ENTER THIS DATA	NJR REF:

PATIENT DETAILS				
NJR Patient Consent Obtained	Yes ☐	No ☐	Not Recorded ☐	
Patient Hospital ID				
Body Mass Index (enter either H&W OR BMI OR tick Not Available box)	Height (IN M) Weight (IN KG)	BMI	Not Available ☐	

PATIENT IDENTIFIERS				
Forename				
Surname				
Gender	Male ☐	Female ☐	Not Known ☐	Not Specified ☐
Date of Birth	DD/MM/YYYY			
Patient Postcode			Overseas Address ☐	
NHS or National Patient Number (if available)				

OPERATION DETAILS				
Hospital				
Operation Date	DD/MM/YYYY			
Anaesthetic Types	General ☐ Regional - Epidural ☐		Regional – Nerve Block ☐ Regional – Spinal (Intrathecal) ☐	
Patient ASA Grade	1 ☐	2 ☐	3 ☐	4 ☐ 5 ☐
Operation Funding	NHS ☐	Independent ☐		

SURGEON DETAILS					
Consultant in Charge					
Operating Surgeon					
Operating Surgeon Grade	Consultant ☐	SPR/ST3-8 ☐	F1-ST2 ☐	Specialty Doctor/SAS ☐	Other ☐
First Assistant Grade	Consultant ☐		Other ☐		

HIP PRIMARY PROCEDURE DETAILS					
Side	Left ☐	Right ☐			
Indications for Implantation (select all that apply)	Osteoarthritis	☐	Trauma – Chronic	☐	
	Inflammatory Arthropathy	☐	Previous Hip Surgery – non Trauma related	☐	
	Congenital Dislocation / Dysplasia of the Hip	☐	Previous Arthrodesis	☐	
	Avascular Necrosis	☐	Previous Infection	☐	
	Trauma – Acute (Neck of Femur)	☐	SUFE	☐	
	Failed Hemi-Arthroplasty	☐	Skeletal Dysplasia	☐	
	Perthes	☐	Other	☐	
	Metastatic Cancer/Malignancy	☐			

SURGICAL APPROACH					
Patient Procedure	Primary Total Prosthetic Replacement Using Cement	☐			
	Primary Total Prosthetic Replacement Not Using Cement	☐			
	Primary Resurfacing Arthroplasty of Joint	☐			
	Primary Total Prosthetic Replacement Not Classified Elsewhere (eg Hybrid)	☐			
Patient Position	Lateral ☐	Supine ☐			
Approach	Hardinge	☐	Trochanteric Osteotomy	☐	
	Posterior	☐	Other	☐	
Minimally Invasive Technique Used?	Yes ☐	No ☐			
Computer Guided Surgery Used?	Yes ☐	No ☐			
THROMBOPROPHYLAXIS REGIME (intention to treat)					
Chemical (In Hospital)	Aspirin	☐	Direct Thrombin Inhibitor (eg Dabigatran)	☐	
	LMWH	☐			
	Pentasaccharide (eg Fondaparinux)	☐	Factor Xa Inhibitor (eg Rivaroxaban/Apixaban)	☐	
	Warfarin	☐	Other	☐	
			None	☐	
Mechanical	Foot Pump	☐	Other	☐	
	Intermittent Calf Compression	☐	None	☐	
	TED Stockings	☐			
BONEGRAFT USED					
Femur	Yes ☐	No ☐			
Acetabulum	Yes ☐	No ☐			
SURGEON'S NOTES					

INTRA OPERATIVE EVENT						
Untoward Intra Operative Event	None	☐	Shaft Fracture	☐	Other	☐
	Calcar Crack	☐	Shaft Penetration	☐		
	Pelvic Penetration	☐	Trochanteric Fracture	☐		

National Joint Registry
www.njrcentre.org.uk
Working for patients, driving forward quality

MDS VERSION 6.0
Hip Operation

Form: MDSv6.0 H2 v004

H2

Hip Single Stage Revision
Hip Stage 1 of 2 Stage Revision
Hip Stage 2 of 2 Stage Revision
Hip Excision Arthroplasty
Insertion of PLAD/Stabiliser

Patient Addressograph

Important:
Please tick relevant boxes. All component stickers should be affixed to the accompanying 'Minimum Dataset Form Component Labels Sheet'. Please ensure that all sheets are stapled together.

All fields are Mandatory unless otherwise indicated

REMEMBER! MAKE A NOTE OF THE NJR REFERENCE NUMBER WHEN YOU ENTER THIS DATA	NJR REF:

PATIENT DETAILS				
NJR Patient Consent Obtained	Yes ☐	No ☐	Not Recorded ☐	
Patient Hospital ID				
Body Mass Index (enter either H&W OR BMI OR tick Not Available box)	Height (IN M) Weight (IN KG)	BMI	Not Available ☐	

PATIENT IDENTIFIERS				
Forename				
Surname				
Gender	Male ☐	Female ☐	Not Known ☐	Not Specified ☐
Date of Birth	DD/MM/YYYY			
Patient Postcode			Overseas Address ☐	
NHS or National Patient Number (if available)				

OPERATION DETAILS					
Hospital					
Operation Date	DD/MM/YYYY				
Anaesthetic Types	General ☐ Regional - Epidural ☐		Regional – Nerve Block ☐ Regional – Spinal (Intrathecal) ☐		
Patient ASA Grade	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
Operation Funding	NHS ☐	Independent ☐			

SURGEON DETAILS					
Consultant in Charge					
Operating Surgeon					
Operating Surgeon Grade	Consultant ☐	SPR/ST3-8 ☐	F1-ST2 ☐	Specialty Doctor/SAS ☐	Other ☐
First Assistant Grade	Consultant ☐	Other ☐			

HIP REVISION PROCEDURE DETAILS					
Procedure Type	Single Stage Revision ☐	Stage 1 of 2 Stage Revision ☐	Stage 2 of 2 Stage Revision ☐	Excision Arthroplasty ☐	
Revision of	Primary Total Arthroplasty ☐		Previous Revision Arthroplasty (excluding excision arthroplasty) ☐		
Side	Left ☐	Right ☐			
Indications For / Findings at Time of Revision		Stem	Socket	Head	
	Aseptic Loosening	☐	☐	-	
	Implant Fracture	☐	☐	☐	
	Head/Socket Mismatch	-	☐	☐	
	Lysis	☐	☐	-	
	Malalignment	☐	☐	-	
	Peri-Prosthetic Fracture	☐	☐	-	
	Dislocation/Subluxation ☐	Wear of Acetabular Component ☐			
	Infection ☐	Dissociation of Liner ☐			
	Unexplained Pain ☐	Adverse Soft Tissue Reaction to Particulate Debris ☐			
		Other ☐			

PRIMARY OPERATION DETAILS			
Primary Operation Date OR Year	DD/MM/YYYY Please enter Date if known		Not Available ☐
Primary Operation Hospital			Not Available ☐

COMPONENTS REMOVED (Do not complete for Stage 2 of 2 Stage Revision)				
Femoral Component Removed	Yes ☐	No ☐	Brand	Not Available ☐
Acetabular Component Removed	Yes ☐	No ☐	Brand	Not Available ☐

SURGICAL APPROACH (Used for Single Stage Revision & Stage 2 of 2 Stage Revision)				
Patient Procedure	Revision Using Cement ☐			
	Revision Not Using Cement ☐			
	Revision of and to Resurfacing Arthroplasty ☐			
	Revision Not Classified Elsewhere (eg Hybrid) ☐			
Patient Position	Lateral ☐	Supine ☐		
Approach	Hardinge ☐	Posterior ☐	Trochanteric Osteotomy ☐	Extended Trochanteric Osteotomy ☐
				Other ☐
THROMBOPROPHYLAXIS REGIME (intention to treat)				
Chemical (In Hospital)	Aspirin ☐	LMWH ☐	Pentasaccharide (eg Fondaparinux) ☐	Warfarin ☐
	Direct Thrombin Inhibitor (eg Dabigatran) ☐	Factor Xa Inhibitor (eg Rivaroxaban/Apixaban) ☐	Other ☐	None ☐
Mechanical	Foot Pump ☐	Intermittent Calf Compression ☐	TED Stockings ☐	Other ☐ None ☐
BONEGRAFT USED				
Femur	Yes ☐	No ☐		
Acetabulum	Yes ☐	No ☐		
SURGEON'S NOTES				

11.2 Ovid Medline Search Terms for Chapter 2 Systematic Review

1. periprosthetic.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

2. peri-prosthetic.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

3. fracture.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

4. fractures.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

5. 1 or 2

6. 3 or 4

7. 5 and 6

8. exp Periprosthetic Fractures/

9. 7 or 8

10. hip.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

11. hips.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

12. exp Hip Fractures/ or exp Hip Joint/ or exp Hip/ or exp Arthroplasty, Replacement, Hip/ or exp Hip Prosthesis/

13. knee.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

14. knees.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

15. tibio-femoral.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

16. tibial-femoral.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

17. exp Knee Prosthesis/ or exp Knee/ or exp Knee Injuries/ or exp Arthroplasty, Replacement, Knee/ or exp Knee Joint/

18. femur.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

19. femoral.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

20. exp Femur/

21. exp Femoral Fractures/

22. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21

23. 9 and 22

24. Odds ratio.mp. or Odds Ratio/

25. Risk/

26. RR.mp.

27. probability.mp. or Probability/

28. rate.mp.

29. hazard.mp.

30. Proportional Hazards Models/ or hazards.mp.

31. HR.mp.

32. incidence.mp. or Incidence/

33. Prevalence/ or prevalence.mp.

34. rates.mp.

35. 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34

36. 23 and 35

11.3 Joanna Briggs Institute Checklists for Systematic Reviews



JBI Critical Appraisal Checklist for Cohort Studies

Reviewer_____Date_____

Author _____Year_____Record Number _____

	Yes	No	Unclear	Not applicable
1. Were the groups similar and recruited from the same population?	☐	☐	☐	☐
2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?	☐	☐	☐	☐
3. Was the exposure measured in a valid and reliable way?	☐	☐	☐	☐
4. Were confounding factors identified?	☐	☐	☐	☐
5. Were strategies to deal with confounding factors stated?	☐	☐	☐	☐
6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	☐	☐	☐	☐
7. Were the outcomes measured in a valid and reliable way?	☐	☐	☐	☐
8. Was the follow up time reported and sufficient to belong enough for outcomes to occur?	☐	☐	☐	☐
9. Was follow-up complete, and if not, were the reasons to loss to follow-up described and explored?	☐	☐	☐	☐
10. Were strategies to address incomplete follow-up utilized?	☐	☐	☐	☐
11. Was appropriate statistical analysis used?	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info ☐

Comments (Including reason for exclusion)

_____

_____

_____



JBI Critical Appraisal Checklist for Case Control Studies

Reviewer_____Date_____

Author _____Year_____Record Number_____

	Yes	No	Unclear	Not applicable
1. Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	☐	☐	☐	☐
2. Were cases and controls matched appropriately?	☐	☐	☐	☐
3. Were the same criteria used for identification of cases and controls?	☐	☐	☐	☐
4. Was exposure measured in a standard, valid and reliable way?	☐	☐	☐	☐
5. Was exposure measured in the same way for cases and controls?	☐	☐	☐	☐
6. Were confounding factors identified?	☐	☐	☐	☐
7. Were strategies to deal with confounding factors stated?	☐	☐	☐	☐
8. Were outcomes assessed in a standard, valid and reliable way for cases?	☐	☐	☐	☐
9. Was the exposure period of interest long enough to be meaningful?	☐	☐	☐	☐
10. Was appropriate statistical analysis used?	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info ☐

Comments (Including reason for exclusion)

_____

_____

_____



JBI Critical Appraisal Checklist for Analytical Cross Sectional Studies

Reviewer_____Date_____

Author _____Year_____Record Number _____

	Yes	No	Unclear	Not applicable
1. Were the criteria for inclusion in the sample clearly defined?	☐	☐	☐	☐
2. Were the study subjects and the setting described in detail?	☐	☐	☐	☐
3. Was the exposure measured in a valid and reliable way?	☐	☐	☐	☐
4. Were objective, standard criteria used for measurement of the condition?	☐	☐	☐	☐
5. Were confounding factors identified?	☐	☐	☐	☐
6. Were strategies to deal with confounding factors stated?	☐	☐	☐	☐
7. Were the outcomes measured in a valid and reliable way?	☐	☐	☐	☐
8. Was appropriate statistical analysis used?	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info ☐

Comments (Including reason for exclusion)

_____

_____

_____

11.4 Ovid Medline Search Strategy for Chapter 5: A Systematic Review of Vancouver B2 and B3 Fractures

1. periprosthetic.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier].
2. peri-prosthetic.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
3. fracture.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
4. fractures.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
5. 1 or 2
6. 3 or 4
7. 5 and 6
8. exp Periprosthetic Fractures/
9. 7 or 8
10. hip.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
11. hips.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
12. exp Hip Fractures/ or exp Hip Joint/ or exp Hip/ or exp Arthroplasty, Replacement, Hip/ or exp Hip Prosthesis/
13. femur.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
14. femoral.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
15. exp Femur/
16. exp Femoral Fractures/
17. 10 or 11 or 12 or 13 or 14 or 15 or 16
18. 9 and 17

11.5 Table of included studies in Chapter 2 Systematic Review: The Risk and Risk Factors for Periprosthetic Femoral Fractures in Total Hip Arthroplasty

Study	Study Design	Institution/Country	PFF after Primary/Revision/Both	Intra-operative/post-operative/both/ combined	Failure Event
Abdel (2016)	Cohort	Mayo Clinic, USA	Revision	Both	PFF
Abdel (2016)	Cohort	Mayo Clinic, USA	Primary	Both	PFF
Bergh (2014)	Cross-sectional	Nordic Arthroplasty Register	Primary	Combined	Revision for PFF
Bozic (2012)	Cross-sectional	Medicare Database, USA	Primary	Combined	PFF
Broden (2015)	Cohort	Danderyd Hospital, Karolinska, Sweden	Primary	Post-operative	PFF
Capello (2014)	Cohort	Indiana University Medical Center, USA	Primary	Intra-operative	PFF
Cook (2008)	Cohort	Edinburgh Arthroplasty Unit	Primary	Post-operative	PFF
Cooper (2010)	Cohort	Hospital for Special Surgery, USA	Primary	Post-operative (within 1 year)	PFF
Gjertson (2007)	Cohort	Norwegian arthroplasty register	Primary	Combined	Revision for PFF
Hailer (2010)	Cohort	Swedish Arthroplasty Register	Primary	Post-operative (within 2 years)	Revision for PFF
Jamsen (2014)	Cohort	Finnish Arthroplasty Register	Primary	Post-operative	Revision for PFF
Katz (2014)	Cohort	Medicare Beneficiaries	Primary	Combined	PFF
Khatod (2015)	Cohort	Kaiser Permanente Integrated Healthcare System	Primary	Combined	PFF
Leonardsson (2009)	Cross-sectional	Swedish Arthroplasty Register	Primary	Post-operative	Revision for PFF
Meek (2011)	Cohort	Scottish National Database	Both	Post-operative	PFF
Miettinen (2016)	Case-control	3 Finnish Institutions	Primary	Intraoperative	PFF (calcar

Palan (2016)	Cohort	National Joint Registry (England & Wales)	Primary	Post-operative	Revision for PFF
Park (2017)	Cohort	Nationwide Inpatient Sample (NIS) data, USA	Primary	Post-operative (early – during inpatient stay)	PFF
Sarvilinna (2003)	Cohort	Finnish Arthroplasty Register	Primary	Post-operative	Revision for PFF
Sheth (2013)	Cohort	Rush University Medical Centre	Primary	Post-operative (within 90 days)	PFF
Singh (2013)	Cohort	Mayo Clinic Registry, USA*	Primary	Post-operative	PFF
Singh (2012)	Cohort	Mayo Clinic Registry, USA*	Revision	Post-operative	PFF
Singh (2011)	Cohort	Mayo Clinic*	Both	Post-operative	PFF
Solgard (2014)	Cohort	Horsholm Hospital, Denmark	Primary	Intra-operative and post-operative (within 6 weeks)	PFF
Thien (2014)	Cohort	Nordic Arthroplasty Register	Primary	Post-operative (within 2 years)	Revision for PFF
Thillemann (2009)	Cross-sectional	3 sources- Danish Arthroplasty Registry, The Register of Medicinal Product Statistics & The National Registry of Patients	Primary	Post-operative	Revision for PFF
Thillemann (2010)	Case-control	Danish Arthroplasty Registry	Primary	Post-operative	Revision for PFF
Watts (2015)	Cross-sectional	Mayo Clinic Registry	Primary	Post-operative	PFF
Lindberg-Larson (2017)	Cohort	Lundbeck Centre for Fast Track THA and TKA database	Primary	Intraoperative and Postoperative (within 90 days)	PFF

11.6 An example flexible parametric model to obtain "real-world" estimates of risk of PFF revision in the presence of competing risks of death and revision for other indications

```
***Expand the dataset
expand 3
bysort case_id: gen cause=_n
****Generate indicator variables for event of interest and competing events
gen revfracture_stem=(cause==1)
gen death=(cause==2)
gen rev_other=(cause==3)
gen event=(cause==status)
list case_id status cause event if indrevppfstemornot==2, sepby(case_id)

*** stset to tell inform stata it is survival data we are dealing with
stset primarytooutcomeyears, failure(event==1)

***Create interaction terms between each of the events and gender
tab patientgender2, gen(sex)
forvalues i=1/2 {
        gen fractsex`i'=revfracture*sex`i'
        gen revothsex`i'=rev_other*sex`i'
        gen deathsex`i'=death*sex`i'
}
* Create interaction terms between each of the events and age group
forvalues i = 5/9 {
gen age`i'revfracture=(ageatprimarycat==`i' & revfracture_stem==1)
gen age`i'revother=(ageatprimarycat==`i' & rev_other==1)
```

```
gen age`i'death=(ageatprimarycat==`i' & death==1)

}
```

*** Create interaction terms between each of the events and cement/uncement group**

```
tab pri_cem_uncem, gen(cement)

forvalues i = 1/2 {

gen fractcement`i'=revfracture*cement`i'

gen revothcement`i'=rev_other*cement`i'

gen deathcement`i'=death*cement`i'

}
```

*** Create interaction terms between each of the events, age group and cement/uncement**

```
forvalues i = 5/9 {

gen age`i'revfracture_cement=(ageatprimarycat==`i' & pri_cem_uncem==1 & revfracture_stem==1)

gen age`i'revother_cement=(ageatprimarycat==`i' &  pri_cem_uncem==1 & rev_other==1)

gen age`i'death_cement=(ageatprimarycat==`i' & pri_cem_uncem==1 & death==1)

gen age`i'revfracture_uncement=(ageatprimarycat==`i' & pri_cem_uncem==2 & revfracture_stem==1)

gen age`i'revother_uncement=(ageatprimarycat==`i' &  pri_cem_uncem==2 & rev_other==1)

gen age`i'death_uncement=(ageatprimarycat==`i' & pri_cem_uncem==2 & death==1)

}
```

*****Fit a flexible parametric model using the stpm2 command**

```
stpm2 revfracture fractsex2 fractcement2 age5revfracture_cement
age6revfracture_cement age7revfracture_cement age8revfracture_cement
age9revfracture_cement ///

        age5revfracture_uncement age6revfracture_uncement
age7revfracture_uncement age8revfracture_uncement
age9revfracture_uncement ///

        rev_other revothsex2 revothcement2 age5revother_cement
age6revother_cement age7revother_cement age8revother_cement
age9revother_cement ///

        age5revother_uncement age6revother_uncement
age7revother_uncement age8revother_uncement age9revother_uncement ///

        death deathsex2 deathcement2 age5death_cement age6death_cement
age7death_cement age8death_cement age9death_cement ///

        age5death_uncement age6death_uncement age7death_uncement
age8death_uncement age9death_uncement, ///

        scale(hazard) nocons rcsbaseoff tvc(revfracture fractcement2
rev_other death) ///  dftvc(3) initstrata(cause) eform nolog
```

*****Predict the cause-specific hazard rates and cumulative incidence function (with 95% confidence intervals).**

```
forvalues i=1/9 {

stpm2cif revfracture_m_c_age`i' revother_m_c_age`i' death_m_c_age`i', ///

cause1(revfracture 1 fractsex2 1 age`i'revfracture_cement 1) ///

cause2(rev_other 1 revothsex2 1 age`i'revother_cement 1) ///

cause3(death 1 deathsex2 1 age`i'death_cement 1) ci

stpm2cif revfracture_m_uc_age`i' revother_m_uc_age`i' death_m_uc_age`i',

cause1(revfracture 1 fractsex2 1 age`i'revfracture_uncement 1) ///

cause2(rev_other 1 revothsex2 1 age`i'revother_uncement 1) cause3(death 1

deathsex2 1 age`i'death_uncement 1) ci ///

stpm2cif revfracture_f_c_age`i' revother_f_c_age`i' death_f_c_age`i', ///

cause1(revfracture 1 fractsex2 0 age`i'revfracture_cement 1 ) ///

cause2(rev_other 1 revothsex2 0 age`i'revother_cement 1) cause3(death 1

deathsex2 0 age`i'death_cement 1) ci
```

```
stpm2cif revfracture_f_uc_age`i' revother_f_uc_age`i' death_f_uc_age`i',
cause1(revfracture1 fractsex2 0 age`i'revfracture_uncement 1) ///
cause2(rev_other 1 revothsex2 0 age`i'revother_uncement 1) cause3(death 1
deathsex2 0 age`i'death_uncement 1) ci
        }
```

*******graph males/females 50-59 cement vs. cementless stems**

```
twoway rarea CIF_revfracture_m_c_age5_lci CIF_revfracture_m_c_age5_uci
_newt, color(eltblue) fi(20) || ///
(line CIF_revfracture_m_c_age5 _newt, sort lcolor(blue) lpattern(solid)) ///
,ytitle("Probability of Fracture") title("Males 50-59 Cemented Stems") ///
xtitle("Time Since Primary THR (Years)") ///
legend(order(1 "Fracture Revision")) ///
ylabel(0(0.005)0.01, angle(0) format(%9.2f)) name(males_50_cemented,
replace)
twoway rarea CIF_revfracture_m_uc_age5_lci
CIF_revfracture_m_uc_age5_uci _newt, color(eltblue) fi(20) || ///
```

```
(line CIF_revfracture_m_uc_age5 _newt, sort lcolor(blue) lpattern(solid)) ///

,ytitle("Probability of Fracture") title("Males 50-59 Cementless Stems")

xtitle("Time Since Primary THR (Years)") ///

legend(order(1 "Fracture Revision")) ///

ylabel(0(0.005)0.01, angle(0) format(%9.2f)) name(males_50_cementless,

replace)

twoway rarea CIF_revfracture_f_c_age5_lci CIF_revfracture_f_c_age5_uci

_newt, color(eltblue) fi(20) || ///

(line CIF_revfracture_f_c_age5 _newt, sort lcolor(blue) lpattern(solid)) ///

,ytitle("Probability of Fracture") title("Females ≥50-59 Cemented Stems") ///

xtitle("Time Since Primary THR (Years)") ///

legend(order(1 "Fracture Revision")) ///

ylabel(0(0.005)0.01, angle(0) format(%9.2f)) name(fem_50_cemented,

replace)

twoway rarea CIF_revfracture_f_uc_age5_lci CIF_revfracture_f_uc_age5_uci

_newt, color(eltblue) fi(20) || ///
```

```
(line CIF_revfracture_f_uc_age5 _newt, sort lcolor(blue) lpattern(solid)) ///

,ytitle("Probability of Fracture") title("Females ≥50-59 Cementless Stems") ///

xtitle("Time Since Primary THR (Years)") ///

legend(order(1 "Fracture Revision")) ///

ylabel(0(0.005)0.01, angle(0) format(%9.2f)) name(fem_50_cementless,

replace)

graph combine males_50_cemented males_50_cementless fem_50_cemented

fem_50_cementless, ycommon xcommon name(_50_cement, replace)
```

11.7 A Systematic Review of Vancouver B2 and B3 Periprosthetic Fractures

■ HIP

A systematic review of Vancouver B2 and B3 periprosthetic femoral fractures

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Aims
The aim of this study was to investigate the outcomes of Vancouver type B2 and B3 fractures by performing a systematic review of the methods of surgical treatment which have been reported.

Materials and Methods
A systematic search was performed in Ovid MEDLINE, Embase and the Cochrane Central Register of Controlled Trials. For inclusion, studies required a minimum of ten patients with a Vancouver type B2 and/or ten patients with a Vancouver type B3 fracture, a minimum mean follow-up of two years and outcomes which were matched to the type of fracture. Studies were also required to report the rate of re-operation as an outcome measure. The protocol was registered in the PROSPERO database.

Results
A total of 22 studies were included based on the eligibility criteria, including 343 B2 fractures and 167 B3 fractures. The mean follow-up ranged from 32 months to 74 months.

Of 343 Vancouver B2 fractures, the treatment in 298 (86.8%) involved revision arthroplasty and 45 (12.6%) were treated with internal fixation alone. A total of 37 patients (12.4%) treated with revision arthroplasty and six (13.3%) treated by internal fixation only underwent further re-operation.

Of 167 Vancouver B3 fractures, the treatment in 160 (95.8%) involved revision arthroplasty and eight (4.8%) were treated with internal fixation without revision. A total of 23 patients (14.4%) treated with revision arthroplasty and two (28.6%) treated only with internal fixation required re-operation.

Conclusion
A significant proportion, particularly of B2 fractures, were treated without revision of the stem. These were associated with a higher rate of re-operation. The treatment of B3 fractures without revision of the stem resulted in a high rate of re-operation. This demonstrates the importance of careful evaluation and accurate characterisation of the fracture at the time of presentation to ensure the correct management. There is a need for improvement in the reporting of data in case series recording the outcome of the surgical treatment of periprosthetic fractures. We have suggested a minimum dataset to improve the quality of data in studies dealing with these fractures.

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As the number of total hip arthroplasties (THA) being performed worldwide continues to increase,[1,2] so does the incidence of periprosthetic femoral fracture. Based on the predictive modelling of National Joint Registry (NJR) data,[2] it has been projected that the numbers of primary and revision THAs in England and Wales will reach 186 893 and 137 056, respectively, by 2030.[2] A higher risk of periprosthetic femoral fracture has been shown in revision THA[3] but also following uncemented femoral fixation,[4] which is increasingly being used.[1,2,5] The incidence of periprosthetic femoral fractures will therefore continue to rise. The Swedish National Hip Arthroplasty Register,[6] which contains data from 1979 onwards, shows periprosthetic fracture as the second most common reason for revision beyond four years after primary arthroplasty.[7]

The management algorithm surrounding the treatment of periprosthetic femoral fractures is complex. Various factors determine the correct form of treatment. The major influences are

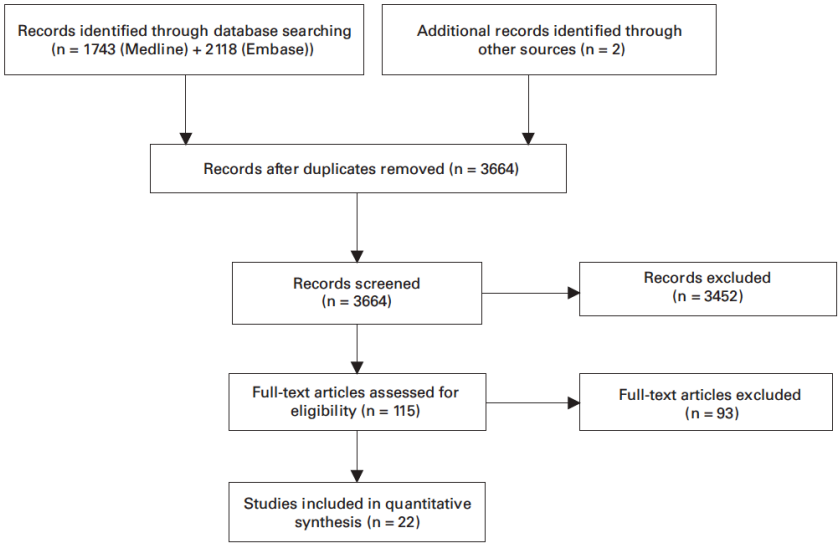


Fig. 1

Prepared Reporting Items for Systematic Reviews and Meta-Analyses flowchart.

the location of the fracture relative to the implant, the state of fixation of the implant and the influence of the quality of the surrounding bone. These three variables are identified in the Vancouver classification and form the basis of the established algorithm of management.[8] B2 fractures may, however, be difficult to identify when implant loosening is not obvious, and the determination of B3 status can be subjective. In this study, one of the objectives was to demonstrate supportive evidence for the importance of attributing an accurate Vancouver classification to the fracture.

A number of studies have indicated a poorer outcome and higher mortality after revision for periprosthetic fracture compared with other indications for revision.[9-11] Drew et al[12] calculated the combined risk of either death or re-operation in the first year after a periprosthetic femoral fracture to be 24%. Furthermore, the costs associated with the treatment of these fractures are significant.[13,14] In todays' challenging healthcare environment, only a successful clinical outcome will provide cost effective management.

Many of these fractures are Vancouver types B2 or B3.[8,15] Data from the Swedish National Hip Arthroplasty Register, showed that 555 of 1049 (53%) periprosthetic femoral fractures were type B2 and 43 (4.1%) were type B3.[16] Due to the presence of a loose stem with either good (Type B2) or poor bone stock (Type B3), revision surgery is generally recommended.

Joint registries can provide an analysis of revision surgery for periprosthetic femoral fractures, but the breadth of data collected is limited. Much of this is related to the difficulties of collecting appropriate data at the time of an emergency admission for fracture. Similarly, registry data will not identify the entire cohort, specifically will often not identify those treated with fixation alone. With the exception of publications based on the Swedish registry,[16,17] most other reported registry studies do not describe details of the classification of the fracture and the technique of fixation used at revision.[18-21]

The results from observational studies may provide detailed information which can be used collectively to assess the outcome of different forms of treatment for type B2 and B3 fractures. Although systematic reviews have assessed the outcomes of B1[22,23] and C[22] fractures, there are no previous formal systematic reviews assessing the outcomes or comparative outcomes of B2 and B3 fractures.

The primary aim of this study was to perform a systematic review of the methods of surgical treatment and outcomes of Vancouver B2 and B3 fractures. The secondary aim was to compare the outcomes in fractures treated with revision of the stem *versus* those treated with internal fixation without revision of the stem. We hypothesised that the appropriate classification of periprosthetic fractures is critical to avoiding unnecessary further surgery and ensuring a cost effective and successful outcome.

Table I. Total numbers and re-operations of Vancouver B2 and B3 fractures by the type of fracture

	Revision with or without ORIF			ORIF without revision	Total
Fracture type	**Cemented**	**Uncemented**	**Unspecified**		
Total Type B2 fractures	82	153	63	45	343
Re-operations Type B2 fractures, n (%)	11 (*13.4*)	19 (*12.4*)	7 (*11.1*)	6 (*13.3*)	43 (*12.5*)
Total Type B3 fractures	49	90	21	7	167
Re-operations Type B3 fractures, n (%)	8 (*16.3*)	12 (*13.3*)	3 (*14.3*)	2 (*28.6*)	25 (*15.0*)

ORIF, open reduction and internal fixation

Materials and Methods

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist for systematic reviews.[24] The review was registered on PROSPERO,[25] an international prospective register of systematic reviews.

A comprehensive electronic search of Ovid MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials and Database of Systematic Reviews[26] from the earliest available year of indexing until August 2016 was conducted. As an example, the key terms used in the Ovid MEDLINE search are shown in supplementary material. The electronic search was supplemented with a manual search of the reference lists of all retrieved review articles for any other relevant citations. Abstracts of all citations were screened and full texts of articles were obtained to decide on inclusion of relevant studies. The attrition flowchart is shown in Figure 1.

Observational studies reporting the outcomes of surgical treatment of periprosthetic femoral fractures after THA, were included if: periprosthetic femoral fractures were classified according to the Vancouver system,[15] they included at least ten patients with a type B2 fracture, and/or ten patients with a type B3 fracture. A minimum of two years mean follow-up was required and studies had to report re-operation (including revision arthroplasty) as an outcome measure.

Studies were excluded if the fractures were not classified according to the Vancouver system, or if the methods of treatment and outcomes were not reported separately according to the classification of the fractures.

Two authors (TK, RGP) independently extracted data relating to the design of the study, the country of conduct, the period of study, case selection, the assessment of outcome and the characteristics of the patients. In cases of disagreement on the data which were extracted, a third author (BES) independently extracted the data. Quality assessment was performed independently by two authors using the validated tool specifically designed by Guo et al[27] to assess the quality of case series, and a minimum dataset was designed to improve data reporting specific to periprosthetic femoral fractures.

Statistical analysis. Extracted data were entered onto RevMan Version 5.3 (Cochrane, London, United Kingdom). Treatment was categorised by the type of fracture (Vancouver B2 or B3) and the type of treatment (revision with or without open reduction and internal fixation (ORIF), ORIF alone). The details of the component used at revision were also recorded. The demographics of the further operations were reported according to the type of fracture and treatment. Risk Ratios (with 95% confidence intervals (CIs)) for re-operation were calculated using the Mantel-Haenszel random effects model[28] to make comparisons between the types of fracture and treatment. Data were represented as Forest plots and two-tailed z tests were used with a level of significance of 5%. Studies which reported treating both types of fracture, or similarly used both revision with or without ORIF and ORIF alone, could be included when calculating Risk Ratios.

Results

A total of 22 studies fulfilled the inclusion criteria and were included in the review. All were case series.[29-50] Two involved the same patients;[32,50] data were extracted from both separately and then combined for analysis.

A total of 510 Vancouver B2 or B3 fractures treated between 1984 and 2012 were included for analysis. The mean follow-up ranged between 32 months and 74 months.

B2 fractures. A total of 343 B2 fractures were reported in 14 case series (see supplementary material). Information about the gender was available for 125 patients (64 women: 61 men). Treatment involved revision of the stem with or without internal fixation in 298 patients (87.6%). A total of 45 were treated with fixation without revision of the stem. For those treated with revision THA, cemented stems were used in 82 (27.6%) and uncemented stems in 153 patients (51.3%). The type of stem was not specified in 63 operations (21.1%).

A total of 43 patients (12.8%) required re-operation following treatment. A total of 37 patients (12.4%) who were treated with revision of the stem with or without internal fixation required re-operation and six (13.3%) who were treated with internal fixation alone required re-operation. Table I shows the re-operations by the type of fracture.

Four studies[38,39,45,49] reported the results of treating Vancouver B2 fractures with either revision of the stem with or without ORIF or with ORIF alone. The calculated Risk Ratio of re-operation was 1.74 (95% CI 0.61 to 4.97, p = 0.30) in favour of revision with or without ORIF (Fig. 2).

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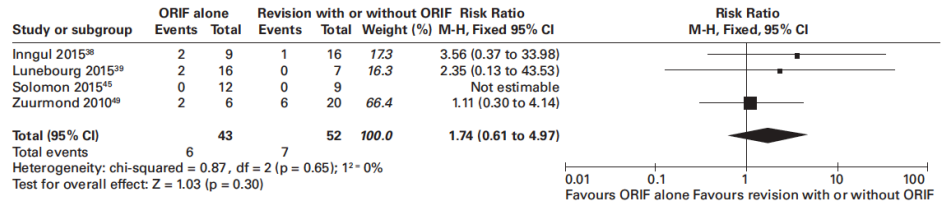


Fig. 2

Forest plot comparing the risk of re-operation for Vancouver B2 fractures treated with revision arthroplasty with or without open reduction and internal fixation (ORIF) *versus* ORIF alone (M-H, Mantel-Haenszel method; CI, confidence intervals; df, degrees of freedom).

Table II. Indications for re-operation by type of fracture

Indication for re-operation	B2 fractures	B3 fractures
Refracture	9	2
Infection	3	3
Subsidence	6	3
Stem loosening (aseptic)	4	1
Nonunion	4	0
Dislocation	4	2
Wound infection/superficial haematoma	4	3
Implant breakage	1	1
Not specified	8	10
Total	43	25

Table III. Revision femoral stem designs used in the treatment of B2 and B3 fractures by the design of the implant

Stem design	Type B2 fractures	Type B3 fractures	Total
Tapered, collarless polished (cemented)	24	3	27
Tapered, polished, collared (cemented)	7	0	7
Non-tapered, collared, rough finish (cemented)	23	0	23
Matte finish (cemented)	0	25	25
Tapered fluted (uncemented)	114	58	172
Distal locking (uncemented)	15	24	39
Proximal femoral replacement (cemented)	0	21	21
Unspecified cemented	28	0	28
Unspecified uncemented	46	8	54
Unspecified	41	21	62
Total	298	160	458

Table II summarises the indications for re-operation by the type of fracture.

B3 fractures. There were 167 Vancouver B3 fractures in the studies which were included (see supplementary material). Information about the gender was available for 99 patients (59 women, 40 men). In 160 cases (95.2%) treatment involved revision of the stem with or without internal fixation. A total of eight patients (4.8%) were treated with internal fixation alone. Of the 160 patients who underwent revision THA, 90 (53.9%) involved uncemented stems, 28 (16.8) involved a cemented stem and 21 (12.6%) were treated with a cemented stem. Revision prostheses were not specified for 21 patients (12.6%). Table III shows the stem designs which were used for revision in patients with both Vancouver B2 and B3 fractures.

There were a total of 25 re-operations (15.0%) (Table I), 23 (14.4%) in patients who were treated with revision of the stem with or without ORIF, including two who had further surgery for a wound infection in B3 fractures treated with a cemented stem. There were two re-operations (28.6%) for patients treated with ORIF alone, one for a further periprosthetic fracture and one for aseptic loosening of the stem. In two studies,[42,46] the results of those treated with both revision of the stem with or without ORIF or ORIF alone were reported. The Risk Ratio based on these two studies was 1.38 (95% CI 0.38 to 5.01, p = 0.63) in favour of revision of the stem with or without ORIF (Fig. 3).

***B2 versus* B3 fractures.** Four studies[33,40,42,43] reported the outcome of sufficient numbers (> 10) of both B2 and B3

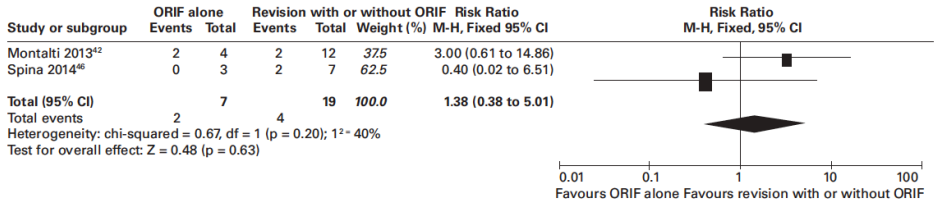


Fig. 3

Forest plot comparing the risk of re-operation for Vancouver B3 fractures treated with revision arthroplasty with or without open reduction and internal fixation (ORIF)*versus* ORIF alone (M-H, Mantel-Haenszel method; CI, confidence intervals; df, degrees of freedom).[42,46]

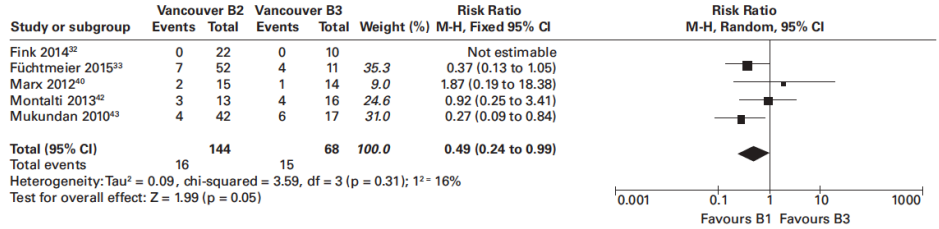


Fig. 4

Forest plot comparing the risk of re-operation for Vancouver B2 and B3 fractures (M-H, Mantel-Haenszel method; CI, confidence intervals; df, degrees of freedom).

fractures for a total of 180 periprosthetic fractures. The Risk Ratio of re-operation regardless of the form of treatment was 0.49 (95% CI 0.24 to 0.99, p = 0.31) in favour of B2 fractures (Fig. 4). The Risk Ratio when excluding patients treated with ORIF alone was 0.52 (95% CI 0.28 to 0.98, p = 0.23) in favour of B2 fractures.

Uncemented tapered fluted stems. Uncemented tapered fluted stems were used for revision in 114 B2 fractures (33.2%) and 58 B3 fractures (34.7%). The overall percentage rate of re-operation was 14/114 for B2 (12.3%) and 9/58 for B3 fractures (15.5%). The indications for re-operation included re-fracture (three), dislocation (three), aseptic loosening (three), wound complications (three) and stem breakage (one). Stem subsidence was reported in 9/172 patients (5.2%), although only three (1.7%) of these required revision. The indication for re-operation was not specified for seven patients.

Quality assessment. The mean quality score was 11.5/18 (standard deviation 2.39). Only two studies[34,49] reported detailed individual case-by-case data including demographic details, diagnosis, treatment and outcomes, both adopting a table format with a row per patient. Only five studies[35,40,41,45,47] had a mean follow-up of more than five years. A total of 14 studies[29-33,37,39-46] included either the names of the specific prostheses or details of the design of the stem which was used for revision. No study reported data to allow analysis of survival.

Discussion

This systematic review shows that as per consensus, most Vancouver B2 and B3 fractures which are reported in the literature are treated with revision THA with or without internal fixation. However, for B2 fractures particularly, a significant proportion (13.1% in this review) were treated with internal fixation alone. This might reflect difficulties in determining whether or not the stem was loose pre-operatively from the available imaging. However, this determination is important. Often the differentiation between a Vancouver B1and B2 fracture is straightforward. However, there are fractures, initially felt to be around well- fixed stems, in which only a careful review of previous radiographs or a thorough history identifying pre-existing thigh pain, will raise the suspicion of associated loosening of the stem. Similarly, there are specific patterns and locations of fractures, such as a relatively transverse fracture through an area of lysis below an apparently well-fixed stem, that should alert the surgeon to the likelihood that the stem is failing and should be revised. We found that for both types of fracture, treatment with internal fixation alone was associated with a higher percentage of re-operations, but the difference in relative risk did not reach statistical significance. Almost a third of B3 fractures treated with internal fixation alone required re-operation. This trend is supported by national data from the Swedish

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National Hip Arthroplasty Register,[17] which indicates a higher percentage of re-operations for B2 fractures treated with ORIF without revision of the stem (32%), than with those treated with revision alone (10%) or revision combined with internal fixation (23%). The overall proportion of patients undergoing a re-operation was higher than reported in this review which may be a reflection of the longer follow-up of registry data as opposed to published observational series. Another possible explanation is that there is bias in the selection of patients which surgeons/centres treat with internal fixation alone, which may be related to the fitness of the patients for a longer more physiologically demanding revision procedure, non-ambulatory patients, or in those with a limited life expectancy. Some authors have also reported good results at five-year follow-up of treating selected B2 fractures around polished, tapered, collarless stems in which anatomical reduction can be achieved, with internal fixation alone.[45] The information available for this systematic review limits our ability to address the question of which, if any, patients sustaining Vancouver B2 or B3 fractures, would be suitable for treatment with internal fixation alone.

The analysis of included studies with sufficient data available for comparison, indicates a higher relative risk of re-operation for B3 fractures compared with B2 fractures, even when comparing those treated with revision of the stem with or without fixation. Anecdotally, this has been appreciated by surgeons experienced in the management of these fractures, but there is little previous information, to quantify this difference into risk of failure. It is important to remember that compromise in the surrounding bone stock, that determines the differentiation of B2 and B3 fractures, is potentially representative of other factors which may contribute to a higher risk of failure, such as multiple previous operations on the hip, previous infection or fracture, severe lysis or osteopenia and other comorbidities, which have not been accounted for as confounders in this analysis.

Uncemented stems were found to be more commonly used for the management of both B2 and B3 fractures. A significant proportion of these were tapered fluted titanium stems with the non-modular Wagner SL stem (Zimmer Biomet, Warsaw, Indiana) being used in almost a quarter of all patients requiring revision of the stem. Tapered fluted titanium stems provide reliable and versatile distal diaphyseal fixation, which overcomes concerns about proximal stress shielding and the difficulties associated with advanced proximal bone loss.[51] These systems facilitate an accurate restoration of biomechanics of the hip with options to re-establish length and version independently, with modular proximal components. Good results have been reported after femoral revision for aseptic loosening.[52-57] Encouraging results with these technologies have also been reported in the management of periprosthetic fractures.[51,58-60] However, in many studies, the results are reported as part of larger observational cohorts, with their use in B2 and B3 fractures as only one of a number of other indications for femoral revision. This is likely to have been under-reported in our review as the papers did not satisfy our inclusion criteria.

In this systematic review, the percentage of patients requiring re-operation using tapered fluted stems for both B2 (12.3%) and B3 (16.7%) fractures was comparable with those in the Swedish National Hip Arthroplasty register for the rate of re-operation for B2 and B3 fractures treated with revision of the stem with or without ORIF, which were 18.5% and 15.5% respectively.[17] One of the complications of these stems is subsidence of the stem. This can be a particular concern in the presence of poor bone quality. The rates and magnitude of subsidence differ in different systems. While significant rates of subsidence have been reported with the 2° taper angle of the Wagner SL stem,[61,62] more aggressive angles of taper available in some systems have shown lower rates of subsidence.[63] The overall proportion of subsidence in the stems used for Vancouver B2 and B3 fractures appears relatively low in this review. Most studies had a follow-up of less than five years and it is likely that significant subsidence would have occurred before that time. It is also important to appreciate that there was variation in the threshold for what could be deemed 'clinically significant' subsidence.

This review has limitations. There is a lack of large prospective studies in this field of study. Hence, the studies which were included were all retrospective case series. A total of 115 studies were assessed for inclusion based on the full-text, of which only 22 were finally included. Many were excluded either due to small numbers of periprosthetic fractures or a lack of matched outcomes by classification of the type of fracture. Only two studies reported individual case-by-case details.[34,49] Specifics such as the details of the original implant, whether the fracture occurred after primary or revision THA, the strategies used for fixation and the details of the implants for each patient would have allowed a more detailed analysis. Furthermore, the time to re-operation or death was not reported in any studies, and comparative analysis of survival was not possible.

Similar to the data from the Swedish National Hip Arthroplasty Register, Cook et al[64] reported 52% B2 and 10% B3 fractures in their study of periprosthetic fractures following 6458 primary THAs. Recent results from the Mayo clinic[4] described 557 periprosthetic femoral fractures from their institutional registry of 32 644 primary THAs, of which 24.5% were B2 and 9.2% were B3. As the incidence of Vancouver B2 and B3 femoral fractures continues to rise so will the requirement for complex reconstructive surgery with high morbidity and resulting high costs in financial and clinical resources.

It is important to appreciate that a significant number of Vancouver B2 fractures may be misclassified as B1 and treated with internal fixation without revision of the stem. These would not have been captured in this study. Therefore, the true re-operation rate for B2 fractures is likely to be higher than we have recorded.

Table IV. Suggested minimum dataset for case series reporting results of periprosthetic fractures

Age at primary (yrs)	Gender	Fracture: post-primary THA, revision, hemiarthroplasty	Yr of primary	Primary Implants	Time to fracture (mths)	Fracture type (Vancouver)	ASA grade + comorbidities	Treatment: stem revision only, stem revision + ORIF, ORIF only, stem revision + socket revision, cement-in-cement revision	Revision implants	ORIF implants (including strut allograft if used)	Impaction grafting (Y/N)	Reoperation/ died/No re-operation (R/D/N) If re-operation, give indication. E.g. infection, dislocation, fracture, stem failure, subsidence, aseptic loosening	Re-operation details e.g. washout, stem revision	Time to re-operation/ death	Date of last follow-up/death	Other outcomes: patient-reported outcome measures subsidence complications

ORIF, open reduction and internal fixation; ASA, American Society of Anesthesiologists; THA, total hip arthroplasty

The Vancouver classification has good intra- and inter-observer reliability[15,65-67] and is a useful tool in guiding decision-making. It can, however, be difficult to classify some fractures accurately. Previous authors have suggested algorithms based on various strategies for treatment which are available and which often depend on the design of the existing femoral stem, the location of the fracture and its precise configuration.[68] This systematic review highlights both the variability in the treatment of B2 and B3 fractures, but also the significance of choosing the correct management strategy to avoid an increased risk of re-operation. We also found that although there are established guidelines for the principles of management, there is a shortage of high quality reporting of outcomes. Comparison of such studies would allow refinement in an algorithmic approach to management.

Currently, the National Joint Registry, the largest arthroplasty register in the world, records all primary THAs performed in England and Wales with matched revision procedures by indication. However, as a large population-based database, the breadth of data on each specific indication for revision is limited. For periprosthetic fractures, only those undergoing revision arthroplasty are entered. Therefore, those treated by internal fixation alone, although a relatively small number in the case of B2 and B3 fractures, are not recorded. The classification of these fractures and the details of any use of additional forms of internal fixation are also not recorded. There is therefore a necessary reliance on detailed observational studies to bridge this gap in information. There are reporting recommendations for case series in colorectal,[69] and more recently plastic surgery.[70] On this basis, we have designed a suggested minimum dataset to aid reporting of case series describing the outcome of periprosthetic fractures (Table IV).

In conclusion, this study is the only systematic review of Vancouver B2 and B3 femoral fractures. A proportion of both types of fracture are treated by internal fixation alone and have a higher rate of re-operation. Despite a large number of case series recording the treatment of B2 and B3 fractures, the breadth and detail of data limited the quantitative comparisons of specific forms of treatment. We have suggested a minimum dataset to be used for case series describing the management of these fractures.

Take home message:

- Vancouver B2 & B3 fractures treated with internal fixation are associated with poorer outcomes.

- Improved reporting of periprosthetic fracture case series will allow better evaluation of treatment modalities in specific patient groups, as well as to allow robust analysis of implants used for revision arthroplasty.

Supplementary material

A table showing the Ovid MEDLINE search strategy, as well as a data extraction chart, is available alongside the online version of this article at www.bjj.boneandjoint.org.uk

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