PhD Thesis

Outcomes of different bearings in total hip arthroplasty

- implant survival, revision causes, and patient-reported outcome

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PREFACE

This thesis is based on studies carried out during my part-time employment at Orthopaedic Research
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The thesis is based on the following three studies

Study I: Varnum C, Pedersen AB, Kjærsgaard-Andersen P, Overgaard S. Comparison of the risk of revision in cementless total hip arthroplasty with ceramic-on-ceramic and metal-on-polyethylene bearings. Acta Orthop. 2015;86(4):477-84.

Study II: Varnum C, Pedersen AB, Makela K, Eskelinen A, Havelin LI, Furnes O, Karrholm J, Garellick G, Overgaard S. Increased risk of revision of cementless stemmed total hip arthroplasty with metal-on-metal bearings. Acta Orthop. 2015;86(4):469-76.

Study III: Varnum C, Pedersen AB, Kjærsgaard-Andersen P, Overgaard S. Are different types of bearings and noises from total hip arthroplasty related to quality of life postoperatively? Manuscript in review.

ABBREVIATIONS

ALVAL	Aseptic lymphocytic vasculitis-associated lesions
AOA NJRR	Australian Orthopaedic Association National Joint Replacement Registry
ARMD	Adverse reaction to metal debris
ASR	Articular Surface Replacement
ASTM	American Society for Testing and Materials
BMI	Body mass index
CCI	Charlson comorbidity index
CI	Confidence interval
CoC	Ceramic-on-ceramic
CoP	Ceramic-on-polyethylene
CRS	Civil Registration System
CT	Computed tomography
DHR	Danish Hip Arthroplasty Registry
DNPR	Danish National Patient Registry
FDA	Food and Drug Administration
HHS	Harris Hip Score
HOOS	Hip disability and osteoarthritis outcome score
HR	Hazard ratio
HXLPE	Highly cross-linked polyethylene
IQR	Inter-quartile range
LDH	Large-diameter-head
MCII	Minimal clinically important improvement
MeSH	Medical subject heading
MoHXLPE	Metal-on-highly cross-linked polyethylene
MoM	Metal-on-metal
MoP	Metal-on-polyethylene
MRI	Magnetic resonance imaging
NARA	Nordic Arthroplasty Register Association
NJR	National Joint Registry for England, Wales, Northern Ireland and Isle of Man
OA	Osteoarthritis
PASS	Patient-acceptable symptom state
PJI	Prosthetic joint infection
PPV	Positive predictive value
PRO	Patient-reported outcome
QoL	Quality of life
RCT	Randomized clinical trial
ROM	Range of motion
RR	Relative risk
SHAR	Swedish Hip Arthroplasty Register
THA	Total hip arthroplasty
UCLA	University of California, Los Angeles
UHMWPE	Ultrahigh-molecular-weight polyethylene
VAS	Visual analogue scale
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index
Y-TZP	Yttria stabalized tetragonal zirconia polycrystals
ZTA	Zirconia-toughened alumina

CONTENT

1. INTRODUCTION

1.1. Total hip arthroplasty

Total hip arthroplasty (THA) is a common and successful treatment of patients suffering from severe osteoarthritis (OA) that significantly reduces pain and improves hip function and quality of life (QoL). It has been proclaimed that THA is the operation of the century.[2] Historically in 1923, Smith-Petersen created a mould arthroplasty made of glass to be inserted between the reshaped articulating surfaces of the head of the femur and the acetabulum. It was thought that the moulded glass would guide nature's repair of the defects in the cartilage. Due to the fragility of the material used, the results were not encouraging, and in 1938 the first vitallium mould arthroplasty was performed.[3] During the 1950-60s, Sir John Charnley introduced the modern low torque friction arthroplasty, which included the use of acrylic cement to fix components to bone, high-density polyethylene as bearing material, and monoblock stem of metal.[2,4] Studies have reported remarkable durability with 77%[5] and 81%[6] survivorship of these THAs at 25-year follow-up with any revision as endpoint, and the concept is still the gold standard.

1.2. Outcome of total hip arthroplasty

Traditionally, the outcome of THA (Figure 1) has been evaluated from the surgeon's perspective. The surgeon-based outcome may be assessed in morbidity including peri- and postoperative complications. Surgical complications count bleeding, prosthetic joint infection (PJI), damage to anatomical structures including involvement of the sciatic nerve, dislocation, anisomelia, and periprosthetic fracture, whereas medical complications include pneumonia, deep venous thrombosis, and pulmonary embolism. Also biomechanical reconstruction, range of motion, prosthetic survival, causes of revision, and mortality are outcomes assessed by the surgeon.

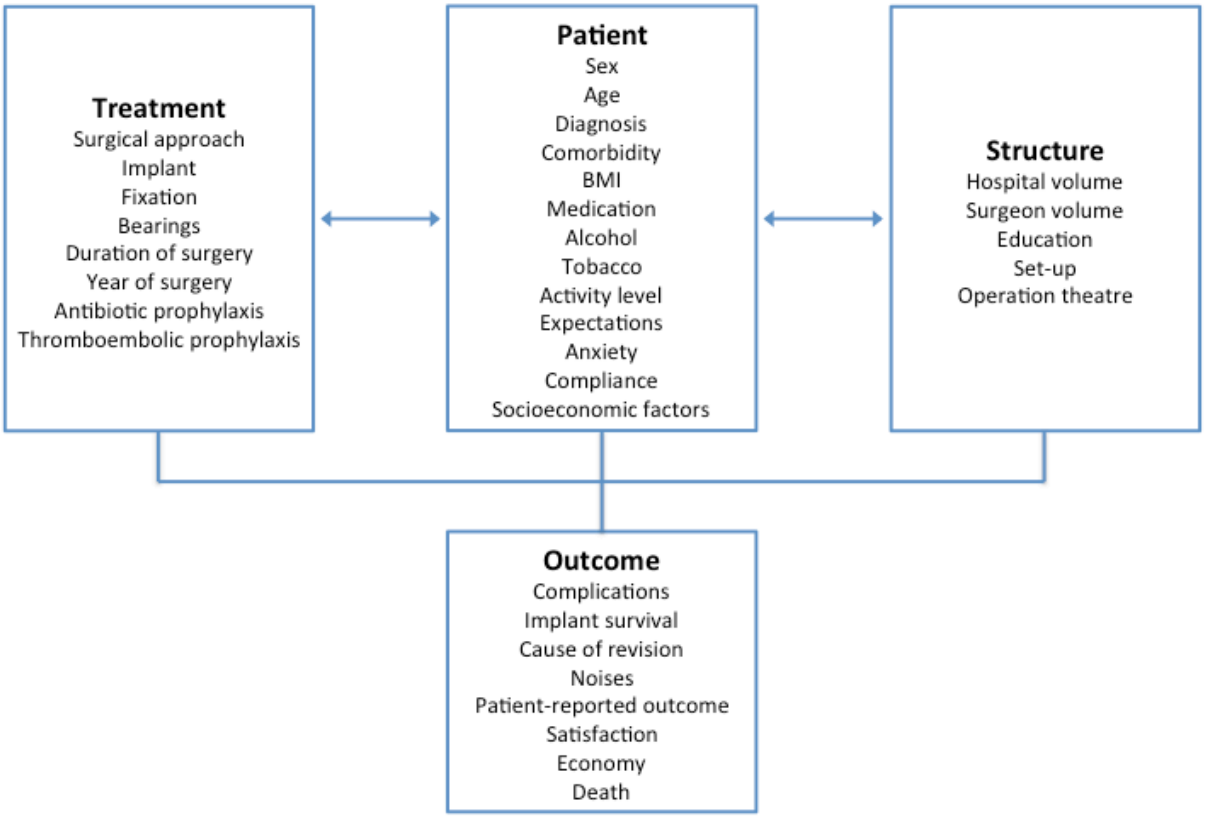

Figure 1. Prognostic factors for the outcome of total hip arthroplasty. The possible influence of these factors is discussed in more detail in section 3.7.3.

Furthermore, noises from the THA[7] and persistent hip-related pain have been used as outcome measures after THA. Studies have shown, that persisting hip-related pain was seen in 28.1% of patients 12 to 18 months after primary THA[8], and that 7% of patients were dissatisfied or highly dissatisfied one year after primary THA[9]. By including measures of pain, disability and satisfaction into the definition of failure, a more balanced assessment of outcome can be made, as patients and orthopaedic surgeons may assess outcome after THA differently. Therefore, patient-reported outcome (PRO), which can be disease-specific or generic, is recognized as a very important tool for evaluating the outcome after THA.[10,11] The US Food and Drug Administration (FDA) have defined a PRO as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response

by a clinician or anyone else".[12] FDA strongly recommends the use of PROs in clinical trials, and PROs have been implemented in national hip arthroplasty registries.[10,13,14] Additionally, the economic outcome of THA may be assessed.[15]

The outcome after THA may be influenced by a number of prognostic factors, which may be related to the patient, treatment, and structure (Figure 1). Prognostic factors may be categorised into non-modifiable, e.g. sex and age, and modifiable, e.g. alcohol consumption, smoking habits, and activity level. Previous literature has shown that the patient-related factors sex, age, diagnosis, comorbitity, and use of medication influence the outcome of THA.[16-23] The outcome may also be affected by the surgical approach, implant design, fixation, type of bearings, and femoral head size.[21,24-31] Furthermore, hospital volume and fast-track set-up may be of importance for the outcome of THA.[32,33] Among all these determinants of the outcome of THA, the focus of this thesis is different types of bearings.

1.3. Types of bearings

1.3.1. Metal-on-polyethylene bearings

Metal-on-polyethylene (MoP), a femoral head of stainless steel articulating on a polyethylene acetabular liner, are by far the most commonly used bearings in THA and are therefore considered the "standard" bearings. The major concern related to the use of MoP bearings is wear and generation of polyethylene wear particles which potentially can lead to osteolysis and aseptic loosening of the implant. Aseptic loosening is the most prevalent cause of revision accounting for 51.8% of registered revisions in the Danish Hip Arthroplasty Registry (DHR).[16]

Generation of polyethylene wear particles can primarily result from three different processes: Abrasion (a harder surface make grooves in a softer material), adhesion (formation of a transfer

film occurring when a softer material is smeared onto a harder surface), and fatigue (generation of particles resulting from subsurface cracks).[34] Wear particles can be found in periprosthetic osteolytic lesions embedded in a membrane also containing macrophages which release pro-inflammatory mediators when having phagocytized ultrahigh-molecular-weight polyethylene (UHMWPE) wear particles. Consequently, osteoclasts are activated to resorb the bone at the bone-implant interface that can result in painful loosening of the implant.[35-40] Previous research has stated that linear polyethylene wear exceeding 0.2 mm/year or volumetric wear surpassing 150 mm3/year predisposes to periprosthetic osteolysis.[41]

In cementless MoP THA, the polyethylene liner is inserted into a metal acetabular shell leading to both frontside and backside wear. Ex vivo, however, linear and volumetric wear from the articulating side were at least three orders of magnitude higher than the wear estimates at the backside. This variation was mainly explained by the difference in maximum sliding distance at the articulating surfaces (measured in mm) compared to the back surface (measured in μm).[42]

In order to reduce abrasive/adhesive and fatigue wear, much effort has been made to improve the tribological properties of polyethylene during the last decades. Charnley introduced the polytetrafluorethylene (Teflon) as material for the acetabular component but due to poor wear resistance, this material was abandoned in favour of high molecular weight polyethylene.[4,43] Charnley recommended the use of gamma sterilization for polyethylene components, a technique that is still used.[44] In hip simulators, wear rates decreased by a factor of more than 30 when the molecular weight of polyethylene increased from $5x10^5$ to $2x10^6$, and a single dose of gamma irradiation at 2.5-5.0 Mrad (1 Mrad=10 kGy) progressively improved the wear resistance in UHMWPE.[45] A drawback of gamma irradiation in air is, that it leads to long-lived free radicals which react with oxygen resulting in progressive oxidation and deterioration of the mechanical properties of the polymer.[46] In order to reduce oxidative degradation, some manufacturers

started to gas-sterilize by ethylene oxide or gas plasma but in contrast to gamma irradiation, these alternative gas-sterilization methods did not cross-link the polyethylene.[47] In a radiographic wear study, higher wear rates was found for uncross-linked, gas-sterilized components when compared with gamma-sterilized controls.[48] Furthermore it was confirmed that, in hip simulator testing, elevated doses of irradiation cross-linking reduced wear rates, and thermal processing after irradiation influenced the mechanical properties and oxidative resistance. Irradiation cross-linking, whether by gamma or electron irradiation, when combined with annealing and remelting thermal treatments resulted, in the late 1990s, in the first generation of highly cross-linked polyethylene (HXLPE).[44,49,50]

Starting around 2005, the newer generations of HXLPE were developed by the use of different methods to stabilize the polymer: Sequential irradiation and annealing process whereby the polyethylene receives a high dosage of radiation cumulatively instead of during one event (X3 material)[51]; solid-state, hydrostatic extrusion that modify the physical and mechanical properties of HXLPE by induction of plastic deformation and orientation of the molecules (ArCom XL material)[52]; and incorporation of vitamin E (α-Tocopherol), which react with peroxy free radicals on lipid chains and arrest the oxidation reactions resulting in increased oxidative stability[53].

1.3.2. Ceramic-on-ceramic bearings

Ceramic-on-ceramic (CoC) bearings were introduced to reduce wear debris. In 1970, Boutin implanted the first THA with all-alumina bearings in France.[54] Today's ceramic bearings consist of aluminium oxide (alumina, Al_2O_3), zirconium oxide (zirconia, ZrO_2) or composites and have been changed in order to reduce fracture risk. The first generation alumina had low density and a very coarse microstructure, whereas the newer third generation had a higher purity and a finer grain structure and was hot isostatic pressed, laser engraved, and proof tested.[55] Alumina

has been used for CoC bearings.[56-58] The safety of a ceramic component is correlated to its mechanical strength, and efforts for improving this strength have been made by developing different manufacturing processes.

Zirconia ceramic is used in the form of yttria stabalized tetragonal zirconia polycrystals (Y-TZP) to impede the hydrothermal degradation of zirconia. Y-TZP has a higher density and finer grain size than alumina, providing about double its fracture toughness and flexural strength. There is clear experimental evidence that the wear rate of zirconia-on-zirconia bearings is too high to use in prosthetic joints, and zirconia is traditionally used for the femoral head in combination with an UHMWPE acetabular liner.[59,60]

Two different composites can be made from alumina and zirconia: A zirconia matrix reinforced with alumina particles (alumina-toughened zirconia) or an alumina matrix reinforced with zirconia particles (zirconia-toughened alumina, ZTA). The hardness of ZTA composites is greater resulting in higher wear resistance. With new processing techniques, it is possible to obtain high-density ZTA nanocomposites with a very homogeneous microstructure, nearly the same hardness as alumina, a higher fracture toughness, high hydrothermal stability, and high crack-resistance.[61,62]

The most frequently used ceramic materials today in THA are the third generation hot isostatic pressed alumina commercially known as BIOLOX forte and the fourth generation commercially known as BIOLOX delta, which is an alumina matrix composite comprised of 75% alumina, 24% zirconia, and 1% elongated oxides of chromium and strontium.[63] Some of the advantages with the use of CoC bearings are the low wear rates both ex vivo and in vivo.[63-66] In addition, wear debris produced from CoC bearings are less biologically active than metal or polyethylene debris.[67,68] The major concerns related to the use of CoC bearings are fracture of the ceramic

components[69-73] and squeaking and other noises[7,74,75]. Also, the sandwich design for ceramic inserts have been reported to have problems in terms of dislodging of the ceramic insert.[76,77]

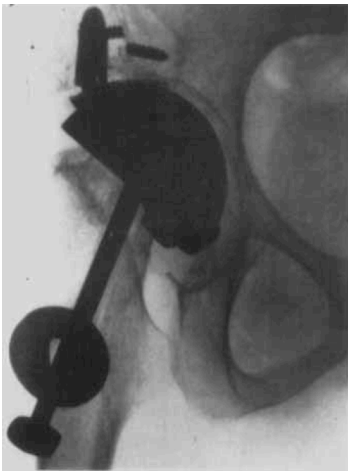

Figure 2. A ball-and-cup arthroplasty performed in 1938. Radiograph 13 years later.[1]

1.3.3. Metal-on-metal bearings

In 1938, Wiles performed the first THA consisting of pre-formed acetabulum and femoral head made of stainless steel attaching it to bone with bolts and screws.[1] During the beginning of the 1960s, McKee and Watson-Farrar implanted THAs with metal-on-metal (MoM) bearings. The components were constructed of chromium-cobalt alloy and fixed to the bone by methylmethracrylate.[78] In the same period, Ring developed a screw fixated cup to be used with the Moore's prosthesis.[79] By mid-1970s, MoM articulations were abandoned in favour of Charnley's technique.[80] Modified alloys marked a new era for MoM bearings, and in 1988 Weber implanted the first MoM THA with Metasul bearings manufactured from carbon rich cobalt chromium molybdenum alloy[81,82], and the Metasul bearings are still used today. The current MoM implants are made of a Cobalt-28 Chromium-6 Molybdenum Alloy (ASTM (American Society for Testing and Materials) F75 or ASTM F1537) and have a high carbon content above 0.20% which has the purpose of decreasing wear[83].

With the reintroduction of MoM bearings it was possible to use large-diameter-heads (LDHs) which were shown to reduce wear ex vivo.[84] Ex vivo, LDHs have been shown to improve range of motion (ROM) and, due to increased jump distance (the distance a femoral head requires for displacement from the acetabular cup before dislocation), decrease the component-to-component impingement and hereby the potential risk of dislocation.[85] However, a randomised clinical trial have shown no difference in total ROM for patients with LDH and hip resurfacing

arthroplasty compared to patients having 28-mm femoral head.[86] In a study from the Finnish Hip Arthroplasty Register, a decreased risk of revision due to dislocation was found, when comparing 32-36 mm and femoral heads larger than 36 mm to 28 mm heads.[29]

The most important predictor of the wear rate in MoM bearings is edge-loading[87], and the chromium and cobalt wear particles may result in different periprosthetic soft-tissue lesions: metallosis[88], aseptic lymphocytic vasculitis-associated lesions (ALVAL)[89], pseudotumours[90] and adverse reaction to metal debris (ARMD)[91]. Metallosis is the gross staining of the periprosthetic soft tissue as a result of metal deposition and is seen at revision surgery. ALVAL is characterized by a diffuse and perivascular infiltrate of T- and B-lymphocytes and plasma cells, high endothelial venules, massive fibrin exudation, accumulation of macrophages, infiltrates of eosinophils, and necrosis and was found in periprosthetic tissues from patients with failed MoM bearings.[89] Pseudotumours are symptomatic reactive periprosthetic soft tissue changes demonstrated on magnetic resonance imaging (MRI) as thin- or thick-walled cysts or solid masses, and their histology resembles that of ALVAL, but a more diffuse lymphocytic infiltrate as well as extensive connective tissue necrosis characterise pseudotumours.[90,92] ARMD is used as an umbrella term and describes joint failures associated with pain, large sterile effusions of the hip and/or macroscopic metallosis/necrosis, thus including metallosis, ALVAL and pseudotumours.[91]

Apart from the local reactions, also systemic effects might be seen. Systemic cobalt toxicity have been described following revision of fractured ceramic bearings and in patients with failed MoM implants, and possible symptoms include impairment of vision and hearing, hypothyroidism, peripheral neuropathy, cardiomyopathy, depression, anxiety, tinnitus, fatigue, and anorexia.[93-99] There is dissemination of cobalt and chromium to sites distant to the orthopaedic implant.[100] It has been found, that patients having THA have a significant increase of chromosomal damage in

peripheral blood lymphocytes, and that the changes may depend in part on the type of prosthesis.[101] However, the incidence of cancer after THA is low predicted from the normal population, and the overall risk of cancer is not higher for MoM than for any other type of bearings. The low risk of cancer must be read with caution, as the follow-up is relatively short (maximum 7-11 years).[102,103]

1.4. Motivation

In order to improve the outcome after THA, this PhD study was initiated. Although improvements of the polyethylene in MoP bearings, alternative bearings such as CoC and MoM have been used in THA, which may result in better implant survival and PRO. Only a few registry-based studies on CoC and stemmed MoM THA have been published.[28,104-107] These studies may be hampered by the lack of information on completeness of data, of examination of implant types, and of causes of revision and may be limited by the short follow-up and the used statistical methods including lack of adjustments for confounders. Moreover, the existing literature on implant survival and PRO including information on hip-related noises from patients having MoP, CoC or MoM THA represents smaller series of patients involving one to few hospitals and clinics.[7,24,27,108-112] These studies are limited by the small sample size, and results from a single institution may reduce the generalizability of the findings. Furthermore, the results may be biased, as some authors have been involved in the development of the implant. To overcome these issues, we decided to perform nation-wide, population-based studies, which can take patient- and surgery-related characteristics into account, in order to provide patients the optimal type of bearings in THA.

2. AIMS OF THE THESIS

The aims of this thesis were:

Study I: To examine the revision risk and to investigate the causes of revision of cementless CoC THAs comparing them to those of "standard" MoP THAs.

Study II: To compare the six-year revision risk for MoM bearings with that for MoP bearings in cementless stemmed THA, and further to study the revision risk for different designs of stemmed MoM THAs and the causes of revision.

Study III: To examine the association between CoC, MoM, and MoP bearings and both generic and disease-specific PROs, and furthermore to examine the incidence and types of noises from the three types of bearings and identify the effect of noises on PROs.

3. METHODOLOGICAL CONSIDERATIONS

3.1. Literature search

The literature search was not based on a systematic review. It was conducted throughout the study period with a final search in January 2016. PubMed was the main database for literature search, and the medical subject heading (MeSH) "Total hip replacement" was combined with the following keywords: "ceramic-on-ceramic", "alumina bearings", "metal-on-metal", "polyethylene", "HOOS", "EQ-5D", "UCLA", and "satisfaction". Also the reference lists of relevant articles and annual reports from national hip arthroplasty registries were reviewed. Furthermore, the Web of Science database was used to search for specific articles. The literature search was limited to articles in English or Danish and mainly to articles published from 2005 and onwards, although some key articles from before 2005 have been included due to historical interest.

3.2. Data sources

3.2.1. The Civil Registration System (study I-III)

Since the establishment in 1968, the Civil Registration System (CRS) has contained individual information on the unique 10-digit identification number issued to all Danish citizens at birth. This personal identification number encodes for date of birth and sex and allows for individual-level linkage between Danish data sources. Moreover, the CRS contains information on address, protection against inquiry from researchers, and continuously updated information on migration and vital status including date of death. The CRS is virtually complete, since the prevalence of disappeared persons is around 0.3%. This ensures complete follow-up in Danish cohort studies when using CRS data for censoring.[113]

3.2.2. The Danish Hip Arthroplasty Registry (study I-III)

The DHR was established January 1, 1995 with the aim of registering and improving the results after THA in Denmark.[114] During 1995 to 2014, approximately 140,000 primary THAs and 22,000 revisions have been reported to the DHR. The coverage is very high and in 2014, 28 orthopaedic departments and 16 private clinics reported to the DHR, and the completeness has been about 95% for both primary procedures and revisions during the last many years compared to the Danish National Patient Registry (DNPR).[16] The authorities reimburse the orthopaedic departments when reporting to the DNPR; therefore, reporting to the DNPR is considered the gold standard. Clinical data on primary THAs, revisions, and at follow-up examinations are prospectively collected. Preoperative data include the unique personal identification number, hospital code, laterality of the affected hip, previous surgery in the same hip, function of walking according to Charnley's groups A, B, and C[115], and diagnosis. In addition, it is possible to register the preoperative Harris Hip Score (HHS)[116], but this is not compulsory. The perioperative data registered in the DHR include the date of surgery; antibiotic and thromboembolic prophylaxis; type of anaesthesia; duration of surgery; type of acetabular and femoral component and their fixation; complications in the acetabulum and the femur; and type, size, and material of the prosthetic femoral head and the acetabular liner. For revisions, defined as a new surgical procedure including complete or partial exchange or removal of the prosthetic components, the following is registered: Indication, prosthetic status before revision, extent of revision, number of earlier revisions, and classification of acetabular and femoral bone loss. Data collected at follow-up include the laterality of the hip, date of the latest surgery, date of follow-up examination, postoperative complications, the patient's assessment of satisfaction with the primary or revision THA, and possibly the HHS. As there are no national guidelines for postoperative follow-up after primary THA or revisions, postoperative follow-up data is registered at different time points for the different departments.

The completeness for both primary THAs and revisions is validated yearly in the annual reports, and data on diagnosis for primary THA and postoperative complications[117] and on deep PJI as cause of revision[118] has been validated. But no validation of the data on prosthetic components including material of the acetabular liner and the femoral head has been made.

3.2.3. The Nordic Arthroplasty Register Association (study II)

To obtain a larger study population, data from the Nordic Arthroplasty Register Association[119] (NARA) was used in study II. Hip arthroplasty registries were established in Sweden in 1979, in Finland in 1980, and in Norway in 1987.[120-122] In 2007, selected individual data on each THA registered in the arthroplasty registries in Denmark, Norway, and Sweden were merged into the NARA database, and Finland were able to deliver data in 2010.[123] Data in the four registries were not fully compatible as there were some differences in variables and in the definition of these. Therefore, a common dataset including data that all registries were able to deliver were defined, and consensus has been made according to definition of several variables. In each national registry, the selected data were anonymised, including deletion of the national civil registration number, before merging into the common NARA database.[124] Thus, identification of patients at an individual level was not possible. As a consequence, the completeness and quality of data in the NARA database depend on the completeness and quality of data in each of the four national registries. Although the healthcare systems, patient populations, and treatment traditions in the Nordic countries are rather homogenous, there is no consensus regarding indication for neither primary THA nor revision procedures.

3.2.4. The Danish National Patient Registry (study I and III)

The DNRP was established in 1977 and contains data linked to the unique personal identification number on all admissions and discharges from somatic hospitals in Denmark, including dates of admissions and discharges, surgical procedures performed, and up to twenty

diagnoses for every discharge. From 1977 to 1993, diagnoses were classified according to the Danish version of the International Classification of Diseases, eighth edition, and since 1994 according to the tenth edition. From 1995 and onwards, data on psychiatric hospitalisation and all outpatients and emergency visits have been included into the registry. The physician who discharges the patient assigns all discharge diagnoses.[125] Data from the DNRP was used to determine the Charlson comorbidity index (CCI) score.[126] Although the positive predictive value (PPV) for diagnosis and treatment vary substantially in the DNPR[125], the overall PPV for the 19 Charlson conditions was 98.0%[127].

3.3. Design and study population

Randomised clinical trials (RCTs) may be considered the gold standard when studying THA as an intervention. However, RCTs are labour-demanding and relatively costly, which may limit their use when examining rare outcomes. In such situations, observational cohort studies based on national registries are suitable as large study populations can be obtained.

Study I and II were designed as population-based cohort studies. As registration of the femoral head and acetabular liner material in the DHR started in 2002, patients operated before 2002 were not included in the studies. In study I, a data extract from 2010 including raw data on all primary THAs operated from 2002 to 2009 (n=58,731) revealed that 55,212 (94%) had registered the material of the femoral head, whereas 46,386 (79%) had registered the material of the acetabular liner. When combining the femoral head and liner material for determination of the couple of bearings, it was found that 14,537 (25%) primary THAs had missing data on bearings. This problem was in part redressed both retrospectively and prospectively by changes in the software (Klinisk Målesystem) used to report data on THA procedures to the DHR. In a new data extract from 2012 including primary THAs from the same time period, the proportion

of THAs registered with missing data on couple of bearings was reduced to 5% (2,942 of 59,431). The latter data extract from the DHR was used in study I. The eligible number of cementless THA in patients diagnosed with primary OA of the hip, inflammatory arthritis, femoral head osteonecrosis, and childhood hip disorder was 25,656. Of these, 11,096 THAs with either CoC (n=1,773) or MoP (n=9,323) bearings were included.
In study II, the eligible number of cementless THA was 85,371 and of these, 32,678 THAs having MoM (n=11,567) and MoP (n=21,111) bearings were included.

Study III was initially designed as a cross-sectional case-comparison cohort study. One case having CoC THA was randomly matched on sex, year of birth, and year of surgery to one patient with MoM and one patient with MoP THA. Matching was performed in order to eliminate the confounding effect of sex, age, and follow-up. After matching, 2,025 CoC, 1,280 MoM, and 1,821 MoP THAs were identified and clearly, it was not possible to find a unique match to each case. Furthermore, a large number of patients with MoM and MoP THA were matched to more than one CoC THA (Table 1), and in some cases and matched patients operated bilaterally both THAs were included (Table 2). Even though patients with MoM and MoP THA were matched to more than one CoC THA, these patients should only receive one questionnaire. Moreover, only the first THA was included in case of bilateral THA. Thus, 1,803 patients with CoC THA, 834 patients with MoM THA, and 1,584 patients with MoP THA were included. Another limitation related to the matching was non-responders, i.e. patients who did not return a fulfilled questionnaire. If the matched case-comparison cohort design should be maintained, the corresponding case and matched patients should be omitted, when one of the three was a non-responder. This would have resulted in a significant reduction of the study population, which then only would have consisted of 621 patients. Therefore, the case-comparison cohort design was abandoned in favour of a cohort study design and instead, adjustments for sex, age, and year of surgery were made when performing the regression analyses.

Table 1. A number of MoM and MoP THAs were controls for more than one CoC THA, e.g. 202 MoM and 180 MoP THAs were each controls for 2 CoC THAs (study III).

Number CoC THA being controls for	MoM n=1,280	MoP n=1,821
1	857	1,606
2	202	180
3	81	26
4	44	8
5	28	1
6	25	0
7	17	0
8	11	0
9	9	0
10	5	0
11	1	0

Table 2. Number of patients with unilateral and bilateral THA (study III).

	CoC n=2,025	MoM n=857	MoP n=1,606
Unilateral THA	1,803	834	1,584
Also contralateral THA	222	23	22

3.4. Inclusion/exclusion criteria

In study I-III, patients having implanted hip resurfacing arthroplasties or dual mobility acetabular systems (Table 3) were excluded due to the different prosthetic concept and design with specific risks and complications, e.g. femoral neck fracture, for hip resurfacing arthroplasties, and specific patient selection, e.g. mentally disabled patients, for dual mobility acetabular systems. Thus, only patients having stemmed THA with a standard cup were included. Further, patients diagnosed with acute or sequelae from traumatic hip disorder were excluded from the study populations, because these patients have a specific risk profile

including comorbidity influencing the outcome of THA. Also patients diagnosed with "other" diagnoses (than OA, femoral head osteonecrosis, inflammatory arthritis, and sequelae from childhood hip disorder), which includes patients having a specific risk profile due to, for instance, primary tumour or metastases, were excluded. As fixation is a well-known confounder and the vast majority of CoC (97.1%) and MoM THAs (86.5%) had cementless fixation, only cementless THAs were included in study I and II. In study III, all fixation methods were included and adjusted for in the analyses.

Table 3. Designs and manufacturers of dual mobility acetabular systems checked for and excluded from the study populations.

Brand	Manufacturer
Acorn Double Mobility Cup	Permedica
Avantage	Biomet
Collegia	Cremascoli-Wright
Dual Mobility Cup	Tornier
EOL	Norton-Ceramconcept
Evora	Science et Médecine
Gyros	DePuy
Modular Dual Mobility	Stryker
Novae-1	Serf
Novae-E	Serf
Novae Sunfit	Serf
Polarcup	Smith & Nephew
Restoration Anatomic Dual Mobility	Stryker
Saturne	Wright
Saturne Reconstruction	Wright
seleXys DS	Mathys
seleXys DS Revision	Mathys
Stafit	Zimmer
Tregor	Aston
Versafitcup Double Mobility	Medacta

3.5. Questionnaires (study III)

The set of questionnaires was supplemented by questions concerning the current height and weight. Patients were also asked to indicate by "yes" or "no", if they had undergone any

reoperation in the specified hip with removal or exchange of the whole or any parts of the implant since primary surgery.

3.5.1. HOOS

The disease-specific hip disability and osteoarthritis outcome score (*HOOS*)[128] was constructed by adding dimensions concerning sport and recreation function and hip-related QoL to the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[129]. In study III, HOOS was chosen as it is well validated and widely used, but other disease-specific questionnaires, e.g. the Oxford Hip Score[130], which is translated into Danish and validated in a Danish registry setting[131,132], could also have been used. In contrast, the HHS is not self-administered and therefore not suitable for a questionnaire survey.

The HOOS is constituted of five subscales (dimensions): pain (HOOS Pain), other symptoms (HOOS Symptoms), activities of daily living (HOOS ADL), sport and recreation function (HOOS Sport), and hip related QoL (HOOS QoL). The validation of the instrument includes assessment of content and construct validity, responsiveness, minimal clinically important improvement (MCII), and patient-acceptable symptom state (PASS).[128,133,134] HOOS is recommended for evaluation of patients diagnosed with OA of the hip treated non-surgically or with THA.[135] For each subscale, a score from 0 to 100 is computed: A score of 100 indicates no problems and 0 indicates extreme problems. If at least 50% of items in the subscale have been answered, the subscale score can be calculated (HOOS scoring instructions available at http://www.koos.nu/index.html). Translation and cross-cultural adaptation of the original Swedish version of HOOS into Danish has been done using existing guidelines[136] although no testing of validity, reliability, and responsiveness in a Danish population has been performed. As the Danish and Swedish cultures are very similar, it is reasonable to assume, that there is no difference on validity, reliability, and responsiveness in the two cultures.

3.5.2. EQ-5D

The EuroQol EQ-5D-3L is a generic, reliable and validated instrument used for measure of QoL and is applicable to a wide range of health conditions and treatments including hip OA, THA, and revision hip arthroplasty.[137-140] The EQ-5D-3L was chosen as the generic questionnaire, as it is used in the Swedish Hip Arthroplasty Register (SHAR) and the National Joint Registry for England, Wales, Northern Ireland and Isle of Man (NJR).[10,14] Furthermore, the ED-5D-3L was used in a Danish registry setting[132], and it takes only a few minutes to fill in. Other relevant generic questionnaires that could have been used is the Short-Form 12[141].

The EQ-5D index describes the health-related QoL from a social perspective and the EQ visual analogue scale (VAS) from the patient's perspective. The EQ-5D index is determined from five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, each with three levels (no problems, some/moderate problems, and extreme problems/unable to) resulting in 3^5=243 possible health states. The EQ-5D is translated into Danish, and based on the time trade-off method[142], a value set ranging from -0.624 to 1, where 1 describes full health, 0 represents being dead, and a negative value represents a health state worse than being dead, constitutes the Danish culture-adjusted EQ-5D index[143]. The EQ VAS is determined when the patients rate their current state of health on a thermometer scale ranging from 0 ("worst imaginable") to 100 ("best imaginable"). A newer version of the EQ-5D (EQ-5D-5L) with five levels (no problems, slight problems, moderate problems, severe problems, and extreme problems/unable to) for each of the five dimensions has been developed in order to improve the sensitivity and to reduce floor and ceiling effects.[144,145] The EQ-5D-5L was compared to the EQ-5D-3L in patients with hip and knee OA referred to total joint replacement and provided stronger evidence of validity specifically for the dimensions mobility, usual activities, and pain/discomfort that are particularly relevant for OA patients.[146]

3.5.3. UCLA activity score

University of California, Los Angeles (UCLA) activity score was first described in 1984, is disease-specific, and has 10 descriptive activity levels ranging from wholly inactive and dependent on others (level 1), to moderate activities such as unlimited housework and shopping (level 6), to regular participation in impact sports such as jogging or tennis (level 10). Regardless of frequency or intensity of participation, the UCLA activity score is based on the highest-rated activity.[147] The UCLA activity score, which includes different types of sporting activities, was included in the questionnaire to supplement the Sport subscale in the HOOS. The activity score is found to correlate well to pedometer data in a population but for individual patients with the same UCLA activity score, the difference in the average steps per day could vary by up to a factor of 15.[148] The UCLA activity score was compared to the International Physical Activity Questionnaire as gold standard and was found to be the most appropriate scale for assessment of physical activity levels in patients undergoing total joint replacement, as it had high reliability and completion rate and showed no floor effects.[149] A validated Danish version of the UCLA activity score, although not published yet, was used.

3.5.4. Questionnaire about noises

Owen et al. defined noises as any audible sound that the patient perceived as originating from the THA.[150] Other authors have defined a squeaking as a squeaking, clicking, or grating sound with origin from the THA during movement[151], thus classifying different qualities of noises as squeaking, whereas noises from THA also have been described as “pops”, “snaps”, and “grinds” by other authors[7]. In 2010, Swanson et al. proposed a scale for grading the frequency and the intensity of the noise, and the authors defined “problem squeaking” as any squeak always audible to others and occurring at least once per week.[152] Furthermore, the Melbourne Orthopaedic Noise Assessment, including questions about noise frequency, noise type, and audibility of the noise to others, was published in 2013.[112] For aim III, a questionnaire to collect

information on noises from THA was created based on the literature.[7,152] All patients were asked if they had experienced noises from the THA. If confirmed, they were asked to characterise the noises as squeaking, creaking, grating, clicking, or other. Furthermore, patients were asked to answer questions about onset (number of months after surgery at which the noises started), frequency (at least once a day, at least once a week, more seldom than once a week), audibility (only audible to the patient, from time to time audible to others, always audible to others), activities triggering the noises (rising from a chair, sitting down, bending, walking, walking up or down the steps, climbing a high step, or other activity), and what degree noises led to reduced physical function and hindered the patient being together with other people ("no", "slight", "moderate", "severe", or "extreme"). Among all authors, consensus was obtained regarding phrasing of the questions. Subsequently, the questions about noises were slightly adjusted through a test phase based on 18 patients randomly selected among patients admitted to Department of Orthopaedic Surgery, Vejle Hospital, Denmark for primary THA surgery. Furthermore, three patients who had undergone revision at the same department of their CoC THA due to noises tested the questions and found these relevant and meaningful. Although the questions about noises do not result in an overall score, a major drawback is that the questions are not properly evaluated in relation to content and construct validity, and no test-retest in a smaller proportion of the patients have been performed. Further, no objective assessment has been made to validate the self-reported noises. However, in the literature no thorough validation of questions on noises from THA has been made, and the definition of "problem squeaking" was made by Swanson et al. without knowing if this definition was meaningful for the patients with squeaking THA.[152]

3.5.5. Choice of PRO

Since 2002, PROs have been included stepwise in the SHAR in order to increase the sensitivity of the registry. Patients undergoing primary THA are asked to complete a self-administered

questionnaire, including Charnley's functional categories, a VAS for pain and satisfaction, and the EQ-5D. This is done preoperatively (except for satisfaction) and at one, six, and ten years postoperatively unless the patient has undergone revision surgery.[10] A study comparing collection of PRO data with either pen-and-paper or internet questionnaires found that the response rates for pen-and-paper and internet questionnaires were 49% and 92%, respectively.[153] This is in contrast to a small series study that reported very high correlation of scores from HHS, WOMAC, Short Form-36, EQ-5D, and UCLA activity score obtained with the paper, touch screen, and web-based modes.[154] However, the use of pen-and-paper questionnaire is costly and laborious due to postage and double manual data entry. With the use of HOOS and EQ-5D-3L questionnaires, Paulsen et al. performed a comparison between automated forms processing and double manual data entry for highly structured forms containing only check boxes, numerical codes and no dates, and no differences in the proportion of errors were found.[155] Moreover, HOOS and EQ-5D-3L were found appropriate for administration in a hip arthroplasty registry.[132] To compare symptoms, function, activity, and QoL before and after primary THA, both a generic and a disease-specific questionnaire can be administered via the Internet with supplement of pen-and-paper questionnaire prepared for automated forms processing.

Several factors may be taken into account when interpreting the PROs. Patients' preoperative expectations to THA may vary considerably, and Judge et al. reported that greater numbers of preoperative expectations were associated with younger age, women, increasing body mass index (BMI), and more education. Patients were more likely to improve after surgery the more preoperative expectations they had.[156] However, other authors report, that there was no association between the level of preoperative expectations and fulfilment of expectations or outcome. Furthermore, there was no relation between depression and expectations.[157] Otherwise, patients with anxiety or depression preoperatively had lower PRO scores after THA

than patients without these mental disorders.[158] In a study from the SHAR, changes in EQ-5D index, EQ VAS, and pain VAS increased with higher educational level[159], and other authors reported higher likelihood of less than excellent or good HHS and thigh pain ≥3 on a VAS for patients with less than a high school education.[160] In another study, Short From-36 was used to compare QoL, and completed level of schooling had no effect on the improvement in QoL after THA[161], which indicates that differences may appear due to different PROs, study designs, follow-up, and cultures. None of these factors were treated separately in study III.

3.6. Statistics

In all studies, the exposure was THA with different types of bearings: CoC and MoP in study I; MoM and MoP in study II; and CoC, MoM, and MoP in study III. In study I and II, the primary outcome was time to revision for any cause, whereas time to revision for aseptic loosening, dislocation, and other causes were secondary outcomes. In study III, the outcome was generic and disease-specific PROs.

Traditionally, time-to-event or survival analysis has been performed with the Cox regression, but competing risk cannot be addressed properly with this method[162]. The Kaplan-Meier estimator used in Cox regression overestimates the risk of revision when the risk of death is high[163], and THA is most common in older patients having higher risk of death compared to younger patients. In study I and II, we therefore chose to perform the survival analysis with regression with the pseudo-value approach taking the competing risk of death into account. Pseudo-values are calculated at prespecified time points. The pseudo-observation is a transformation of the time-to-event data in which each time-to-event observation is represented by the amount of information it contains when the observation is deleted from the dataset. Subsequently, a model for relative risk (RR) for the uncensored data is applied via a generalised

estimating equation obtained in a generalised linear model for the pseudo-values with normal distribution and robust variance estimation.[164,165] The pseudo-value method relies on, as any time-to-event analysis, the censoring being independent. In the current context independent censoring is satisfied since the risk of revision was assumed to be constant over calendar time. The measure of association of Cox regression is the hazard ratio (HR), which may be a little difficult to interpret and may often be interpreted as a measure of the RR. One assumption when performing the Cox regression is proportional hazards meaning that the HR is constant over time, and this assumption was not fulfilled in study I and II. When using regression with the pseudo-value approach, there is no assumption of proportional hazards to be satisfied. Another advantage is, that the measure of association of regression with the pseudo-value approach is a real RR, which may ease the interpretation of the results. However, a drawback with this method, and contrary to the Cox regression, is that it is not possible to have survival curves adjusted for confounders.

In study III, multivariate linear regression has been performed to determine adjusted mean differences of PRO scores between the types of bearings. For the HOOS subscales, EQ-5D index, and EQ VAS the resulting scores are continuous. For the UCLA activity score, the resulting score is between one and ten, but each individual score corresponds to one activity statement, and the difference in activity level between score two and three is not the same as, for instance, between score seven and eight. Therefore, one could argue that the appropriate analysis would have been one for ordered categorical outcome, e.g. ordinal logistic regression. One of the drawbacks with the use of such a model is, that the outcome is an odds ratio, which is more difficult to interpret than mean and mean difference from linear regression. Furthermore, in studies using the UCLA activity score the outcome has been described as means.[149,166] Hence, no comparison of the results in study III with other studies would have been possible, if ordinal logistic regression had been used. Therefore, linear regression was performed to analyse the UCLA activity score in

study III knowing full well that the results may be interpreted with caution as the UCLA activity score had been treated as a continuous variable.

3.7. Bias and confounding

Several factors may influence the validity of our results. The association observed could have several explanations that have to be considered before inferring a causal association. These factors include selection problems potentially leading to selection bias, information problems potentially leading to information bias, chance, and confounding (Figure 3).

3.7.1. Selection bias

In general, selection problems in a cohort study can occur due to lost to follow-up. However, in study I and II we have complete follow-up of all patients included in the study population. Thus, selection bias is not likely. In contrast, selection bias may influence the results in study III, as patients who did not answer the questionnaire (non-responders) were lost to follow-up. Non-responders had a greater proportion of patients younger than 50 years and smaller proportion of patients aged 70 years or older, which may result in lower activity scores in study III, as younger patients are more active than older. Among non-responders, a smaller proportion was diagnosed with OA and a greater proportion with other diagnoses, which corresponds well with differences in the age groups. Furthermore, there was a smaller proportion without comorbidity and a greater proportion with high comorbidity, which may give higher PRO scores in the study. Among non-responders there was a smaller proportion with CoC bearings, and a greater proportion of patients with MoP bearings than responders, which may be explained by the greater proportion of patients with high comorbidity that are more likely to be treated with MoP THA.

In study I, another selection problem can occur because the use of CoC bearings may be reserved for young and active patients as recommended by some authors[167], or some departments may have CoC as their "standard" bearings, whereas other departments may reserve these bearings for only very rare cases, e.g. very young patients suffering from childhood hip disorders[168]. In study II, there is a greater proportion of males, a greater proportion diagnosed with OA, and a smaller proportion diagnosed with childhood hip disorders operated with MoM compared to MoP bearings. Furthermore, in Denmark not all orthopaedic departments have used MoM bearing in THA, and within the Nordic countries there is a huge variation in the use of MoM THA: In study II, 72% of patients were operated in Finland, 23% in Denmark, and 5% in Sweden and Norway. These differences may reflect surgeons' preferences, the "culture" for using alternative/new implants, and socioeconomic circumstances and may result in better outcome for patients treated in countries, in hospitals, and by surgeons with greater experience with the specific bearings.

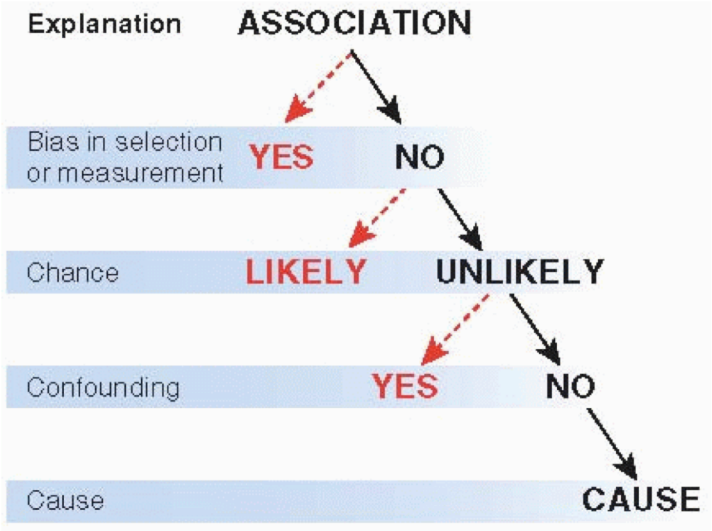

Figure 3. Bias, chance, and confounding should be excluded before concluding that a causal association is likely. From Fletcher RH, Fletcher SW, Fletcher GS. Clinical Epidemiology: The Essentials. 5th edition. Lippincott Williams & Wilkins 2015.

3.7.2. Information bias

In registry-based cohort studies, information problems can occur due to misclassification of

exposure or outcome. However, only if misclassification of exposure is dependent of misclassification of outcome (hence, when misclassification is differential), the results may be influenced by information bias. We may have misclassification of both exposure and outcome, but if these were independent of each other (non-differential misclassification), the RR estimates would go towards the null hypothesis.

In studies I-III, misclassification of bearings can occur, if data are missing or registered incorrectly. The lack of validation of data, e.g. bearings, implant design, femoral head size, and causes of revision, in the DHR and the NARA database may give rise to concerns related to the quality of these data. In study I and II, misclassification is obviously related to the unambiguous registration of a couple of bearings. However, the misclassification of causes of revision was unlikely to be related to the registration of the type of bearings for primary THAs due to the prospective registration of data in DHR and the NARA dataset. The resulting non-differential misclassification may produce bias towards the null hypothesis. Moreover, the two worst-case scenarios that all patients registered with missing bearings had either CoC or MoP (study I) and MoM or MoP (study II) have been calculated. In neither of the studies, the RR for revision of any cause was significantly changed in any of these scenarios.

Although the proportion of missing data in study III was low, non-differential misclassification may be present, as there was no difference in missing subscale scores between bearing groups. Misclassification was minimised by using well validated questionnaires (HOOS, EQ-5D-3L, and UCLA activity score) and relevant questions about noises from the THA. Five to nine answer categories on a scale have been proposed to be ideal in most circumstances[169] and in 43 of 68 items, five steps were present in the response scale. Furthermore, no evident external interests were present. The resulting high response rate (85%) reduces the misclassification.

Recall bias may be a problem for retrospective items. Thus in study III, in question no. 7 about onset of noises from the THA, 50-52% of patients with noises from the THA indicated that the onset of noises was "unknown", which illustrates the probable recall bias.

3.7.4. Chance

Chance, or random error, is inherent in all observations. The statistical precision of an estimate is expressed as a confidence interval (CI) that represents the range of values that is likely to include the true value. Statistical precision increases with the statistical power of the study, which is dependent of the sample size. We have performed large cohort studies resulting in increased precision of the estimates, but sample size calculation has not been performed.

3.7.3. Confounding

Three conditions must be present for confounding to occur:

1. The confounding factor must be associated with both the exposure and the outcome.
2. The confounding factor must be distributed unequally among the groups being compared.
3. A confounder cannot be an intermediary step in the causal pathway from exposure to outcome.

In a study by Johnsen et al. from the DHR, males had a 20% higher RR of any revision compared to females, and patients younger than 60 years had increased RR of revision after 0.5-year follow-up. Diagnosis was found to be a time-dependent predictor, although no difference in RR of revision was found for any diagnosis after 0.5-year follow-up, whereas high CCI predicted higher RR of revision.[18] For sex, age, diagnosis, and comorbidity, the definition of confounding is fulfilled, and adjustments were made for these four patient-related confounders in order to eliminate the confounding effect on the results (Table 4). Adjustment for comorbidity has not

Table 4. Confounders adjusted for in study I-III.

Confounders	Study I	Study II	Study III
Patient-related			
Sex	X	X	X
Age	X	X	X
Diagnosis	X	X	X
Comorbidity	X		X
BMI			X
Surgery-related			
Fixation			X
Femoral head size	X		X
Duration of surgery	X		
Year of surgery	X		X

been performed in study II, as the NARA database do not contain any information allowing for determination of the CCI score or other evaluation of the comorbidity. BMI and THA due to OA may be associated[170], and BMI >35 kg/m^2 has been found to be a predictor for revision due to PJI: RR=2.1 (95% CI: 1.1–4.3) for BMI 35–39.9 and RR=4.2 (95% CI: 1.8–9.7) for BMI ≥40.[171] In study III, mean BMI varied between the three bearing groups indicating that BMI is a confounder. But information on height and weight is not registered in the DHR or in the NARA database, which explains that BMI is not adjusted for in study I and II. This may result in an underestimated RR of revision for MoM compared to MoP THA, if patients having MoM THA have lower BMI as found in study III. In contrast, BMI have been adjusted for in study III. Among the surgery-related factors, the fixation technique has been shown to influence the risk of revision.[16,19] The confounding effect of fixation is eliminated in study I and II, because only cementless THAs have been included, whereas adjustments have been made in study III. Larger femoral head sizes increase the jump distance[85] and decrease risk of revision due to dislocation (RR=0.09 (95% CI: 0.05–0.17) for femoral head sizes >36 mm compared to head size of 28

mm)[29]. In study II, 92% of MoM THAs had femoral head sizes ≥38 mm and 97% of MoP THAs had head sizes <38 mm. Therefore, femoral head size was considered a proxy for the bearings and was not adjusted for. Duration of surgery, which may reflect the surgeon's skills and the complexity of the patient case, was found to be a predictor for revision due to PJI after primary THA (RR=2.0 (95% CI: 1.5–2.8) for duration of surgery longer than two hours compared to less than one hour)[172], and the confounding effect of duration of surgery was reduced by adjustments in study I, but duration of surgery was not registered in the NARA database and therefore not adjusted for. The confounding effect of year of surgery may be related to the introduction of new implants or bearings during recent years, e.g. BIOLOX Delta or incorporation of vitamin E in HXLPE, and surgeons may have been better to register data in the DHR resulting in higher completeness. Also the confounding effect of year of surgery was reduced by adjustments.

Although adjusting for many patient- and treatment-related confounders, unmeasured confounding may be due to patient-related prognostic factors including medication (postoperative use of statin was associated with lower RR of revision)[23]; alcohol use (associated with non-traumatic osteonecrosis of the femoral head, and this diagnosis has a higher RR of revision)[173,174]; smoking habits (a strong association between smoking and risk of revision of MoM THA has been found)[175]; physical activity before and after primary surgery (some predictors of high activity at 5 years after surgery were younger age, male sex, and lower BMI)[166]; patients' expectations (the more preoperative expectations the patients had, the more likely they were to improve after surgery)[156]; anxiety (preoperative depressive symptoms predicted smaller changes in HOOS subscale scores and patients were less satisfied 12 months postoperatively)[158,176]; socioeconomic factors including education (high educational level was associated with higher health-related QoL and less pain)[159]. Treatment-related prognostic factors potentially leading to confounding include surgical approach (worse scores on HOOS and EQ-5D were reported after lateral approach than after posterior approach, and lateral approach

was shown to increase the risk of revision du to aseptic loosening and decrease the risk of revision due to dislocation)[31,177,178]; type of polyethylene as both cross-linked and highly cross-linked polyethylene have been included (the use of highly cross-linked polyethylene reduces polyethylene wear substantially)[179]; antibiotic and thromboembolic prophylaxis[180-182]. The structure-related prognostic factors, which may result in confounding, include hospital volume (hospitals operating ≤50 procedures per year had an increased risk of revision after two-, five-, 10-, and 15-year follow-up)[32]; set-up including fast-track[33]; surgeon's skills including learning-curve and positioning of components[183-185]; operation theatre (airflow, plastic adhesive draping, separate skin and deep knives)[186]. Furthermore, information from any radiological examinations including MRI and blood concentrations of chromium and cobalt may also be prognostic factors. Except from blood concentrations of chromium and cobalt and results of MRIs and ultrasound examinations, which have been included in the DHR since 2013 for MoM THA, none of these prognostic factors are registered in the used hip arthroplasty registries.

4. MAIN RESULTS

4.1. Study I

Risk of any revision

11,096 patients having cementless THA with CoC (n=1,773 (16%)) and MoP (n=9,323 (84%)) bearings were included. The median follow-up was 5.0 (interquartile range (IQR): 3.1-6.5) years

Table 5. Crude and adjusted[a] RR of revision for any cause, with 95% CIs, in THA with CoC and MoP bearings.

	Patients in the beginning of the period (n)	Revisions performed within the period (%)	Crude RR (95% CI)	Adjusted[a] RR (95% CI)
At 2-year follow-up (0 to 2 years postoperatively)				
CoC	1,773	48 (2.7)	0.91 (0.67-1.24)	1.18 (0.65-2.13)
MoP	9,323	274 (2.9)	1 (ref.)	1 (ref.)
At 4-year follow-up (2 to 4 years postoperatively)				
CoC	1,519	15 (1.0)	0.95 (0.72-1.26)	1.12 (0.70-1.81)
MoP	7,065	62 (0.9)	1 (ref.)	1 (ref.)
At 6-year follow-up (4 to 6 years postoperatively)				
CoC	1,135	4 (0.4)	0.91 (0.68-1.21)	1.03 (0.60-1.77)
MoP	4,501	26 (0.6)	1 (ref.)	1 (ref.)
At 8.7-year follow-up (6 to 8.7 years postoperatively)				
CoC	543	4 (0.8)	1.02 (0.74-1.39)	1.33 (0.72-2.43)
MoP	2,230	11 (0.5)	1 (ref.)	1 (ref.)

[a]Adjustments were made for sex, age, diagnosis of primary THA, comorbidity, year of surgery, femoral head size, and duration of surgery.

for CoC and 3.9 (IQR: 2.0-5.9) years for MoP bearings (p<0.001 based on a Wilcoxon rank-sum test). The entire study population had 444 revisions (4.0%): 4.0% (71 of 1,773) for CoC THA and 4.0% (373 of 9,323) for MoP THA. At 8.7-year follow-up, the cumulative incidence for any revision was 5.4% (95% CI: 4.0-7.1) for CoC THA and 5.3% (95% CI: 4.7-5.9) for MoP THA. No significant difference in the RR of revision for any cause was found for CoC THA compared to MoP THA at two-, four-, six-, and 8.7-year follow-up (Table 5).

Causes of revision

Eight CoC THAs were revised due to component failure. The proportion of revision due to component failure was higher for CoC than for MoP bearings (p<0.001 based on a chi-square test) (Table 6). Of the eight patients registered with component failure as revision cause, six (0.34%) patients had ceramic fracture and two (0.11%) patients had impingement between the stem-neck and the rim of the liner. No statistically significant difference in the risk of revision due to aseptic loosening (adjusted RR 0.84, 95% CI: 0.21-3.4), dislocation (adjusted RR 1.2, 95%

Table 6. Main indications for THA revision registered in the DHR. For CoC and MoP bearings, the number and percentage (%) for the specific cause of revision is given.

	CoC n=71 (%)	MoP n=373 (%)	p-value
Aseptic loosening	10 (0.6)	43 (0.5)	0.6
Osteolysis without loosening	0 (0.0)	3 (0.0)	0.5
Deep infection	6 (0.3)	61 (0.7)	0.1
Femoral bone fracture	9 (0.5)	56 (0.6)	0.6
Dislocation	22 (1.2)	156 (1.7)	0.2
Component failure	8 (0.5)	6 (0.1)	<0.001
Pain	9 (0.5)	26 (0.3)	0.1

CI: 0.29-5.3), and all other revision causes (adjusted RR 1.1, 95% CI: 0.14-8.8) was found for CoC compared to MoP bearings.

4.2. Study II

Risk of any revision

The study population included 32,678 patients having cementless stemmed THA with MoM (n=11,567 (35%)) and MoP (n=21,111 (65%)) THAs. The median follow-up was 3.6 (IQR: 2.4-

Table 7. Crude and adjusted[a] RR of revision for any cause, with 95% CIs, in THA with MoM and MoP bearings.

	Patients in the beginning of the year (n)	Revisions performed within the year (%)	Crude RR (95% CI)	Adjusted[a] RR (95% CI)
At 1-year follow-up (0 to 1 year postoperatively)				
MoM	11,567	198 (1.7)	0.81 (0.68-0.95)	0.83 (0.70-1.00)
MoP	21,111	448 (2.1)	1 (ref.)	1 (ref.)
At 2-year follow-up (1 to 2 years postoperatively)				
MoM	11,295	91 (0.8)	0.92 (0.80-1.06)	0.94 (0.81-1.09)
MoP	20,495	123 (0.6)	1 (ref.)	1 (ref.)
At 3-year follow-up (2 to 3 years postoperatively)				
MoM	9,640	66 (0.7)	1.01 (0.89-1.15)	1.02 (0.89-1.18)
MoP	15,653	72 (0.5)	1 (ref.)	1 (ref.)
At 4-year follow-up (3 to 4 years postoperatively)				
MoM	7,251	44 (0.6)	1.09 (0.96-1.23)	1.10 (0.96-1.26)
MoP	11,976	45 (0.4)	1 (ref.)	1 (ref.)
At 5-year follow-up (4 to 5 years postoperatively)				
MoM	4,638	49 (1.1)	1.32 (1.17-1.50)	1.37 (1.19-1.57)
MoP	9,137	22 (0.2)	1 (ref.)	1 (ref.)
At 6-year follow-up (5 to 6 years postoperatively)				
MoM	2,466	18 (0.7)	1.44 (1.27-1.63)	1.49 (1.30-1.71)
MoP	6,811	19 (0.3)	1 (ref.)	1 (ref.)

[a]Adjustments were made for sex, age, and diagnosis of primary THA.

4.8) years for MoM and 3.4 (IQR: 2.0-5.8) years for MoP bearings (p<0.001 based on a Wilcoxon rank-sum test). 1,236 (3.8% of 32,678 patients) first time revisions following primary THA were registered during the study period: 4.1% (470 of 11,567 patients) for MoM and 3.6% (766 of 21,111 patients) for MoP bearings. The cumulative incidence of any revision was 7.0% (95% CI: 6.0-8.1) for MoM and 5.1% (95% CI: 4.7-5.6) for MoP at eight-year follow-up. The RR of any revision was statistically significantly increased for MoM after five- and six-year follow-up (Table 7).

Stratified analyses and causes of revision

The MoM cup/stem combinations of Articular Surface Replacement (ASR)/Summit, ASR/Corail, and "other" had statistically significantly higher RR of revision for any reason compared to MoP THAs (Table 8). The cementless MoM THAs had higher proportion of revisions due to aseptic loosening (p<0.001 based on a chi-square test) and "other" causes (p=0.03 based on a chi-square

Table 8. Median follow-up for combination of acetabular and femoral components in MoM THA. Crude and adjusted[a] RR of revision for any cause at six-year follow-up with, 95% CIs, compared to MoP THA.

	n=32,678 (%)	Median follow-up (IQR)	Any revision (n)	Crude RR (95% CI)	Adjusted[a] RR (95% CI)
All MoP THAs	21,111 (65)	3.4 (2.0-5.8)	766	1 (ref.)	1 (ref.)
Recap/Bi-Metric	4,990 (15)	3.2 (2.2-4.4)	138	0.90 (0.76-1.06)	0.96 (0.80-1.15)
M²a/Bi-Metric	2,407 (7)	4.8 (3.0-6.1)	95	1.16 (0.87-1.53)	1.25 (0.93-1.67)
Pinnacle/Corail	910 (3)	2.9 (2.0-3.9)	31	1.21 (0.89-1.65)	1.25 (0.90-1.74)
Conserve Plus/Profemur	418 (1)	3.2 (2.7-3.9)	18	1.53 (1.00-2.33)	1.47 (0.95-2.27)
ASR/Summit	401 (1)	3.9 (2.8-4.8)	56	6.35 (4.74-8.49)	7.27 (5.18-10.2)
Birmingham/Synergy	369 (1)	4.2 (3.4-5.1)	10	1.07 (0.51-2.24)	1.26 (0.56-2.84)
ASR/Corail	307 (1)	3.7 (2.7-4.5)	35	5.00 (3.54-7.07)	5.17 (3.53-7.56)
Others	1,765 (6)	3.7 (2.5-4.9)	87	1.77 (1.39-2.26)	1.75 (1.29-2.36)

[a]Adjustments were made for sex, age, and diagnosis of primary THA.

test). A lower frequency of revisions due to dislocation ($p<0.001$ based on a chi-square test) was found for MoM THA regardless of femoral head size compared to MoP THAs. At six-year follow-up, the RR of revision due to dislocation was lower (0.27, 95% CI: 0.19-0.39) for MoM than for MoP bearings, but the RR of revision due to aseptic loosening (5.5, 95% CI: 3.8-7.9) and all other revision causes (1.2, 95% CI: 1.0-1.5) was higher when comparing MoM to MoP bearings.

4.3. Study III

Comparison between bearing groups

The response rate was 85% (3,089 of 3,625). In the study population (n=3,089), 45% received CoC, 17% MoM, and 38% MoP THA. There was similar distribution of sex within the three bearing groups: 44-46% were females, and 54-56% were males ($p=0.68$ based on a chi-square test). Mean age difference was -1.6 (95% CI: -2.3 to -1.0) years for CoC and -1.9 (95% CI: -2.7 to -1.0) years for MoM THA compared to patients with MoP THA. Mean follow-up was 6.9 years for CoC and MoP THA and 5.1 years for MoM THA. For HOOS Symptoms, the adjusted mean score was significantly lower for the CoC group compared to the MoP group (adjusted mean difference (aMD) -2.3 (95% CI, -4.1 to -0.5)). No other statistical significant adjusted differences were found for the other HOOS subscales, EQ-5D index, EQ-5D VAS, or UCLA activity score when comparing the CoC and MoM groups to the MoP group.

Noises

27% of patients with CoC, 29% of patients with MoM, and 12% of patients with MoP bearings had experienced noises from the THA. Stratified analyses for the three types of bearings with and without noises showed significantly lower adjusted mean scores of all HOOS subscales, EQ-5D index, and EQ-5D VAS for patients experiencing noises from the CoC, MoM or MoP THA compared to patients having MoP THA without noises. For all subscales, the aMD was largest for

MoP THA with noises. Only for the ULCA activity score, no difference was found for CoC and MoM THA with noises compared to MoP THA without noises (Table 9).

Table 9. Association between experience of noise from THA with CoC, MoM, and MoP bearings and mean differences of PRO subscales with 95% CIs.

		Noisy CoC (95% CI)	Noisy MoM (95% CI)	Noisy MoP (95% CI)	Silent MoP (95% CI)
HOOS Symptoms					
Mean difference	Crude	-12.9 (-14.9 to -10.8)	-11.4 (-15.2 to -7.65)	-16.8 (-20.6 to -13.0)	0 (ref.)
	Adjusted	-13.6 (-15.8 to -11.4)	-12.0 (-16.2 to -7.83)	-16.1 (-20.0 to -12.2)	0 (ref.)
HOOS Pain					
Mean difference	Crude	-7.33 (-9.21 to -5.45)	-5.11 (-8.31 to -1.90)	-14.0 (-18.1 to -9.97)	0 (ref.)
	Adjusted	-7.79 (-10.0 to -5.59)	-5.11 (-8.56 to -1.67)	-13.4 (-17.5 to -9.37)	0 (ref.)
HOOS ADL					
Mean difference	Crude	-7.29 (-9.63 to -4.95)	-5.52 (-9.19 to -1.84)	-14.2 (-18.3 to -10.1)	0 (ref.)
	Adjusted	-8.53 (-11.2 to -5.89)	-7.58 (-11.8 to -3.40)	-13.6 (-17.9 to -9.27)	0 (ref.)
HOOS Sport					
Mean difference	Crude	-9.45 (-13.0 to -5.94)	-7.16 (-11.8 to -2.47)	-21.2 (-26.9 to -15.5)	0 (ref.)
	Adjusted	-11.3 (-15.6 to -7.13)	-11.6 (-17.8 to -5.44)	-19.7 (-25.4 to -13.9)	0 (ref.)
HOOS QoL					
Mean difference	Crude	-12.1 (-15.0 to -9.24)	-12.3 (-16.8 to -7.76)	-20.1 (-24.6 to -15.5)	0 (ref.)
	Adjusted	-11.8 (-14.7 to -8.94)	-12.2 (-17.3 to -7.10)	-19.1 (-24.0 to -14.3)	0 (ref.)
EQ-5D index					
Mean difference	Crude	-0.059 (-0.085 to -0.032)	-0.067 (-0.100 to -0.034)	-0.113 (-0.144 to -0.081)	0 (ref.)
	Adjusted	-0.061 (-0.088 to -0.035)	-0.073 (-0.117 to -0.030)	-0.108 (-0.137 to -0.079)	0 (ref.)
EQ VAS					
Mean difference	Crude	-3.07 (-5.80 to –0.38)	-2.81 (-6.63 to 1.01)	-9.99 (-14.5 to -5.51)	0 (ref.)
	Adjusted	-4.56 (-7.20 to -1.92)	-6.29 (-9.72 to -2.87)	-9.44 (-13.5 to -5.38)	0 (ref.)
UCLA activity score					
Mean difference	Crude	0.08 (-0.20 to 0.35)	0.16 (-0.16 to 0.47)	-0.53 (-0.89 to -0.17)	0 (ref.)
	Adjusted	-0.12 (-0.38 to 0.15)	-0.44 (-0.88 to 0.00)	-0.56 (-0.88 to -0.25)	0 (ref.)

5. DISCUSSION

5.1. Discussion of bearings

When the surgeon together with the patients shall choose the couple of bearings, pros and cons may be weighted. MoP bearings were introduced in the Charnley era and are still the most commonly used bearings. Hence, the clinical experience with these bearings is very long, and MoP THA may be considered a safe treatment. The most prominent challenge with MoP bearings has been wear and generation of polyethylene wear particles possibly resulting in osteolysis and aseptic loosening of the implant, if wear rate is too high. However, the newer generations of polyethylene have shown promising durability as regards wear.[179,187] From CoC bearings, there are fewer wear particles generated and these are supposed to be more bioinert than polyethylene wear particles, which may reduce the problem with aseptic loosening. On the other hand, the risk with CoC bearings is fracture of the head or insert which is a serious complication. In study I, the prevalence of revision due to ceramic fracture was 0.34%, which is in accordance with a study by Traina et al., who reported a prevalence of ceramic fracture of 0.5%[188]. Ceramic fracture is a serious complication because there is a high risk of more than one revision following ceramic fracture.[189] There exist no consensus about the best strategy for revision surgery in patients with ceramic fracture[73] although it has been recommended to implant CoC or ceramic-on-polyethylene (CoP) bearings.[188] A high complication rate was seen by Lee et al. when using MoP bearings during revision for ceramic fracture.[190] Another drawback to take into account in relation to CoC bearings is noises. Noises have been described particularly from CoC bearings[152,191,192], but in study III it is revealed, that the prevalence of self-reported noises from both CoC and MoM THA is high (27-29%), whereas noises from MoP THA were prevalent in 12%. The reported high frequency of noises question, what the patient in fact report as a noise. But it seems to bother the patients reporting noises, as noisy THAs resulted in lower PROs

compared to silent MoP THAs in study III, thus indicating that noises from the THA may be of clinical significance. CoC bearings are recommended by some authors to be used in young and active patients[167], and as found in study I, patients with CoC were younger than patients with MoP demonstrating that patients are selected to this bearing. This had, however, no influence on the activity level, which was similar for patients with CoC and MoP bearings after mean follow-up of 6.9 years (study III). Some surgeons may reserve CoC bearings to a highly selected group of very young patients suffering from childhood hip disorder. Hannouche et al. published a series of 105 CoC THAs in patients younger than 20 years at the time of primary THA, and the 10-year survival rate with aseptic loosening as endpoint was 90.3% (95% CI: 82.4%–98.9%).[168]

Since 2012 the use of MoM bearings has been abandoned in Denmark because of the concerns for the long-term prognosis. The higher risk of revision of MoM compared to MoP THA was confirmed in study II. However, PRO scores from patients having MoM THA were similar to PRO scores from patients having MoP THAs, which may be due to revision of the unsuccessful MoM THA (study III).

Another thing to account for when choosing the bearings for the patient is the cost-effectiveness, as CoC and MoM bearings in general are more expensive than MoP bearings. However, Pulikottil-Jacob et al. reported that the differences in quality-adjusted life-years between different bearings and fixation methods were extremely small. It was recommended that the choice of prosthesis should be determined by the rate of revision, local costs and the preferences of the surgeon and patient.[15]

MoP are still considered "standard" bearings by most surgeons.[193,194] CoC bearings may be recommended in younger patients, whereas the use of MoM bearings is not recommended, before population-based studies with long-term follow-up have shown similar survival as for

CoC and MoP bearings. In addition, CoP bearings were found to have lower 13-year HR=0.80 (95% CI: 0.74-0.88) for any revision compared to MoP THA[16], but population-based studies are lacking.

5.2. Choice of outcome

This thesis has focused on the association between bearings and the risk of revision and PROs but in relation to THA, several outcomes may be of relevance: Radiological findings, metal-ion levels, second revision, economy, and mortality. When asking a scientific question, the chosen outcome shall be appropriate to give an answer. In study I and II, the outcome was firstly revision for any and secondly for specific causes. Studies on implant survival or annual reports from hip arthroplasty registries answer the question: "What is the longevity of the implant?", but from these studies it is not possible to answer: "What is the QoL after THA?" However, survival studies are very important to identify any early failure of a new implants, as the lost survival will never be regained with longer follow-up. This is illustrated in study II and other studies reporting lower survival rates for MoM THA[105,107]. If THA is only defined as a failure, when the implant is revised, the patient with a poor outcome and no awaiting revision surgery will not be captured, which results in an overestimation of the success of the THA.[11] Therefore, PROs shall be used in combination with survival in order to give a more balanced and real measure of the success after THA.

In study III, the outcome was disease-specific and generic PRO scores and noises from the THA, as the aim was to examine if type of bearings was a prognostic factor for PRO scores and noises. Only a few studies have reported the influence of type of bearings on PRO scores[111,195], but one could argue that PROs are too coarse to possibly answer, if there might be difference in the patients' perception of THA with different types of bearings.

5.3. Results compared to other studies

5.1.1. Ceramic-on-ceramic total hip arthroplasty

The main concerns of CoC are fracture of the components whereas reduced wear is an advantage. This may in the long-term run result in fewer revisions compared to MoP bearings. NJR is the registry with the largest number of CoC THA registered, and the cumulative incidence of revision of any cause was 4.22% (95% CI: 3.85-4.62) at 10-year follow-up. This was lower than in study I, where we found a cumulative incidence of revision of 5.4% (95% CI: 4.0–7.1) for CoC at 8.7-year follow-up. When comparing the HR for revision of any cause, the HR for CoC compared to MoP THA was 0.81 (95% CI: 0.70-0.94) after 13-year follow-up in the DHR[16], whereas the HR for CoC compared to metal-on-highly cross-linked polyethylene (MoHXLPE) in the Australian Orthopaedic Association National Joint Replacement Registry (AOA NJRR) was 1.08 (95% CI: 1.02-1.14) after 14-year follow-up[193]. The differences in HR from these two registries may be due to inclusion of both conventional and highly cross-linked polyethylene in the analyses from the DHR. These findings are in contrast to those in study I, where no difference in RR of revision was found for CoC compared to MoP THA. This might be due to shorter follow-up and better adjustments for confounding in our study. In another study based on data from six national and regional registries, cementless CoC THA with femoral head sizes >28 mm had similar risk of revision as MoHXLPE THA after nine-year follow-up, but CoC THA with femoral head ≤28 mm had increased risk of revision (HR=1.36 (95% CI: 1.09-1.68)).[106] This was in contrast to study I, where no difference in RR of any revision was found for any femoral head size ≤28 mm or >28 mm. Furthermore, a meta-analysis including 18 randomised clinical trials having a minimum two-year follow-up and an average age younger than 65 years in the included studies found no difference in risk ratio for revision of CoC THA when compared to MoHXLPE.[196] Hence, these results are in accordance with study I.

The risk of revision due to dislocation later than one year after index surgery after median follow-up of seven (range: 1-13) years was examined in a study from the New Zealand Joint Registry including 8,177 CoC THAs. In patients younger than 65 years having 28 mm femoral heads, more revisions for late dislocation was found for CoC THAs compared to MoM THAs ($p=0.014$), whereas no other statistically significant differences were found for CoC THAs when stratified by age and head size.[197] In study I, no difference in RR of revision due to dislocation was found for CoC compared to MoP THA, but no stratification for femoral head size was made. Furthermore, other differences in causes of revision were examined in study I, and we found a higher frequency of revision due to component failure for CoC than for MoP bearings ($p<0.001$).

The weakness of the current knowledge of CoC bearings is the relatively short follow-up. A difference in revision rate between MoP and CoC may first become evident after 15 to 20 years due to the very low wear in the new generations of polyethylene. Thus, patients who may benefit from CoC THA may be relatively young with a life expectancy longer than 15 to 20 years.

5.1.2. Metal-on-metal total hip arthroplasty

MoM bearings in THA were reintroduced as alternative bearings to MoP. Although one advantage is the possibility to use large head sizes and the following reduced the risk of dislocation, there major concern is related to increased risk of revision. In the NJR, the cumulative incidence of revision was 12.7% (12.3-13.2) at seven-year and 20.2% (95% CI: 19.2-21.2) at 10-year follow-up.[194] These cumulative incidences are higher than that of 7.0% (95% CI: 6.0–8.1) for MoM at eight years found in study II, and these differences may be caused by the use of different component designs. In the AOA NJRR, the HR of any revision was 1.36 (95% CI: 1.21-1.54) after 14 years.[193] This is in accordance with results in study II where the RR of revision was 1.49 (95% CI: 1.30–1.71), although the follow-up was only six years. Furnes et al. published a study with seven-year follow-up including data from six national and regional registries, and a

significantly increased HR=2.15 (95% CI: 1.63-2.83) was found for MoM THA with femoral head size >36 mm compared to MoHXLPE in patients aged from 45-64 years.[28] Furnes et al. had excluded patients with the ASR acetabular component. When patients having the ASR acetabular component were excluded in study II, no difference in RR for any revision was found for MoM compared to MoP THA at six-year follow-up. In study II, both cross-linked and highly cross-linked polyethylene was included. As revision rates for metal-on-conventional polyethylene are higher than that for MoHXLPE[193], the revision rate for MoP THA in study II may be higher than in the study by Furnes et al., who only included MoHXLPE and therefore, the resulting RR of revision for MoM THA in study II may be smaller than in the study by Furnes et al.

The causes of revision were examined in study II, and MoM had a higher RR of revision due to aseptic loosening than MoP THA. This confirmed the findings in the study based on data from the NJR by Smith et al.[107] Lombardi et al. published a study from a single institution including 1,440 MoM THAs with mean follow-up of seven years. The 12-year survival rate was 87% (95% CI: 84-90), and the two most common indications for revision were ARMD (48%; 47 of 108 hips revised) and aseptic loosening or failure of ingrowth (31%; 34 of 108).[198] According to the NJR, the highest patient-time incidence-rates for specific causes of revision was found for MoM THA revised for adverse soft tissue reaction to particulate debris.[194] However, in the NARA database it was not possible to register the cause of revision as due to adverse soft tissue reaction to particulate debris or metal-related pathology.

The discrepancies between registries may reflect national variations in the use of or reluctance to use MoM bearings, indications for primary surgery and revisions, different implant designs, and selection of patients.

5.1.3. Patient-reported outcomes

As indicated in section 3.5.5., PROs may be influenced by a number of factors. Preoperative selection of patients for specific bearings may be, among other factors, related to the activity level. Differences in PROs may therefore possibly reflect this selection. In a study from the NJR including 4,596 PROs linked primary THAs with a mean follow-up of seven months, there was no difference in change (postoperative compared to preoperative) for EQ-5D index score between patients having MoP, CoP, or CoC bearings, but there were statistically significant differences in median postoperative EQ-5D index scores with CoC having the highest and CoP THA the lowest score.[195] However, the differences in postoperative EQ-5D index scores between bearings are small (maximum 0.052) and may be without clinical significance, as MCII in a Danish registry setting was determined to be 0.31 one year after primary THA[134]. Similar findings after longer follow-up are reported in study III, although patients having MoM and not CoP were included. In a series including 208 consecutive, large-diameter CoC THAs from a single institution, there were 143 silent hips (69%), 22 (11%) with noises other than squeaking, 17 (8%) with unreproducible squeaking and 26 (13%) with reproducible squeaking. The HOOS subscales and UCLA activity scores were compared for patients with silent and noisy THAs, and no statistically significant difference was found for the UCLA activity score, HOOS Pain, HOOS ADL, and HOOS QoL. However, patients with noisy THA had lower scores for HOOS Symptoms and HOOS Sport.[112] In study III, similar prevalence of noises from CoC THA was found but except from the UCLA activity score, significant lower scores for all subscales were found when comparing noisy CoC to silent MoP THAs.

6. CONCLUSION

The main conclusions of the thesis are:

Study I: At 8.7 years of follow-up, CoC THA had a 33% higher risk of revision for any reason than MoP THA, but this was not statistically significant. CoC THA had a significantly higher incidence of revision due to component failure. The incidences of ceramic head and liner fracture were 0.28% and 0.17%, respectively.

Study II: A higher RR of revision for any reason at six-year follow-up was found for MoM THA than for MoP THA, but after exclusion of patients with the ASR acetabular component, the risk of revision was similar between the two groups of bearings. At six-year follow-up, there was a much higher risk of revision with prosthetic design combinations of ASR/Summit and ASR/Corail than for MoP THA, whereas the risk of revision was similar for the Recap/Bi-Metric combination and for MoP THA.

Study III: No significant difference in mean scores in the five HOOS subscales, EQ-5D index, EQ VAS, or UCLA activity score was found between patients with CoC, MoM, and MoP THA after mean follow-up of 6.9, 5.1, and 6.9 years, respectively. There were significantly lower mean subscale scores for all types of bearings and subscales when comparing noisy THA to silent MoP THA, except for patients having noisy CoC and MoM THA who had similar mean UCLA activity scores as patients with silent MoP THA.

7. FUTURE PERSPECTIVES

The DHR has a very high coverage and completeness and contains well validated data on diagnosis for primary THA.[16,117] However, a number of prognostic factors for the outcome of THA have not been validated, thus further studies may be performed in order to validate data on, for instance, implant design, types of bearings, and coating with/without hydroxyapatite. Since PJI is the only revision cause that has been validated[118], future studies may be conducted to validate other revision causes.

CoC and MoM bearings were introduced in order to reduce problems related to aseptic loosening of MoP THA. As aseptic loosening most commonly occurs with longer follow-up, there is a continuing need for large population-based studies comparing survival of THA with different types of bearings - including CoP. There are several prognostic factors for outcome in relation to bearings that are of interest and deserve further investigation: As CoC THA are recommended for young and active patients by some authors[167], the association between CoC bearings and activity level before and after surgery should be examined in more detail in a cohort study. For MoM THA, the association of results of chromium and cobalt ion measurements, ultrasound examinations, and MRIs may now be assessed in nationwide population-based cohort studies, as these variables are contained in the DHR since 2013.

When younger patients are treated with THA, the risk of more than one revision is increased. Ceramic fracture is a specific revision cause only related to the use of CoC bearings and in study II, revision due to aseptic loosening was more frequently for MoM bearings. Therefore, the types of bearings may be a prognostic factor also for the second revision, which may call for further investigation.

Although the treatment with THA is successful, not all patients will have their expectations fulfilled or be satisfied after THA. Therefore, patient selection for surgery is very important and may be influenced by many factors, which together result in a patient's risk profile in relation to the outcome after THA. PROs may be very useful to identify this risk profile, and PROs should be incorporated more systematically in the DHR.

8. SUMMARY IN ENGLISH

Total hip arthroplasty (THA) is a common and successful treatment of patients suffering from severe osteoarthritis that significantly reduces pain and improves hip function and quality of life. Traditionally, the outcome of THA has been evaluated by orthopaedic surgeons and assessed in morbidity and mortality rates, and implant survival. As patients and surgeons may assess outcome after THA differently, patient-reported outcomes (PROs) have gained much more interest and are today recognized as very important tools for evaluating the outcome and satisfaction after THA. One of the prognostic factors for the outcome of THA is the type of bearings. This PhD thesis focuses on the influence of different types of bearings on implant survival, revision causes, PROs, and noises from THA.

The aims of the thesis were:

Study I: To examine the revision risk and to investigate the causes of revision of cementless ceramic-on-ceramic (CoC) THAs comparing them to those of "standard" metal-on-polyethylene (MoP) THAs.

Study II: To compare the six-year revision risk for metal-on-metal (MoM) with that for MoP bearings in cementless stemmed THA, and further to study the revision risk for different designs of stemmed MoM THAs and the causes of revision.

Study III: To examine the association between CoC, MoM, and MoP bearings and both generic and disease-specific PROs, and furthermore to examine the incidence and types of noises from the three types of bearings and identify the effect of noises on PROs.

In study I and III, we used data from the Danish Hip Arthroplasty Registry combined with data from the Civil Registration System and the Danish National Patient Registry. In study II, data from the Nordic Arthroplasty Register Association, containing data from hip arthroplasty

registries in Denmark, Norway, Sweden, and Finland, was used.

In study I, 11,096 patients operated from 2002 through 2009 with cementless THA were included. Of these, 16% had CoC THA and 84% had MoP THA. At 8.7-year follow-up, no difference in RR of revision for any cause was found for CoC compared to MoP THA. One cause of revision related only to CoC THA is ceramic fracture. Medical records were reviewed for patients who had revision surgery due to component failure, and six patients (0,34%) had been revised due to ceramic fracture. No other difference in prevalence of causes of revision was found when comparing CoC to MoP THA.

Study II included 32,678 patients who were operated from 2002 through 2010 with cementless stemmed THA with either MoM bearings (11,567 patients, 35%) or MoP bearings (21,111 patients, 65%). At six-year follow-up, the RR of revision for any cause was significantly higher for MoM compared to MoP THA. When comparing different combinations of cup/stem with MoM to MoP bearings, there was an increased RR of revision for any cause for the ASR/Summit, ASR/Corail, and "other" combinations. There was a higher prevalence of revision due to aseptic loosening for MoM compared to MoP THA. In contrast, the prevalence of revision due to dislocation was lower for MoM THA.

In study III, a set of questionnaires including HOOS, EQ-5D, UCLA activity score, and a questionnaire about noises from the THA was send to patients having THA with CoC, MoM, or MoP bearings. The response rate was 85% and among the 3,089 patients responding, 45% received CoC, 17% MoM, and 38% MoP THA. No differences in mean subscale scores were found for CoC and MoM compared to MoP THA, except for CoC THA that had a lower mean HOOS Symptoms score than MoP THA. 27% of patients with CoC, 29% of patients with MoM, and 12% of patients with MoP bearings had experienced noises from the THA. For the three types of

bearings, PROs from patients with noisy THA were significantly lower when compared to silent MoP THA, except for noisy CoC and MoM THA that had the same mean UCLA activity score as silent MoP THA.

9. SUMMARY IN DANISH

Total hoftealloplastik (THA) er en almindelig og succesfuld behandling af patienter med svær hofteartrose. Ved denne behandling reduceres hoftesmerterne betydeligt samtidig med, at funktionen i hofteleddet og livskvaliteten forbedres. Resultatet af THA er traditionelt blevet vurderet af ortopædkirurgerne ud fra komplikationer, dødelighed og implantatoverlevelse. Idet patienter og kirurger kan bedømme resultatet af THA forskelligt, er interessen omkring patientrapporterede outcome (PRO) øget, og PRO er i dag anerkendt som et meget vigtigt redskab i bedømmelsen af resultatet af og tilfredsheden med THA. En af de prognostiske faktorer for resultatet af THA er artikulationen svarende til liner og caput. Denne ph.d.-afhandling fokuserer på artikulationens betydning for implantatoverlevelse, revisionsårsager, PRO og lyde fra hofteprotesen.

Formålene med denne afhandling var:
Studie I: At undersøge revisionsrisikoen og –årsagerne for ucementeret THA med keramik-keramik artikulation sammenlignet med standardartikulationen af metal-polyethylen.
Studie II: At sammenligne 6-års revisionsrisikoen for metal-metal artikulation med den for metal-polyethylen artikulation i ucementereret THA, og videre at undersøge revisionsrisikoen for forskellige designs af THA med metal-metal artikulation samt undersøge revisionsårsagerne.
Studie III: At undersøge sammenhængen mellem keramik-keramik, metal-metal og metal-polyethylen artikulationer og både generiske og sygdomsspecifikke PROs, og videre at undersøge prævalensen og typer af lyde fra THA med de tre artikulationstyper og klarlægge indflydelsen af lyde på PROs.

I studie I og III har vi anvendt data fra Dansk Hoftealloplastik Register kombineret med data fra CPR-registeret og Landspatientregisteret. I studie II blev der anvendt data fra Nordic

Arthroplasty Register Association, der indeholder data fra hoftealloplastikregistrene i Danmark, Norge, Sverige og Finland.

I studie I blev der inkluderet 11.096 patienter, der blev opereret med isættelse af ucementeret THA i perioden 2002-2009. 16% af patienterne havde keramik-keramik artikulation, og 84% havde metal-polyethylen artikulation. Efter 8,7 års follow-up var der ingen forskel i relativ risiko (RR) for revision uanset årsag for keramik-keramik sammenlignet med metal-polyethylen artikulation. Keramikfraktur er en revisionsårsag, der kun er relateret til keramik-keramik artikulation. Patientjournaler fra patienter, der var blevet revideret pga. komponentsvigt, blev gennemgået, og seks patienter (0,34%) blev revideret pga. keramikfraktur. Der var ingen andre forskelle i prævalensen af revisionsårsager, når keramik-keramik blev sammenlignet med metal-polyethylen artikulation.

I studie II blev der inkluderet 32.678 patienter, der i perioden 2002-2010 blev opereret med ucementeret THA med enten metal-metal artikulation (11.567 patienter, 35%) eller metal-polyethylen artikulation (21.111 patienter, 65%). Efter 6 års follow-up var RR for revision uanset årsag signifikant højere for THA med metal-metal sammenlignet med metal-polyethylen artikulation. Når forskellige cup/stem-kombinationer med metal-metal artikulation blev sammenlignet med metal-polyethylen artikulation, var der forøget RR for revision uanset årsag for ASR/Summit, ASR/Corail og "andre" kombinationer. Der var højere prævalens af revision pga. aseptisk løsning for metal-metal artikulation sammenlignet med metal-polyethylen. Derimod var der lavere prævalens af revision pga. luksation for metal-metal artikulation.

I studie III blev der udsendt et sæt af spørgeskemaer bestående af HOOS, EQ-5D, ULCA aktivitetsscore og et spørgeskema om lyde fra THA til patienter, som havde THA med keramik-keramik, metal-metal eller metal-polyethylen artikulation. Svarprocenten var 85, og blandt de 3.089 patienter, der svarede, havde 45% keramik-keramik, 17% metal-metal og 38% metal-

polyethylen artikulation. Der var ingen forskel i gennemsnitlig sub-skala score for keramik-keramik og metal-metal sammenlignet med metal-polyethylen artikulation – med undtagelsen af, at patienter med keramik-keramik artikulation havde lavere gennemsnitlig score sv.t. HOOS Symptomer end patienter med metal-polyethylen artikulation. 27% af patienterne med keramik-keramik, 29% af patienterne med metal-metal og 12% af patienterne med metal-polyethylen artikulation havde oplevet lyde fra deres THA. For alle tre artikulationstyper var PRO fra patienter med lyde fra THA signifikant lavere end PRO fra patienter med metal-polyethylen artikulation uden lyde – med undtagelse af, at keramik-keramik og metal-metal THA med lyde havde samme gennemsnitlig UCLA aktivitetsscore som metal-polyethylen THA uden lyde.

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11. ORIGINAL PAPERS

Study I

Comparison of the risk of revision in cementless total hip arthroplasty with ceramic-on-ceramic and metal-on-polyethylene bearings

Data on 11,096 patients from the Danish Hip Arthroplasty Registry

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Background and purpose — Ceramic-on-ceramic (CoC) bearings were introduced in total hip arthroplasty (THA) to reduce problems related to polyethylene wear. We compared the 9-year revision risk for cementless CoC THA and for cementless metal-on-polyethylene (MoP) THA.

Patients and methods — In this prospective, population-based study from the Danish Hip Arthroplasty Registry, we identified all the primary cementless THAs that had been performed from 2002 through 2009 (n = 25,656). Of these, 1,773 THAs with CoC bearings and 9,323 THAs with MoP bearings were included in the study. To estimate the relative risk (RR) of revision, we used regression with the pseudo-value approach and treated death as a competing risk.

Results — 444 revisions were identified: 4.0% for CoC THA (71 of 1,773) and 4.0% for MoP THA (373 of 9,323). No statistically significant difference in the risk of revision for any reason was found for CoC and MoP bearings after 9 years of follow-up (adjusted RR = 1.3, 95% CI: 0.72–2.4). Revision rates due to component failure were 0.5% (n = 8) for CoC bearings and 0.1% (n = 6) for MoP bearings (p < 0.001). 6 patients with CoC bearings (0.34%) underwent revision due to ceramic fracture.

Interpretation — When compared to the "standard" MoP bearings, CoC THA had a 33% higher (though not statistically significantly higher) risk of revision for any reason at 9 years.

Aseptic loosening is the most frequent cause of revision after total hip arthroplasty (THA) (Australian Orthopaedic Association 2013, Danish Hip Arthroplasty Registry 2013). This is associated with polyethylene wear debris, which can stimulate an adverse local host response that results in bone resorption and aseptic loosening of the prosthesis (Jacobs et al. 1994). Ceramic-on-ceramic (CoC) bearings were introduced for THAs in 1970 (Boutin 1972) to reduce the problem of wear due to friction and that of loosening, which was a result of osteolysis caused by wear particles (Hannouche et al. 2005).

Although CoC bearings have shown low wear rates and are used in young and active patients (Hannouche et al. 2005), there are some concerns of fracture of the ceramic acetabular liner (Min et al. 2007) or fracture of the ceramic head (Habermann et al. 2006). Furthermore, dislodgement of the acetabular ceramic insert has been reported for the sandwich design (Akagi et al. 2004). Finally, squeaking and other noises can occur in THAs with CoC bearings (Jarrett et al. 2009). All these concerns may lead to revision surgery.

Survivorship of CoC THAs after a mean follow-up time of 5–12 years has been described in some previous studies (Garcia-Rey et al. 2009, Johansson et al. 2011, D'Antonio et al. 2012), but these studies had small sample sizes and involved very few hospitals and clinics, thus reducing the generalizability of the findings. Based on data from the Danish Hip Arthroplasty Registry (DHR), we therefore conducted a population-based cohort study to determine the revision risk and to investigate the causes of revision of cementless CoC THAs, comparing them to those of "standard" MoP THAs.

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Patients and methods

There are approximately 5.6 million inhabitants in Denmark. All Danish citizens are guaranteed tax-funded, "free" medical care on admission to hospitals or outpatient clinics. Every Danish citizen is given a personal 10-digit identification number that allows unambiguous linkage between all the medical databases in Denmark.

Data sources

The DHR is a nationwide, population-based clinical database that was founded on January 1, 1995 and validated in 2004 (Pedersen et al. 2004). The DHR holds prospectively collected data on primary THAs, revisions, and—to some extent—postoperative complications. In 2012, 50 orthopedic departments and private clinics reported to the registry (Danish Hip Arthroplasty Registry 2013). In annual reports, the completeness of the data is calculated at the individual level as the proportion of THAs reported to the DHR out of the total number of THAs reported to the National Patient Registry (NPR) and/or the DHR. The NPR is considered to be the gold standard—due to the fact that the hospital is reimbursed only after registration of a surgical procedure. In 2012, the degree of completeness was 97% for primary THAs and 90% for THA revisions (Danish Hip Arthroplasty Registry 2013).

The Civil Registration System (CRS) was established in 1968. It contains data on vital status and residence for the entire Danish population (Pedersen et al. 2006). Thus, the CRS provides complete follow-up information on the entire study population.

The NPR was established in 1977. It contains data on all admissions and discharges from hospitals in Denmark, including the dates of admission and discharge, the surgical procedures performed, and up to 20 diagnoses for every discharge. Since 1994, diagnoses have been classified according to the Danish version of the International Classification of Diseases, tenth edition (Andersen et al. 1999). Since 1995, data on outpatients and emergency visits have been included in the registry. Data from the NPR were used to determine the complete hospitalization history of patients included in the study population. As a measure of comorbidity, we computed the Charlson comorbidity index (CCI) score for each patient at the time of surgery (Charlson et al. 1987, Thygesen et al. 2011). This index is based on 19 major disease categories, including cardiovascular, cerebrovascular, chronic pulmonary, liver, renal, and gastrointestinal diseases, diabetes, and solid and hematological tumors. Admissions from each category are weighted with 1, 2, 3, or 6 points. These weights are summed to provide the index score. We defined 3 comorbidity levels: a score of 0 (low), given to patients with no previous record of diseases included in the CCI; a score of 1–2 (medium); and a score of 3 or more (high) (de Groot et al. 2003).

Study population

For patients registered with CoC bearings, the fixation method was cementless in 97.1%, hybrid in 2.7%, and "other" in 0.1%. The study population included patients undergoing cementless THA with either CoC or MoP bearings who were being operated for 1 of the following diagnoses: primary osteoarthritis (OA), inflammatory arthritis, femoral head osteonecrosis, and sequelae from childhood hip disorder.

In the DHR, the registration of THA bearings started in 2002. This study population consisted of all primary cementless THAs registered in the DHR with surgery between January 1, 2002 and September 15, 2009 (n = 25,656). When a patient received bilateral THA operations, only the first was included in the study due to the statistical assumption of independent observations. Thus, 3,572 THAs were excluded due to bilaterality. Patients diagnosed with hip fracture (n = 2,097) and "other" diagnoses (n = 201) and patients with ceramic-on-polyethylene (n = 5,171), metal-on-metal (n = 2,100), or "other" types of bearings (n = 565) were excluded. Furthermore, patients with an acetabular component with a dual-mobility liner (n = 306) were excluded. We also excluded 520 patients who were registered with missing information regarding bearings. Of these, 18 patients had a metal liner and could therefore not have CoC or MoP bearings. Hence, 502 patients with missing information on articulation could possibly have had either CoC or MoP bearings. Patients who were registered without information on diagnosis (n = 16), femoral head size (n = 4), and duration of surgery (n = 8) were also excluded.

11,096 cementless THAs (1,773 CoC and 9,323 MoP) with complete patient information on sex, age group, diagnosis, comorbidity, year of surgery, femoral head size, and duration of surgery were included in the final analysis.

Types of ceramic bearings

According to the manufacturer (CeramTec, Plochingen, Germany), BIOLOX forte was introduced in 1995 and BIOLOX delta in 2004. Distributors of the prosthetic components were contacted to obtain information on the types of ceramic bearings that were used with the specific acetabular and femoral components from 2002 to September 15, 2009. Distributors were supplied with information on the specific component brand and its period in use. At the patient level, the femoral head size was also taken into account to determine the ceramic bearing type implanted.

Medical records

In order to identify patients with fracture of a ceramic component, medical records were reviewed for 14 patients who had revision surgery due to component failure.

Statistics

Patients were followed from the date of primary surgery until revision, death, emigration, or the end of the study period

(September 15, 2010), whichever came first. Revision was defined as a new surgical procedure including complete or partial exchange or removal of the prosthetic components. When death is treated as censored information in survival analysis, it will result in overestimation of the revision rates (Gillam et al. 2010). We therefore performed multivariable regression with the pseudo-value approach (Klein et al. 2007), treating death as a competing risk to estimate the relative risk (RR) for any revision with 95% confidence intervals (CIs), and a cumulative incidence curve was constructed. Adjustments were made for the patient- and surgery-related factors presented in Table 1. Subanalyses were performed at 2, 4, 6, and 8.7 years of follow-up in order to evaluate early and medium-term revision risk. We performed stratified analyses on potentially influencing factors, including sex; age under or over 60 years; comorbidity; osteoarthritis (OA) as diagnosis; femoral heads 28 mm or smaller; and femoral heads larger than 28 mm. All stratified analyses were performed at 8.7 years of follow-up—except for femoral head sizes larger than 28 mm, which had a maximum follow-up of 7.5 years. The primary outcome was revision for any reason. Revisions for aseptic loosening, dislocation, and other causes at 8.7-years follow-up were analyzed and these were secondary outcomes.

Revision rates per 100 person-years (with CI) were calculated as the number of revisions within each group divided by the total risk time for the same group. Chi-square test was performed to compare proportions between the 2 bearing groups, and the 2-sample Wilcoxon rank-sum test was used to compare ages and follow-up times because of skewness. For ages and follow-times, medians and interquartile ranges (IQR) are given. Any p-value < 0.05 was considered significant. Statistical analyses were carried out with Stata software, release 13.1.

Ethics

The study was approved by the Danish Data Protection Agency (journal no. 2010-41-4926).

Table 1. Characteristics of patients with ceramic-on-ceramic (CoC) and metal-on-polyethylene (MoP) total hip arthroplasty. Values are numbers of patients and percentages (%) for each group

	CoC n = 1,773	MoP n = 9,323	p-value
Sex			0.001
Female	835 (47)	4,792 (51)	
Male	938 (53)	4,531 (49)	
Age groups, years			< 0.001
≤ 49	356 (20)	539 (6)	
50–59	576 (33)	2,068 (22)	
60–69	744 (42)	4,238 (46)	
70–79	91 (5)	2,069 (22)	
≥ 80	6 (0)	409 (4)	
Diagnosis			< 0.001
Primary OA	1,471 (83)	8,373 (90)	
Femoral head osteonecrosis	67 (4)	258 (3)	
Arthritis	53 (3)	193 (2)	
Childhood hip disorders	182 (10)	499 (5)	
Charlson comorbidity index at surgery			< 0.001
Low	1,350 (76)	6,324 (68)	
Medium	363 (21)	2,447 (26)	
High	60 (3)	552 (6)	
Year of surgery			< 0.001
2002	167 (10)	867 (9)	
2003	210 (12)	922 (10)	
2004	339 (19)	1,088 (12)	
2005	345 (19)	1,187 (13)	
2006	238 (13)	1,235 (13)	
2007	190 (11)	1,277 (14)	
2008	153 (9)	1,426 (15)	
2009, until September 15	131 (7)	1,321 (14)	
Femoral head size, mm			< 0.001
≤ 27	1 (0)	139 (2)	
28	652 (37)	6,066 (65)	
32	922 (52)	1,926 (21)	
36	193 (11)	1,066 (11)	
≥ 40	5 (0)	126 (1)	
Duration of surgery, min			< 0.001
≤ 59	505 (29)	3,925 (42)	
60–89	899 (51)	4,202 (45)	
90–119	286 (16)	917 (10)	
≥ 120	83 (5)	279 (3)	

Results

Description of the study population (Tables 1 and 2)

16% of the patients had CoC bearings and 84% had MoP bearings. The median follow-up time was 5.0 (3.1–6.5) years for CoC bearings and 3.9 (2.0–5.9) years for MoP bearings (p < 0.001). More males received CoC THAs than MoP THAs. The median patient age was 59 (52–65) years for CoC and 65 (59–70) years for MoP (p < 0.001). A greater proportion of patients with CoC THAs had been diagnosed with sequelae from a childhood hip disorder (p < 0.001) and more CoC patients than MoP patients had a CCI score equal to zero (p < 0.001). 60% of patients with CoC THA had their surgery during the period 2002–2005, whereas only 44% of patients with MoP THA had surgery then (p < 0.001). Patients with CoC THA had a higher proportion of 32-mm or larger femoral head sizes than patients with MoP THA (63% vs. 33%; p < 0.001). The most frequent cup/stem combinations were Plasmacup SC/Bicontact (42%), Lineage/Anca-Fit (16%), and Trident PLS/Symax (7%) for CoC THA and Trilogy/collarless Bi-Metric (34%), Mallory-Head/collarless Bi-Metric (19%), and Pinnacle/Corail (5%) for MoP THA. For patients with CoC THA, 81% (1,428 of 1,773) had a liner and 77% (1,373 of 1,773) had a femoral head made of BIOLOX forte.

Risk of any revision (Table 3)

The entire study population had 444 revisions (4.0%): 4.0% (71 of 1,773) for CoC THA and 4.0% (373 of 9,323) for MoP THA. Revision rates were 0.84 (0.66–1.06) per 100 person-years for CoC bearings and 0.97 (0.88–1.08) per 100 person-years for MoP bearings. At 8.7 years of follow-up, the cumu-

Table 2. Specific designs of acetabular and femoral components and type of ceramic used in total hip arthroplasty with ceramic-on-ceramic bearings. Values are numbers of patients and percentage (%) of total number

	No. n = 1,773	Company	Period in use	No. of BIOLOX forte	No. of BIOLOX delta	No. of either BIOLOX forte or delta	No. of unknown ceramic components
Acetabular component							
Plasmacup SC	792 (45)	Aesculap	2002–2009	764	28	-	-
Lineage	312 (18)	Wright	2004–2009	312	0	-	-
Trident PSL [a]	125 (7)	Stryker	2004–2008	125	0	-	-
Exceed ABT	93 (5)	Biomet	2006–2009	-	93	-	-
Trident hemispherical [a]	73 (4)	Stryker	2005–2007	73	0	-	-
Duraloc Option	63 (4)	DePuy	2002–2005	63	0	-	-
Mallory-Head	51 (3)	Biomet	2002–2009	-	28	-	23
Trilogy	51 (3)	Zimmer	2002–2009	0	51	-	-
Anca-Fit	47 (3)	Wright	2002–2005	47	0	-	-
C2a Taper [b]	44 (2)	Biomet	2007–2009	44	-	-	-
Pinnacle	41 (2)	DePuy	2004–2009	0	41	-	-
Prototyl-E	19 (1)	Wright	2009	-	-	19	-
12 other cups	62 (3)		2002–2009	-	-	-	62
In total				1,428	241	19	85
Femoral component							
Bicontact	769 (43)	Aesculap	2002–2009	720	29	20	-
Anca-Fit	409 (23)	Wright	2002–2009	391	18	-	-
Symax	195 (11)	Stryker	2004–2008	195	0	-	-
Bi-Metric	178 (10)	Biomet	2002–2009	-	-	-	178
Corail	102 (6)	DePuy	2002–2009	31	15	56	-
Profemur R	18 (1)	Wright	2006–2007	18	0	-	-
S-ROM	18 (1)	DePuy	2002–2004	18	0	-	-
18 other stems	84 (5)		2002–2009	-	-	-	84
Total				1,373	62	76	262

[a] Ceramic liner titanium-enchased.
[b] Sandwich design of the ceramic liner.

Table 3. Crude and adjusted relative risk (RR) of revision for any cause, with 95% confidence intervals (CIs), in total hip arthroplasty (THA) with ceramic-on-ceramic (CoC) and metal-on-polyethylene (MoP) bearings [a]

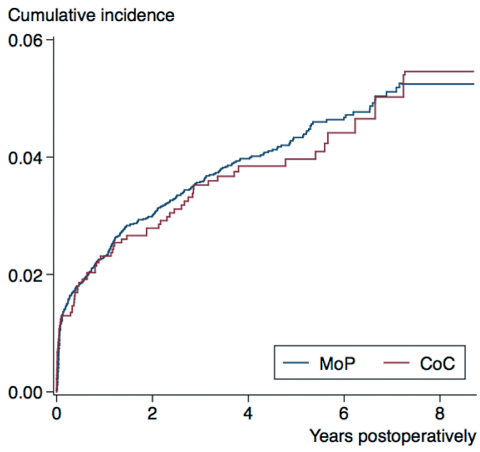
	Patients at the start of the period (n)	Revisions performed within the period (%)	Crude RR (95% CI)	Adjusted RR (95% CI)
At 2-year follow-up (0 to 2 years postoperatively)				
CoC	1,773	48 (2.7)	0.91 (0.67–1.24)	1.18 (0.65–2.13)
MoP	9,323	274 (2.9)	1 (ref.)	1 (ref.)
At 4-year follow-up (2 to 4 years postoperatively)				
CoC	1,519	15 (1.0)	0.95 (0.72–1.26)	1.12 (0.70–1.81)
MoP	7,065	62 (0.9)	1 (ref.)	1 (ref.)
At 6-year follow-up (4 to 6 years postoperatively)				
CoC	1,135	4 (0.4)	0.91 (0.68–1.21)	1.03 (0.60–1.77)
MoP	4,501	26 (0.6)	1 (ref.)	1 (ref.)
At 8.7-year follow-up (6 to 8.7 years postoperatively)				
CoC	543	4 (0.8)	1.02 (0.74–1.39)	1.33 (0.72–2.43)
MoP	2,230	11 (0.5)	1 (ref.)	1 (ref.)

[a] Adjustments were made for sex, age, diagnosis of primary THA, comorbidity, year of surgery, femoral head size, and duration of surgery.

lative incidence for any revision was 5.4% (4.0–7.1) for CoC THA and 5.3% (4.7–5.9) for MoP THA (Figure). At 2, 4, 6, and 8.7 years of follow-up, there was no significant difference in the risk of revision of CoC THA and MoP THA for any reason.

Stratified analyses: risk of revision for any reason

For women, men, patients who were younger than 60 years, patients aged 60 years or older, patients diagnosed with OA, or patients who had no comorbidity (CCI score = 0), any comorbidity (CCI score > 0), or 28-mm or smaller femoral head,



Cumulative incidence for any revision of cementless total hip arthroplasty with ceramic-on-ceramic (CoC) and metal-on-polyethylene (MoP) bearings. See Table 3 for the relative risk of any revision at 2, 4, 6, and 8.7 years of follow-up.

Table 4. The main indications for total hip arthroplasty (THA) revision registered in the Danish Hip Arthroplasty Registry. For each type of THA bearing, numbers and percentages (%) are given regarding the causes of revision listed. The bearings included were ceramic-on-ceramic (CoC) and metal-on-polyethylene (MoP)

	CoC n = 71	MoP n = 373	p-value
Aseptic loosening	10 (0.6)	43 (0.5)	0.6
Osteolysis without loosening	0 (0.0)	3 (0.0)	0.5
Deep infection	6 (0.3)	61 (0.7)	0.1
Femoral bone fracture	9 (0.5)	56 (0.6)	0.6
Dislocation	22 (1.2)	156 (1.7)	0.2
Component failure	8 (0.5)	6 (0.1)	< 0.001
Pain	9 (0.5)	26 (0.3)	0.1
Other	7 (0.4)	22 (0.2)	0.2

no significant differences in revision risk were found for CoC bearings and MoP bearings at 8.7 years of follow-up. At 7.5 years of follow-up, the revision risk was similar in the 2 bearing groups for femoral head sizes greater than 28 mm.

Causes of revision (Tables 4 and 5)

8 CoC THAs were revised due to component failure. The proportion of revisions due to component failure was higher for CoC bearings than for MoP bearings ($p < 0.001$). Of the 8 patients who were registered as having component failure as the cause of revision, 6 patients had ceramic fracture and 2 patients had impingement between the stem-neck and the rim of the liner. In the 6 patients with ceramic fracture, 3 patients had an isolated ceramic head fracture, 1 patient had an isolated ceramic liner fracture, and 2 patients had fracture of both the ceramic head and liner. Thus, 5 patients had ceramic head fracture and 3 had ceramic liner fracture. Ceramic component fracture occurred at a median of 4.0 (1.4–7.2) years after primary surgery, and all the patients who had ceramic fracture had a 28-mm femoral head implanted. The causes of revision of MoP THA in patients registered with component failure as the cause of revision were: subluxation/instability (n = 2), subsidence of the cementless stem (n = 1), deep infection (n = 1), wear of the polyethylene liner (n = 1), and malposition of the acetabular component (n = 1).

Compared to MoP THA patients, patients with CoC THA had half the proportion of revision due to deep infection. The proportion due to dislocation was also lower, but these findings were not statistically significant.

Only 2 patients in the CoC group had revision registered as being due to "mechanical noises" and "squeaking". For MoP, no revisions were performed because of noise from the THA.

There were no statistically significant differences in the risk of revision due to aseptic loosening (adjusted RR = 0.84, CI: 0.21–3.4), dislocation (adjusted RR = 1.2, CI: 0.29–5.3), and all other causes (adjusted RR = 1.1, CI: 0.14–8.8) between CoC bearings and MoP bearings at 8.7 years.

Discussion

In this nationwide, population-based study from the DHR involving 11,096 patients, CoC bearings did not have a statistically significantly higher overall risk of revision than MoP bearings after the maximum follow-up period of 8.7 years.

Table 5. Characteristics of patients who were revised for fracture of the ceramic component

				Acetabular liner			Femoral head			
Patient no.	Sex	Age at primary surgery	Years from primary surgery to revision	Component brand	Component fractured	Type of ceramic	Component brand	Component fractured	Type of ceramic	Size, mm
1	F	53	4.8	Duraloc Option	No	BIOLOX forte	S-ROM	Yes	BIOLOX forte	28
2	F	60	7.2	Plasmacup SC	Yes	BIOLOX forte	Bicontact	No	BIOLOX forte	28
3	M	46	1.4	Plasmacup SC	No	BIOLOX forte	Bicontact	Yes	BIOLOX forte	28
4	F	65	5.7	Plasmacup SC	No	BIOLOX forte	Bicontact	Yes	BIOLOX forte	28
5	F	52	3.2	Anca-Fit	Yes	BIOLOX forte	Anca-Fit	Yes	BIOLOX forte	28
6	M	42	2.4	Mallory-Head	Yes	Unknown	Bi-Metric collarless	Yes	BIOLOX delta	28

The main findings compared to other studies

In the Australian Orthopaedic Association National Joint Replacement Registry (AOA NJRR), the cumulative incidence of revision of CoC THA, with OA as diagnosis, at 10 years was 5.3%, which is similar to our findings after 8.7 years of follow-up. In studies with smaller series, a 5-year survival of 98% (Johansson et al. 2011) and a 6.7-year survival of 94–98% (Garcia-Rey et al. 2009) were found, corresponding to our findings. The main cause of revision in both studies was aseptic loosening. In contrast to this study, Khatod et al. (2014) found an 87% higher risk of aseptic revision in 510 CoC THAs than in 20,631 THAs with metal-on-highly cross-linked polyethylene. The median follow-up period in their study of 2.9 (IQR: 1.2–5.1) years and inclusion of all types of fixation method makes comparison between these findings and our findings difficult. Aseptic loosening can be caused by wear debris (Jacobs et al. 1994), and hip simulator studies have shown reduced wear rates for CoC bearings compared to MoP bearings.

The steady-state wear rate for alumina liners in an alumina head-alumina cup combination was 0.004 mm^3 per million cycles over 14 million cycles in a hip simulator study—in contrast to 13 mm^3 per million cycles for polyethylene liners in MoP bearings in the same study (Clarke et al. 2000). In other hip simulator studies, under severe microseparation conditions, BIOLOX forte showed steady-state wear rates of 1.3 mm^3 per million cycles (Stewart et al. 2001); in contrast, the steady-state wear rates for BIOLOX delta components was 0.12 mm^3 per million cycles (Stewart et al. 2003). Mean wear rates for BIOLOX forte CoC bearings retrieved after a minimum of 6 months in situ were reported to be 0.6 mm^3/year for femoral heads and 0.5 mm^3/year for acetabular liners (Lusty et al. 2007). Thus, simulator studies have shown less wear with CoC bearings, which—together with more bio-inert debris than polyethylene wear debris (Christel 1992)—may reduce the risk of aseptic loosening in CoC THAs, although this has not yet been shown in any study and should only become apparent with longer follow-up time. In the present study and in the above-mentioned studies with short- to medium-term follow-up (Garcia-Rey et al. 2009, Johansson et al. 2011, Khatod et al. 2014), revision due to aseptic loosening could certainly be related to fixation of the components rather than to wear.

A serious complication with ceramic implants is fracture, which may lead to reoperation and to a poor prognosis. One study showed that at a mean follow-up of 5 years after revision due to ceramic head fracture in 24 patients with BIOLOX forte ceramic bearings, 5 patients needed a second revision and 2 of them underwent a third revision (Koo et al. 2014). The reported incidence of ceramic component fracture varies from 0.01% to 3.5% (Ha et al. 2007, D'Antonio and Sutton 2009, Traina et al. 2011). In reports with the highest incidence of ceramic liner fracture, a sandwich design with a layer of polyethylene interposed between the ceramic liner and the acetabular shell was implanted (Ha et al. 2007, Lopes et al. 2012). The risk of fracture using BIOLOX forte (which is made of alumina) has been reduced with the introduction of BIOLOX delta, which is made of zirconia platelet-toughened alumina—making the material more resistant to fracture in ex vivo studies (Piconi et al. 2003). In the present study, 5 of the 6 patients who were revised due to ceramic fracture had BIOLOX forte-on-BIOLOX forte bearings. Other studies have found a prevalence of BIOLOX forte component fracture of 0–2% in smaller series (Yeung et al. 2012, Epinette and Manley 2014). All 6 patients with ceramic fracture had 28-mm femoral heads implanted, which are more prone to fracture than larger head sizes (D'Antonio and Sutton 2009, Traina et al. 2011). Furthermore, Traina et al. (2011) reported that 28-mm femoral heads designed to accept a short neck taper have a higher prevalence of fracture than heads that result in a longer taper. The DHR does not contain information on neck length, and such data are not included in this study. Apart from the material itself, there may be additional causes of ceramic fractures: both head and liner fractures could be due to trauma; debris (e.g. blood or fat) could be interposed between the neck taper or metal shell and the ceramic component; or there could have been course handling of the ceramic component during surgery. Moreover, head failure is associated with dislocation or a mismatch in design between the metal taper of the femoral neck and the ceramic head; and liner failure may be due to malpositioning of the implant or malseating of the ceramic liner into the metal shell (Traina et al. 2011).

None of the patients registered with component failure as the cause of revision had revision due to stem breakage. 1 patient with MoP bearings had revision due to component failure: wear of the polyethylene liner. 2 patients with MoP THA were revised due to problems related to the primary surgery: cup malpositioning and subsidence of the cementless stem, which may have been too small. 1 patient with MoP THA who was registered with component failure as the cause of revision actually had revision due to deep infection ~~-w~~hich is a clear misclassification of the cause of revision. The incidence of revision due to deep infection of MoP THA was more than twice the incidence of revision due to deep infection of CoC THA. This finding was not statistically significant, but the trend has been seen in the National Joint Registry for England, Wales and Northern Ireland (2014).

CoC THAs have been described to make "squeaking", "clicking", "grinding", "popping", and "snapping" noises (Jarrett et al. 2009, Schroder et al. 2011). This complication might lead to revision surgery. We found only 2 patients (0.1%) who underwent revision due to noises from the CoC bearings. This is in accordance with a newly published meta-analysis, which has found an incidence of revision for squeaking of 0.2% (Owen et al. 2014). Our data are not conclusive in terms of the types of noises that lead to revision, as this information is not reported to the DHR.

Methodological considerations

The strengths of our study include the population-based design with prospectively collected data, the large sample size, and the complete follow-up, which limit possible selection and information bias. The medical databases that provide data to our study have independently registered data and they have documented moderate-to-high overall validity (Andersen et al. 1999, Pedersen et al. 2004, Pedersen et al. 2006). In addition, the DHR has a coverage (hospitals/clinics reporting to the registry) of over 95% and a completeness of 97% for primary THA (Danish Hip Arthroplasty Registry 2013); thus, the results are widely generalizable. In addition, all the CoC THAs that were revised for ceramic fracture were validated by searching in the medical files.

Our study also had several limitations. Although the DHR has been validated regarding a number of parameters, no validation regarding the registration of type of bearings has been made. We excluded 502 THAs that had no information registered concerning the bearings. We performed additional regression analyses for the 2 worst-case scenarios, presuming that these 502 THAs had either CoC or MoP bearings. Including the 502 THAs in the CoC group, the adjusted RR for revision for any reason was 1.2 (CI: 0.48–2.8) at 8.7 years for CoC THA compared to MoP THA. Including the 502 THAs in the MoP group provided an adjusted RR for revision for any reason of 1.3 (CI: 0.69–2.5) at 8.7 years for CoC THA compared to MoP THA. In both scenarios—before exclusion of the 502 patients as well as after their exclusion—no statistically significant difference in the RR of revision for any reason at 8.7 years was found. It is assumed that exclusion of the 28 patients with unregistered information on diagnosis, femoral head size, and/or duration of surgery would have no influence on the results in this large study population. We only included patients with cementless THAs in order to reduce the confounding effect of fixation. Adjustments for many confounders have been made, but there is still the possibility of unmeasured confounding, because the registries do not contain data on height, weight, BMI, and level of physical activity before and after surgery. Registration of causes of revision of THAs has never been validated in the DHR. Misclassification of causes of revision and also the lack of registration of revision in the DHR was unlikely to be related to the registration of the type of bearings for primary THAs; this produced a bias towards null. Furthermore, the median follow-up was longer for the CoC group than for the MoP group. This should be taken into account when interpreting the results, as the number of revisions—and especially revision due to aseptic loosening—would most likely increase with longer follow-up.

Conclusion

At 8.7 years of follow-up, CoC THA had a 33% higher risk of revision for any reason than MoP THA, but this was not statistically significant. CoC THA had a significantly higher incidence of revision due to component failure. The incidences of ceramic head and liner fracture were 0.28% and 0.17%, respectively.

CV, ABP, PKA, and SO designed the study protocol. CV and ABP collected the data. Analyses were planned by CV, ABP, PKA, and SO and were carried out by CV. CV wrote the initial draft of the manuscript, which was critically revised by CV, ABP, PKA, and SO.

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Study II

II

Increased risk of revision of cementless stemmed total hip arthroplasty with metal-on-metal bearings

Data from the Nordic Arthroplasty Register Association

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Background and purpose — Data from the national joint registries in Australia and England and Wales have revealed inferior medium-term survivorship for metal-on-metal (MoM) total hip arthroplasty (THA) than for metal-on-polyethylene (MoP) THA. Based on data from the Nordic Arthroplasty Register Association (NARA), we compared the revision risk of cementless stemmed THA with MoM and MoP bearings and we also compared MoM THA to each other.

Patients and methods — We identified 32,678 patients who were operated from 2002 through 2010 with cementless stemmed THA with either MoM bearings (11,567 patients, 35%) or MoP bearings (21,111 patients, 65%). The patients were followed until revision, death, emigration, or the end of the study period (December 31, 2011), and median follow-up was 3.6 (interquartile range (IQR): 2.4–4.8) years for MoM bearings and 3.4 (IQR: 2.0–5.8) years for MoP bearings. Multivariable regression in the presence of competing risk of death was used to assess the relative risk (RR) of revision for any reason (with 95% confidence interval (CI)).

Results — The cumulative incidence of revision at 8 years of follow-up was 7.0% (CI: 6.0–8.1) for MoM bearings and 5.1% (CI: 4.7–5.6) for MoP bearings. At 6 years of follow-up, the RR of revision for any reason was 1.5 (CI: 1.3–1.7) for MoM bearings compared to MoP bearings. The RR of revision for any reason was higher for the ASR (adjusted RR = 6.4, CI: 5.0–8.1), the Conserve Plus (adjusted RR = 1.7, CI: 1.1–2.5) and "other" acetabular components (adjusted RR = 2.4, CI: 1.5–3.9) than for MoP THA at 6 years of follow-up.

Interpretation — At medium-term follow-up, the survivorship for cementless stemmed MoM THA was inferior to that for MoP THA, and metal-related problems may cause higher revision rates for MoM bearings with longer follow-up.

Wear particles from the polyethylene liner in metal-on-polyethylene (MoP) bearings in total hip arthroplasty (THA) are associated with osteolysis and aseptic loosening of the implant (Jacobs et al. 1994). Surgeons therefore became interested in alternatives such as metal-on-metal (MoM) bearings. The main justification for using large-diameter-head (LDH) MoM bearings in THA was less wear and the hope of lower revision rates. However, a lower risk of revision has only been found for revision due to dislocation (Kostensalo et al. 2013), whereas the total risk of revision has been found to be increased in some studies (Smith et al. 2012, Huang et al. 2013). In addition, LDH MoM was introduced in order to achieve increased range of motion and better function (Burroughs et al. 2005, Davis et al. 2007), but that has not been shown clinically (Penny et al. 2013).

Several concerns about the use of MoM bearings in hip surgery have been voiced in recent years: excessive failure rates for certain brands and implant combinations used with MoM components have been reported (Langton et al. 2011, Australian Orthopaedic Association 2013). Some designs are associated with increased frequency of aseptic loosening (Australian Orthopaedic Association 2013), and large head sizes placed on conventional stems may cause taper junction failure (Langton et al. 2012). Exposure to chromium and cobalt may cause adverse reactions to metal debris (ARMD) (Langton et al.

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2010) such as pseudotumors (Pandit et al. 2008) and hypersensivity reactions (Willert et al. 2005) locally in the hip joint. Furthermore, metal ions may be genotoxic (Daley et al. 2004).

Only a few population-based studies on MoM bearings in stemmed THAs from hip arthroplasty registries have been published (Smith et al. 2012, Mokka et al. 2013b, Furnes et al. 2014), with only 1 population-based study focusing on causes of revision resulting from specific combinations of acetabular and femoral components (Mokka et al. 2013b). We compared the 6-year revision risk for MoM bearings with that for MoP bearings in cementless stemmed THA. In addition, we studied different designs of stemmed MoM THAs and the causes of revision in a population-based follow-up study using data from the Nordic Arthroplasty Register Association (NARA).

Patients and methods

The background population included approximately 26 million inhabitants of Denmark (5.6 million), Norway (5.0 million), Sweden (9.5 million), and Finland (5.4 million).

Sources of data

Individual anonymized data relating to each patient who underwent THA as recorded in the arthroplasty registries of Denmark, Norway, Sweden, and Finland were merged into the NARA database (Herberts et al. 1989, Havelin et al. 2000, Lucht 2000, Puolakka et al. 2001). The data provided by each registry were transformed according to common definitions of minimal datasets required for this study (Havelin et al. 2009). Nationally, the primary THA data were linked to potential revision data for each patient and de-identified, including deletion of the national civil registration number, before inclusion in the NARA database. Data were treated with full confidentiality, and identification of patients at the individual level is not possible in this database.

Study population

The study population consisted of patients who received stemmed THA with cementless stem and cementless cup with either MoM or MoP bearings, and with one of the following diagnoses: primary osteoarthritis (OA), femoral head osteonecrosis, inflammatory arthritis, or sequelae from childhood hip disorder. In MoP bearings, the polyethylene liner could be made of either ultra-high-molecular-weight polyethylene or (highly) cross-linked polyethylene.

Since the registration of THA bearings was common for all databases in 2002, our study population consisted of patients who underwent primary THA surgery between January 1, 2002 and December 31, 2010 (Figure 1). When a patient received bilateral THA operations, only the first was included in the study due to the statistical assumption of independent observations (Ranstam et al. 2011). Of the 2,331 patients excluded

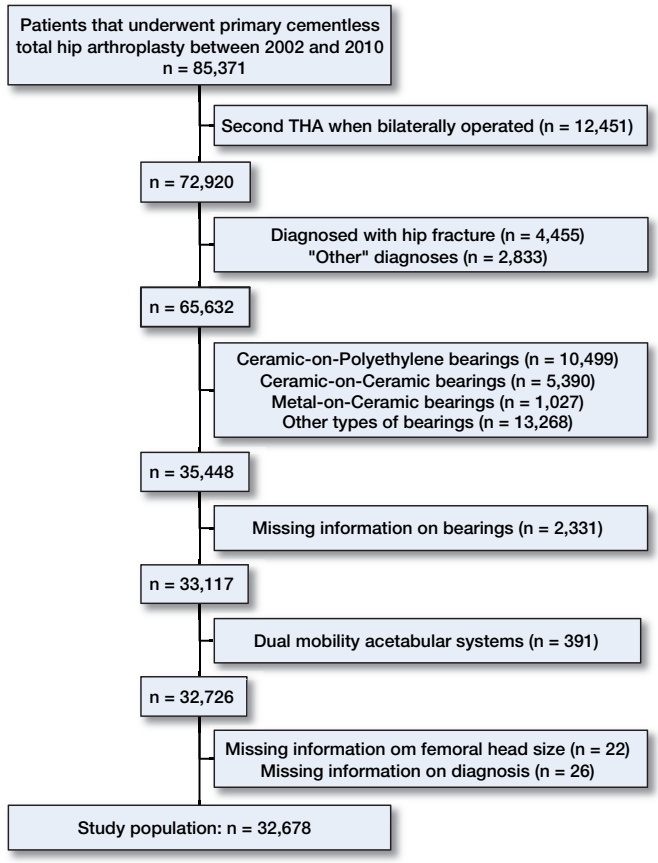

Figure 1. Inclusion of patients in the study population.

with unregistered pairs of bearings, 505 of these had a ceramic head and 114 had a ceramic liner, eliminating the possibility of having MoM or MoP bearings. Thus, 1,712 patients with an unambiguous couple of bearings could potentially have either MoM or MoP bearings.

Of the 309,944 primary stemmed THAs in the NARA database performed from 2002 through 2010, 32,678 primary cementless stemmed THAs (11,567 MoM and 21,111 MoP) with complete information on sex, age group, diagnosis, year of surgery, and femoral head size were included in the study.

Statistics

Patients entered the study on the date of primary surgery and were followed until revision, death, emigration, or the end of study period (December 31, 2011), whichever came first. Revision was defined as a new surgical intervention including partial or complete removal or exchange of the implant. Revision for any reason was considered to be the primary endpoint and aseptic loosening, dislocation, and all other causes of revision were considered to be secondary endpoints. Time since operation was chosen as the underlying time scale in the time-to-event analysis, and death was considered to be a competing risk.

For the presentation of demographic data and procedure characteristics, descriptive statistics were used. The chi-square test was used to compare proportions, and the 2-sample Wilcoxon rank-sum test was used to compare ages and follow-up times between groups because of skewness. For ages and follow-up times, medians and interquartile ranges (IQRs) are presented. Revision rates (per 100 person-years) were assessed for each group of bearings or specific components as the number of revisions divided by the total risk time. Cumulative incidence curves were computed using the Aalen-Johansen estimator to allow for competing risk. Competing risk analyses were used, as the Kaplan-Meier estimator is known to overestimate revision rates (Gillam et al. 2010, National Joint Registry for England and Wales 2011). The cumulative incidence curves were ended when the number of patients at risk was below 50, due to the expected statistical uncertainty in the estimates.

Pseudo-values based on the Aalen-Johansen estimator were calculated at the prespecified time points 1, 2, 3, 4, 5, and 6 years. The pseudo-observation is a transformation of the time-to-event data in which each time-to-event observation is represented by the amount of information it contains when the observation is deleted from the dataset. Once the pseudo-observations have been computed, a model for relative risk (RR) for the uncensored data was applied via a generalized estimating equation. In practice, the generalized estimating equation can be obtained in a generalized linear model for the pseudo-values with normal distribution and robust variance estimation (Klein et al. 2007, Parner and Andersen 2010). Adjustments were made for sex, age, and diagnosis for primary THA when comparing MoM bearings and MoP bearings.

Subanalyses were performed for postoperative follow-up at 1 to 6 years. We performed stratified analyses on sex and age, on OA as diagnosis, and on different component designs focusing on the most prevalent cups and the most prevalent pairs of cups and stems. We also performed stratified analyses on component designs within the MoM group, with the most frequently used acetabular component and combination of acetabular and femoral components as reference. The stratified analyses within the MoM group were adjusted for sex, age, diagnosis for primary THA, and femoral head size (categorized as ≤ 37 mm, 38–39 mm, 40–43 mm, 44–47 mm, 48–51 mm, and ≥ 52 mm). Furthermore, a stratified analysis on femoral head size was performed within the MoM group. All analyses were stopped at 6 years of follow-up as one acetabular component (Conserve Plus) had a maximum follow-up period of 6 years. When performing stratified analyses, each stratum had at least 10 registered revisions.

In August 2010, DePuy Orthopaedics voluntarily recalled the Articular Surface Replacement (ASR) acetabular component used in both hip resurfacing arthroplasty and THA, due to a 5-year revision rate of approximately 12% for the ASR Hip Resurfacing System and approximately 13% for the ASR XL Acetabular System (DePuy Companies 2013). Thus, after exclusion of patients with the ASR acetabular component, additional regression analysis as described above was performed to determine the RR of any revision for MoM THA compared to MoP THA at 6 years of follow-up, with adjustment for sex, age, and diagnosis for primary THA. Also, stratified analysis on femoral head size was performed after exclusion of ASR patients, comparing risk of any revision at 6 years of follow-up within the MoM group.

Any p-value < 0.05 was considered significant, and 95% confidence intervals (CIs) were computed. Statistical analyses were carried out using Stata statistical software, release 13.1.

Results

Description of the study population

The characteristics of the study population are presented in Table 1. Of the whole population, 35% had MoM THAs and 65% had MoP THAs. The proportion of males who had MoM THAs was higher than the proportion who had MoP THAs. The median patient ages in the 2 groups were 62 (56–69) years for MoM and 62 (56–68) years for MoP (p < 0.001). The most common diagnosis for THA was OA accounting for 92% of all MoM bearings and 89% of all MoP bearings (p < 0.001). In the MoM group, 3% were diagnosed with sequelae from childhood hip disorders. The corresponding figure in the MoP group was 6% (p < 0.001). Regarding femoral head size, 92% of MoM THAs had 38-mm or larger femoral heads, and 97% of MoP THAs had head sizes smaller than 38 mm (p < 0.001). From 2002 through 2006, 23% received MoM bearings and 35% received MoP bearings, whereas from 2007 through 2010 77% received MoM bearings and 65% received MoP bearings (p < 0.001). The 3 most frequently used design combinations of acetabular and femoral components in the MoM group were Recap/Bi-Metric (43%), M2a/Bi-Metric (21%), and Pinnacle/Corail (8%), and they were Trilogy/Bi-Metric (17%), Trilogy/CLS Spotorno (13%), and Mallory-Head/Bi-Metric (8%) in the MoP group. Most MoM THAs were performed in Finland (72%) and Denmark (23%), whereas MoP THAs were mainly performed in Denmark (57%) and Sweden (36%) (Table 1). The median follow-up was 3.6 (2.4–4.8) years for MoM bearings and 3.4 (2.0–5.8) years for MoP bearings (p < 0.001).

Risk of revision for any reason

During the study period, we registered 1,236 first-time revisions following primary THA (3.8% of 32,678 patients): 4.1% for MoM bearings (470 of 11,567 patients) and 3.6% for MoP bearings (766 of 21,111 patients), corresponding to revision rates of 1.11 (CI: 1.0–1.2) per 100 person-years for MoM THA and 0.91 (CI: 0.85–0.97) per 100 person-years for MoP THA. The cumulative incidence of any revision was 7.0% (CI: 6.0–8.1) for MoM and 5.1% (CI: 4.7–5.6) for MoP at 8 years of follow-up (Figure 2). The RR of revision for any reason was statistically significantly higher for MoM after 5 and 6 years of follow-up (Table 2, see Supplementary data).

Table 1. Patient- and surgery-related characteristics for the patients who received cementless total hip arthroplasty with metal-on-metal (MoM) bearings or metal-on-polyethylene (MoP) bearings. Values are numbers of patients and percentages (%) within each group

	MoM n = 11,567	MoP n = 21,111	p-value
Sex			< 0.001
Female	5,227 (45)	10,689 (51)	
Male	6,340 (55)	10,422 (49)	
Age groups (years)			< 0.001
< 40	282 (2)	576 (3)	
40–49	969 (8)	1,768 (8)	
50–59	3,188 (28)	5,578 (27)	
60–69	4,712 (41)	8,249 (39)	
70–79	2,200 (19)	4,007 (19)	
≥ 80	216 (2)	933 (4)	
Diagnosis			< 0.001
Primary OA	10,595 (92)	18,694 (89)	
Femoral head osteonecrosis	232 (2)	631 (3)	
Arthritis	404 (3)	427 (2)	
Childhood hip disorders	336 (3)	1,359 (6)	
Femoral head size (mm)			< 0.001
≤ 27	7 (0)	221 (1)	
28–31	118 (1)	10,374 (49)	
32–35	117 (1)	5,842 (28)	
36–37	707 (6)	4,068 (19)	
38–39	2,317 (20)	17 (0)	
40–43	679 (6)	403 (2)	
44–47	2,431 (21)	44 (0)	
48–51	3,124 (27)	38 (0)	
≥ 52	2,067 (18)	104 (1)	
Year of surgery			< 0.001
2002	17 (0)	484 (2)	
2003	39 (0)	1,394 (7)	
2004	109 (1)	1,647 (8)	
2005	887 (8)	1,867 (9)	
2006	1,641 (14)	2,097 (10)	
2007	2,305 (20)	2,385 (11)	
2008	2,691 (23)	2,837 (13)	
2009	2,357 (21)	3,661 (17)	
2010	1,521 (13)	4,739 (23)	
Country			< 0.001
Denmark	2,636 (23)	12,103 (57)	
Norway	88 (1)	1,141 (6)	
Sweden	454 (4)	7,597 (36)	
Finland	8,389 (72)	270 (1)	

Stratified analyses: risk of revision for any reason

Compared to MoP THA, at 6-year follow-up MoM THA had a higher risk of revision for any reason in women less than 60 years of age (1.8, CI: 1.3–2.4) and women who were 60 years old or more (1.9, CI: 1.5–2.4), in men less than 60 years old (1.4, CI: 1.1–1.9), and in patients who were diagnosed with OA of the hip (1.5, CI: 1.3–1.8). The revision risk was similar for MoM THA and MoP THA in men who were 60 years old or more.

For different designs of acetabular components in MoM THAs at 6-year follow-up, the RR of revision for any reason was higher for the ASR cup, for the Conserve Plus cup, and for "other" designs of cups than for the cups used in all the MoP THAs (Figure 3 and Table 3, see Supplementary data). The MoM cup/stem combinations of ASR/Summit, ASR/Corail, and "other" had statistically significantly higher RR of revision for any reason than MoP THAs in general (Figure 4 and Table 3, see Supplementary data). When comparing acetabular components in the MoM group with the most frequently used as reference (Recap), the ASR, Conserve Plus, and "other" cups had significantly higher revision risk at 6-year follow-up (Table 4, see Supplementary data). In the cementless stemmed MoM THAs, the cup and stem combinations of M2a/Bi-Metric, ASR/Summit, ASR/Corail, and other combinations of components had significantly higher RR of revision for any reason than the Recap/Bi-Metric combination (Table 4, see Supplementary data).

For Pinnacle, 75% had femoral head sizes smaller than 38 mm, and 86% of the M2a cups had femoral head sizes of 38–39 mm. For Recap, ASR, Birmingham, Durom, and Conserve Plus acetabular components, the vast majority had femoral head sizes of 44 mm or larger (95%, 93%, 87%, 87%, and 89% respectively) (Table 5, see Supplementary data). In the MoM group and with femoral head size of 38–39 mm as reference, a significantly higher RR of revision for any reason at 6 years was found for femoral head sizes between 44 and 47 mm. Other head sizes did not reach statistical significance in similar comparisons (Table 6).

Causes of revision

The cementless MoM THAs had a higher proportion of revisions due to aseptic loosening ($p < 0.001$) and "other" causes ($p = 0.03$). We found a lower frequency of revision due to dislocation for MoM THA than for MoP THA, irrespective of femoral head size ($p < 0.001$). At 6-year follow-up, the RR of revision due to dislocation was lower for MoM bearings than for MoP bearings (0.27, CI: 0.19–0.39), but the RR of revision due to aseptic loosening (5.5, CI: 3.8–7.9) and all other causes of revision (1.2, CI: 1.0–1.5) was higher for MoM bearings than for MoP bearings (Table 7, see Supplementary data).

For patients with the ASR acetabular component, 10% (75 of 759 patients) had revision surgery because of aseptic loosening, 1.3% (10 of 759 patients) had revision because of deep infection, and 0.9% (7 of 759 patients) had revision because of pain.

Exclusion of the ASR acetabular component

After exclusion of 759 patients with the ASR acetabular component, the cumulative incidence of revision for MoM THA at 8-year follow-up was 5.0% (CI: 4.3–5.8). Comparing MoM THA with MoP THA, the adjusted RR of revision for any reason at 6-year follow-up was 1.1 (CI: 0.97–1.3). Repeated analysis with different femoral head sizes did not show any significant difference in RR of revision for any reason at 6-year follow-up for any head size compared to 38–39 mm (Table 6).

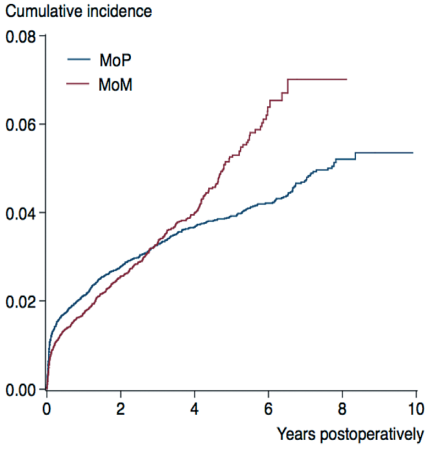

Figure 2. Cumulative incidence for any revision of cementless total hip arthroplasty with metal-on-metal (MoM) bearings and metal-on-polyethylene (MoP) bearings.

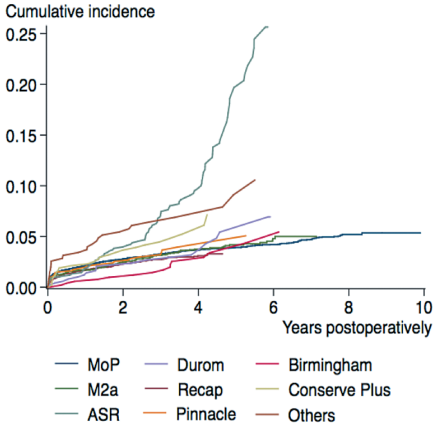

Figure 3. Cumulative incidence for revision (for any reason) of metal-on-polyethylene (MoP) total hip arthroplasty (THA) and specific designs of cementless acetabular components in stemmed THA with metal-on-metal bearings.

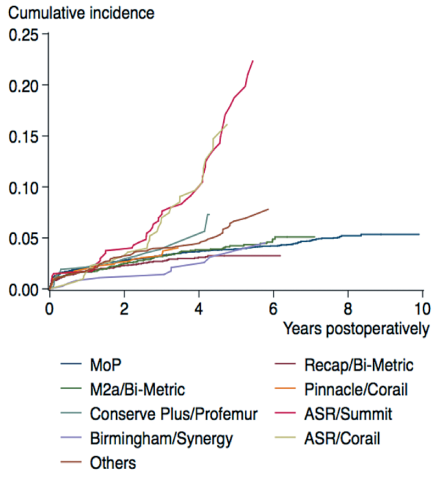

Figure 4. Cumulative incidence for revision (for any reason) of metal-on-polyethylene (MoP) total hip arthroplasty (THA) and combinations of specific designs of cementless acetabular and femoral components in stemmed THA with metal-on-metal bearings.

Discussion

In this population-based study from the NARA database, the RR of revision for any reason at 6 years of follow-up was 49% higher for MoM THA than for MoP THA, whereas the RR of revision for any reason was similar for both after exclusion of ASR acetabular components. There was a high risk of revision with prosthetic design combinations of ASR/Summit and ASR/Corail relative to MoP THA. In all patients with MoM THA, we found a higher risk of revision for femoral head sizes between 44 and 47 mm than for a femoral head size of 38–39 mm.

Risk of revision for any reason

In the Australian Orthopaedic Association National Joint Replacement Registry (AOA NJRR), the cumulative percentage of revision of MoM THA was 9.6 (CI: 9.2–10.0) at 5 years and 15.5 (CI: 14.8–16.2) at 10 years (Australian Orthopaedic Association 2013), which is more than the cumulative incidence of revision at 8 years found in our study. The lower incidence found by us could be due to differences in the use of specific component designs. In the present study, the Recap constituted 47% of all acetabular components in the MoM

Table 6. Median follow-up and revision rate for different sizes of the femoral head used in cementless stemmed total hip arthroplasty (THA) with metal-on-metal (MoM) bearings. Crude and adjusted relative risk (RR) of revision for any reason with 95% confidence intervals (CIs) at 6-year follow-up

	No. (%)	Median follow-up (IQR)	Any revision (n)	Risk time, years	Revision rate per 100 years (95% CI)	Crude RR (95% CI)	Adjusted RR (95% CI)
All MoM THAs							
≤ 37	949 (8)	3.3 (2.2–4.3)	46	3,313	1.39 (1.04–1.85)	1.48 (0.98–2.25)	1.48 (0.95–2.32)
38–39	2,317 (20)	4.9 (3.3–6.1)	93	10,673	0.87 (0.71–1.07)	1 (ref.)	1 (ref.)
40–43	679 (6)	3.0 (2.1–4.3)	20	2,189	0.91 (0.59–1.42)	1.07 (0.65–1.77)	1.14 (0.65–2.02)
44–47	2,431 (21)	3.4 (2.3–4.5)	128	8,443	1.52 (1.27–1.80)	1.77 (1.27–2.48)	1.68 (1.17–2.40)
48–51	3,124 (27)	3.3 (2.3–4.5)	108	10,668	1.01 (0.84–1.22)	1.27 (0.90–1.80)	1.38 (0.93–2.04)
≥ 52	2,067 (18)	3.2 (2.3–4.4)	75	6,917	1.08 (0.86–1.36)	1.14 (0.79–1.62)	1.33 (0.92–1.93)
MoM THAs after exclusion of patients having the ASR acetabular component							
≤ 37	938 (9)	3.3 (2.2–4.3)	45	3,257	1.38 (1.03–1.85)	1.38 (0.91–2.08)	1.40 (0.90–2.19)
38–39	2,314 (21)	4.9 (3.3–6.1)	93	10,661	0.87 (0.71–1.07)	1 (ref.)	1 (ref.)
40–43	643 (6)	3.0 (2.1–4.2)	15	2,049	0.73 (0.44–1.21)	0.74 (0.44–1.26)	0.75 (0.42–1.32)
44–47	2,136 (20)	3.4 (2.3–4.4)	83	7,302	1.14 (0.92–1.41)	1.06 (0.76–1.49)	1.00 (0.68–1.48)
48–51	2,866 (26)	3.3 (2.3–4.4)	75	9,696	0.77 (0.62–0.97)	0.83 (0.58–1.18)	0.90 (0.59–1.39)
≥ 52	1,918 (18)	3.2 (2.2–4.3)	59	6,365	0.93 (0.72–1.20)	0.83 (0.58–1.19)	0.97 (0.66–1.43)

group and the ASR only 7% of them, whereas the ASR cup was used far more frequently in Australia. In contrast, the Recap cup with the second lowest revision rate at 7 years was used to a lesser extent (Australian Orthopaedic Association 2013). In both the NARA database and the AOA NJRR, the ASR cup had the highest cumulative incidence of revision but was used with different frequency, which could explain the different revision rates in these 2 registries. A study from the National Joint Registry of England and Wales (Smith et al. 2012) excluded the ASR implants from the analysis and found an overall 5-year revision rate of 6.2% (CI: 5.8–6.6) for MoM THA, which was higher than the 8-year cumulative revision rate found in our study after exclusion of the ASR implant. This could also be caused by differences in use of certain component designs and implant combinations, and also differences in follow-up and surgical technique.

Stratified analyses: risk of revision for any reason

We found that the cumulative incidence of revision of the ASR acetabular component increased to more than 25% at 5.8 years. The ASR cup had similar cumulative incidence of revision in the AOA NJRR, and Langton et al. (2011) found a 6-year failure rate of 48.8% for the ASR cup used with a conventional stem. In a recent study, the cumulative 7-year survivorship was 38% (CI: 33–44) for MoM THA with the ASR cup with femoral head sizes smaller than 50 mm. The most common cause of revision was ARMD, accounting for 86% of revisions, and use of the Corail stem had an increased risk of ARMD (Reito et al. 2013). Although we have no information of the presence of ARMD in our study, patients with the ASR/Summit combination had a much higher cumulative incidence of revision than patients with the ASR/Corail combination, which may be explained by the shorter follow-up for ASR/Corail. In the present study, ASR components were mainly revised due to aseptic loosening.

The acetabular component with the best survivorship in our study was the Recap cup, with a cumulative incidence of revision of 3.4% (CI: 2.8–4.0) at 6-year follow-up. This is slightly better than reported in Australia, where the Recap acetabular component had the lowest cumulative incidence of revision (6.3%, CI: 4.4–8.9) at 7 years among monobloc cups (Australian Orthopaedic Association 2013). In a recent study with a small series of Recap/M2a-magnum LDH MoM THAs including 80 hips with a mean follow-up of 6 years, 11 hips were considered to have definite ARMD, and revision had been performed in 3 of these cases (Mokka et al. 2013a). Another 32 hips were considered to have probable or possible ARMD. This indicates a high prevalence of ARMD in patients with the Recap cup after medium-term follow-up, with the possible consequence of increasing revision rates due to metal-related pathology with longer follow-up.

The Pinnacle acetabular component was the only non-monobloc cup analyzed separately when we performed stratified analyses. The cumulative incidence of revision of the Pinnacle cup of 5.1% (CI: 2.9–8.2) found in our study at 5 years of follow-up was similar to that found in Australia where the 5-year revision risk was 3.9% (CI: 2.2–7.0) for Pinnacle/S-Rom and 4.6% (CI: 3.6–5.8) for Pinnacle/Articul-Eze (Australian Orthopaedic Association 2013). In England and Wales, the 5-year revision rate following Pinnacle/Corail cementless THA with MoM bearings was 4.2% (99% CI: 2.3–6.0) (Jameson et al. 2013). The adjusted hazard rate of revision for this implant combination was 1.9 (99% CI: 1.4–2.7) when compared to MoP bearings (Jameson et al. 2013). In the present study, the RR of revision of the Pinnacle/Corail MoM THA was similar to that of MoP THA.

Femoral head size is a major risk factor for revision of MoM THA, with increasing revision rates with increasing head size (Graves et al. 2011, Smith et al. 2012, Australian Orthopaedic Association 2013). When we compared MoM THA with different femoral head sizes to MoM THA with 38- to 39-mm heads, the RR of revision for any revision was statistically significantly higher for head sizes of 44–47 mm. This femoral head size was the most prevalent with the ASR cup. After exclusion of patients with the ASR implant, only femoral head sizes smaller than 38 mm had higher RR of revision than head sizes of 38–39 mm, and the larger head sizes had similar or even lower RR of revision when compared to 38–39 mm—although the differences were not significant. As the Pinnacle cup had the majority of the smallest head sizes and revision risk changed when the ASR implant was excluded, it appears that component design is an important factor when interpreting revision risk with different femoral head sizes in MoM THA.

Causes of revision

The most common cause of revision of MoM THA at 8 years of follow-up in Australia was metal-related pathology, followed by aseptic loosening and infection for femoral head sizes larger than 32 mm (Australian Orthopaedic Association 2013). It is not possible to identify revisions performed for "metal-related pathology" in the NARA database, but it is possible that some of these MoM-bearing complications are registered as revisions performed for "other" reasons. In the study from the National Joint Registry of England and Wales, the most common reason for revision of cementless stemmed MoM THA was aseptic loosening (Smith et al. 2012). In our study, the frequency of revision due to aseptic loosening and "other" causes was higher for MoM THA than for MoP THA. The frequency and RR of revision due to dislocation was, however, lower for MoM bearings than for MoP bearings. In a recent study from the Finnish Arthroplasty Register, the RR of revision due to dislocation was 0.09 (CI: 0.05–0.17) for head sizes larger than 36 mm compared to 28 mm (Kostensalo et al. 2013). Thus, the low risk of revision of MoM THA due to dislocation might be explained by the fact that MoM THAs in that study mainly had head sizes larger than 37 mm.

Methodological considerations

Some strengths of the present study were the population-based design with prospective collection of data and a large sample size. The complete follow-up of the study population limited possible selection bias. The study also had several limitations that should be considered when interpreting the results. The exclusion of 1,712 patients—who could have had either MoM or MoP bearings but were registered without unambiguous information on bearings—may have led to information bias. We analyzed the 2 worst-case scenarios by assuming that all 1,712 THAs had received either MoM or MoP bearings. Inclusion of all 1,712 THAs in the MoM group gave an adjusted RR of revision for any reason at 6-year follow-up of 1.4 (CI: 1.3–1.6) for MoM THA vs. MoP THA. Inclusion of all 1,712 THAs in the MoP group gave an adjusted RR of revision for any reason at 6-year follow-up of 1.4 (CI: 1.3–1.6) for MoM THA vs. MoP THA. Thus, in both cases, the risk of revision would have been higher for MoM bearings than for MoP bearings, as was found after exclusion of the patients. The exclusion of the 48 patients with unregistered information on diagnosis or femoral head size can be assumed to have had no influence on the results of the study, due to the large study population.

The distribution of THAs with MoM and MoP bearings varied between countries. Finland and Denmark contributed the majority of MoM THAs, and Sweden and Denmark contributed the majority of MoP THAs. From previous studies (Havelin et al. 2009, Makela et al. 2014), we know that there is variation in outcome in terms of implant survival between the Nordic countries, which may in part be caused by differences in demography and implant selection. Most of the implants included in this study were, however, used in several countries. We also adjusted for sex, age, and diagnosis, and performed subanalyses on specific implants. Even so, any differences between countries caused by factors that not were captured in the NARA database could have influenced our results, but it was not our aim to evaluate differences between countries. Since the healthcare systems, patient populations, and treatment traditions in the Nordic countries are rather homogenous, we believe that any influence of skewed inclusion of patients from the countries involved in this study would be small.

Although we adjusted for several confounders, there is still the possibility of unidentified confounding. The regression model used to compare MoM THA with MoP THA did not include adjustment for femoral head size, despite the fact that it is a well-documented risk factor (Smith et al. 2012, Australian Orthopaedic Association 2013): As 92% of MoM THAs had femoral head sizes greater than 37 mm and 97% of MoP THAs had head sizes smaller than 38 mm, femoral head size could be considered to be a proxy for the bearings used in THA, and it was therefore not adjusted for in the model. Furthermore, the NARA database does not contain any information on potential confounders such as blood concentrations of chromium and cobalt, comorbidity, height, weight, BMI, or physical activity before or after surgery. In addition, we had no information from any radiographic examinations or magnetic resonance imaging, either for revised or unrevised hips, and we could not account for silent, unrevised metal reactions.

Another limitation was the short follow-up, resulting in a high proportion of revisions due to surgical and technical errors. Registry studies are unable to detect silent, unrevised metal reactions, and with longer follow-up, a change in causes of revision may result in an increased proportion of revisions related to mechanical wear and ARMD. Also, the number of revisions was low, and the sensitivity to random effects of single revision cases could thereby be increased when performing stratified analyses. Furthermore, the revision causes registered have not been validated in the national registries contributing to the NARA database, and revisions due to "metal-related pathology" such as ARMD have not been registered.

Conclusion

We found a higher RR of revision for any reason at 6-year follow-up for MoM THA than for MoP THA, but after exclusion of patients with the ASR acetabular component, the risk of revision was similar between the 2 groups of bearings. At 6-year follow-up, there was a much higher risk of revision with prosthetic design combinations of ASR/Summit and ASR/Corail than for MoP THA, whereas the risk of revision was similar for the Recap/Bi-Metric combination and for MoP THA. In MoM THA, we found a higher risk of revision for femoral head sizes between 44 and 47 mm than for 38–39 mm. After exclusion of patients with the ASR acetabular component, the risk of revision was similar for different femoral head sizes in MoM THA.

We recommend that stemmed LDH MoM bearings should not be used until further studies with longer follow-up are performed to identify the risk of complications.

Supplementary data

Tables 2–5, and 7 are available at Acta's website (www.actaorthop.org), identification number 7928.

The study idea was conceived by CV, ABP, KM, and SO. All the authors contributed to the development and design of the study. ABP collected the data. Analyses were directed by CV, ABP, JK, and SO and were performed by CV. All the authors participated in interpretation and discussion of the results. CV wrote the initial draft of the manuscript. All the authors critically revised the manuscript for intellectual content.

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Supplementary article data

Increased risk of revision of cementless stemmed total hip arthroplasty with metal-on-metal bearings

Data from the Nordic Arthroplasty Register Association

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Table 2. Crude and adjusted relative risk (RR) of revision for any reason, with 95% confidence intervals (CIs), in total hip arthroplasty (THA) with metal-on-metal (MoM) and metal-on-polyethylene (MoP) bearings. MoP bearings were considered the "standard" for THAs

	Patients at the beginning of the year (n)	Revisions performed within the year (%)	Crude RR (95% CI)	Adjusted RR (95% CI)
At 1-year follow-up (0–1 year postoperatively)				
MoM	11,567	198 (1.7)	0.81 (0.68–0.95)	0.83 (0.70–1.00)
MoP	21,111	448 (2.1)	1 (ref.)	1 (ref.)
At 2-year follow-up (1–2 years postoperatively)				
MoM	11,295	91 (0.8)	0.92 (0.80–1.06)	0.94 (0.81–1.09)
MoP	20,495	123 (0.6)	1 (ref.)	1 (ref.)
At 3-year follow-up (2–3 years postoperatively)				
MoM	9,640	66 (0.7)	1.01 (0.89–1.15)	1.02 (0.89–1.18)
MoP	15,653	72 (0.5)	1 (ref.)	1 (ref.)
At 4-year follow-up (3–4 years postoperatively)				
MoM	7,251	44 (0.6)	1.09 (0.96–1.23)	1.10 (0.96–1.26)
MoP	11,976	45 (0.4)	1 (ref.)	1 (ref.)
At 5-year follow-up (4–5 years postoperatively)				
MoM	4,638	49 (1.1)	1.32 (1.17–1.50)	1.37 (1.19–1.57)
MoP	9,137	22 (0.2)	1 (ref.)	1 (ref.)
At 6-year follow-up (5–6 years postoperatively)				
MoM	2,466	18 (0.7)	1.44 (1.27–1.63)	1.49 (1.30–1.71)
MoP	6,811	19 (0.3)	1 (ref.)	1 (ref.)

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Table 3. Median follow-up and revision rate for different designs of acetabular components in cementless metal-on-metal (MoM) total hip arthroplasty (THA). Crude and adjusted relative risk (RR) of revision for any reason at 6-year follow-up with 95% confidence intervals (CIs), compared to metal-on-polyethylene (MoP) bearings

	n = 32,678 (%)	Median follow-up (IQR)	Any revision (n)	Risk time, years	Revision rate per 100 years (95% CI)	Crude RR (95% CI)	Adjusted RR (95% CI)
Brands of acetabular components in MoM THAs compared to acetabular components in MoP THAs							
All MoP acetabular components	21,111 (65)	3.4 (2.0–5.8)	766	84,404	0.91 (0.85–0.97)	1 (ref.)	1 (ref.)
Recap	5,384 (16)	3.3 (2.3–4.5)	152	18,172	0.84 (0.71–0.98)	0.91 (0.78–1.07)	0.96 (0.81–1.15)
M2a	2,652 (8)	4.7 (3.0–6.0)	103	11,671	0.88 (0.73–1.07)	1.13 (0.86–1.48)	1.20 (0.91–1.58)
Pinnacle	925 (3)	2.9 (2.0–3.9)	31	2,779	1.12 (0.78–1.59)	1.19 (0.88–1.62)	1.20 (0.86–1.66)
ASR	759 (2)	3.9 (2.8–4.7)	100	2,872	3.48 (2.86–4.24)	5.89 (4.72–7.34)	6.38 (4.99–8.15)
Birmingham	521 (2)	4.0 (2.9–5.0)	15	2,093	0.72 (0.43–1.19)	1.23 (0.70–2.17)	1.34 (0.73–2.45)
Durom	497 (2)	3.2 (1.8–5.0)	18	1,692	1.06 (0.67–1.69)	1.50 (0.91–2.47)	1.50 (0.88–2.57)
Conserve Plus	478 (1)	3.3 (2.7–4.0)	25	1,555	1.61 (1.09–2.38)	1.83 (1.25–2.67)	1.70 (1.14–2.54)
Others	351 (1)	3.6 (2.8–4.6)	26	1,368	1.90 (1.29–2.79)	2.41 (1.57–3.70)	2.38 (1.45–3.92)
Combinations of brands of acetabular and femoral components in MoM THAs compared to MoP THAs							
All MoP THAs	21,111 (65)	3.4 (2.0–5.8)	766	84,404	0.91 (0.85–0.97)	1 (ref.)	1 (ref.)
Recap/Bi-Metric	4,990 (15)	3.2 (2.2–4.4)	138	16,652	0.83 (0.70–0.98)	0.90 (0.76–1.06)	0.96 (0.80–1.15)
M2a/Bi-Metric	2,407 (7)	4.8 (3.0–6.1)	95	10,683	0.89 (0.73–1.09)	1.16 (0.87–1.53)	1.25 (0.93–1.67)
Pinnacle/Corail	910 (3)	2.9 (2.0–3.9)	31	2,723	1.14 (0.80–1.62)	1.21 (0.89–1.65)	1.25 (0.90–1.74)
Conserve Plus/Profemur	418 (1)	3.2 (2.7–3.9)	18	1,315	1.37 (0.86–2.17)	1.53 (1.00–2.33)	1.47 (0.95–2.27)
ASR/Summit	401 (1)	3.9 (2.8–4.8)	56	1,540	3.64 (2.80–4.72)	6.35 (4.74–8.49)	7.27 (5.18–10.2)
Birmingham/Synergy	369 (1)	4.2 (3.4–5.1)	10	1,566	0.64 (0.34–1.19)	1.07 (0.51–2.24)	1.26 (0.56–2.84)
ASR/Corail	307 (1)	3.7 (2.7–4.5)	35	1,117	3.13 (2.25–4.36)	5.00 (3.54–7.07)	5.17 (3.53–7.56)
Others	1,765 (6)	3.7 (2.5–4.9)	87	6,606	1.32 (1.07–1.63)	1.77 (1.39–2.26)	1.75 (1.29–2.36)

Table 4. Stratified analyses with crude and adjusted relative risk (RR) of revision for any reason with 95% confidence intervals (CIs) at 6-year follow-up among total hip arthroplasties (THAs) with metal-on-metal (MoM) bearings

	n = 11,567 (%)	Any revision (n)	Crude RR (95% CI)	Adjusted RR (95% CI)
Brands of acetabular components in MoM THAs. As Recap was the most prevalent, it was used as reference				
Recap	5,384 (47)	152	1 (ref.)	1 (ref.)
M2a	2,652 (23)	103	1.24 (0.94–1.66)	1.82 (0.97–3.43)
Pinnacle	925 (8)	31	1.31 (0.94–1.82)	1.41 (0.60–3.32)
ASR	759 (7)	100	6.45 (5.03–8.28)	6.73 (4.95–9.14)
Birmingham	521 (4)	15	1.35 (0.76–2.41)	1.43 (0.73–2.81)
Durom	497 (4)	18	1.65 (0.99–2.75)	1.57 (0.83–2.95)
Conserve Plus	478 (4)	25	2.00 (1.35–2.97)	1.77 (1.07–2.92)
Others	351 (3)	26	2.64 (1.70–4.11)	2.57 (1.37–4.81)
Combination of brands of acetabular and femoral components in MoM THAs. The combination Recap/Bi-Metric was the most prevalent and was therefore used as reference				
Recap/Bi-Metric	4,990 (43)	138	1 (ref.)	1 (ref.)
M2a/Bi-Metric	2,407 (21)	95	1.29 (0.95–1.76)	2.11 (1.14–3.89)
Pinnacle/Corail	910 (8)	31	1.35 (0.97–1.88)	1.44 (0.49–4.22)
Conserve Plus/Profemur	418 (4)	18	1.71 (1.10–2.65)	1.57 (0.92–2.70)
ASR/Summit	401 (3)	56	7.09 (5.17–9.72)	8.15 (5.06–13.1)
Birmingham/Synergy	369 (3)	10	1.19 (0.56–2.53)	1.36 (0.53–3.51)
ASR/Corail	307 (3)	35	5.59 (3.88–8.06)	5.24 (3.39–8.09)
Others	1,765 (15)	87	1.98 (1.51–2.60)	1.95 (1.22–3.10)

Table 5. Distribution of femoral head size for different designs of acetabular components. Values are numbers of patients and percentages (%) within each acetabular component

	Femoral head size, mm						
	≤ 37	38–39	40–43	44–47	48–51	≥ 52	Total
Recap	23 (0)	24 (0)	268 (5)	1,487 (28)	2,116 (40)	1,466 (27)	5,384
M2a	22 (1)	2,283 (86)	3 (0)	76 (3)	150 (6)	118 (4)	2,652
Pinnacle	695 (75)	1 (0)	196 (21)	25 (3)	6 (1)	2 (0)	925
ASR	14 (2)	3 (0)	37 (5)	298 (39)	258 (34)	149 (20)	759
Birmingham	3 (1)	1 (0)	63 (12)	184 (35)	179 (34)	91 (18)	521
Durom	17 (3)	3 (1)	46 (9)	156 (31)	172 (35)	103 (21)	497
Conserve Plus	4 (1)	0 (0)	50 (10)	146 (31)	184 (38)	94 (20)	478
Others	171 (49)	2 (1)	16 (5)	59 (17)	59 (16)	44 (12)	351
Total	949 (8)	2,317 (20)	679 (6)	2,431 (21)	3,124 (27)	2,067 (18)	11,567

Table 7. Main indications for total hip arthroplasty (THA) revisions. For each type of THA bearing, the number and percentage (%) of the total number of THAs for each specific cause of revision is given. Bearings included metal-on-metal (MoM) and metal-on-polyethylene (MoP)

	MoM n = 470 (%)	MoP n = 766 (%)	p-value
Aseptic loosening	218 (1.9)	121 (0.6)	< 0.001
Deep infection	66 (0.6)	127 (0.6)	0.7
Periprosthetic femoral fracture	57 (0.5)	122 (0.6)	0.3
Dislocation	39 (0.3)	276 (1.3)	< 0.001
Pain only	19 (0.2)	28 (0.1)	0.5
Other	71 (0.6)	92 (0.4)	0.03

Study III

Are different types of bearings and noises from total hip arthroplasty related to quality of life postoperatively?

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ABSTRACT

Background and purpose

Patient-reported outcome (PRO) is recognized as a very important tool for evaluating the outcome and satisfaction after total hip arthroplasty (THA). We aimed to compare PRO scores from patients having ceramic-on-ceramic (CoC) and metal-on-metal (MoM) to scores from patients with metal-on-polyethylene (MoP) THA and examine the influence of noises from THA on PROs.

Patients and methods

We conducted a nationwide cross-sectional prospective questionnaire survey in a cohort of patients identified from the Danish Hip Arthroplasty Registry. The PROs included were: Hip Dysfunction and Osteoarthritis and Outcome Score (HOOS), EQ-5D-3L, EQ VAS, UCLA activity score, and questions about noises from the THA.

Results

The response rate was 85%, and the number of responders was 3,089. Of these, 45% had CoC, 17% MoM, and 38% MoP THA with a mean follow-up of 6.9, 5.1, and 6.9 years, respectively. No differences in mean subscale scores were found for CoC and MoM compared to MoP THA, except for CoC THA that had a lower mean HOOS Symptoms score than MoP THA. For the 3 types of bearings, PROs from patients with noisy THA were significantly lower when compared to silent MoP THA, except for noisy CoC and MoM THA that had the same mean UCLA activity score as silent MoP THA.

Interpretation

The most unfavorable PRO scores were found for noisy MoP THA, which may have a clinical significance.

INTRODUCTION

Pain and functional disability due to osteoarthritis (OA) of the hip joint can be treated effectively with a total hip arthroplasty (THA) (Rissanen et al. 1996). The outcome of THA has traditionally been assessed in prosthetic survivorship and complications rather than in patient-reported outcome (PRO). As patients and orthopaedic surgeons may assess outcome after THA differently, PROs have gained much more interest and are today recognized as very important tools for evaluating the outcome and satisfaction after THA (Rolfson et al. 2011, Wylde and Blom 2011).

Due to problems related to polyethylene wear particles (Jacobs et al. 1994), ceramic-on-ceramic (CoC) and metal-on-metal (MoM) have been introduced used as alternatives to metal-on-polyethylene (MoP) bearings. In population-based studies from hip arthroplasty registers, the medium-term survival for CoC THA equaled that for MoP THA. In contrast, medium-term survivorship for MoM THA was significantly lower, especially for specific component brands, when compared to MoP THA. The main revision cause for CoC THA was dislocation (1.2%) and for MoM THA aseptic loosening (1.9%) (Varnum et al. 2015a, Varnum et al. 2015b). As survival and revision causes differed for different types of bearings, one could question if also PROs were different between bearings in THA. To our best knowledge, only 1 study including 911 patients from a single center in United Kingdom examined the influence of different bearings on PROs at a mean follow-up of 29 months after index surgery. No significant relationship between bearings and PROs was observed (Smith et al. 2012). The study was, however, limited by the relatively small number of patients and the lack of generalizability.

An alternative outcome reported for THA is noises. For CoC bearings, the reported prevalence of squeaking was 4.2% in a meta-analysis (Owen et al. 2014), but other studies reported

prevalences from less than 1% (Capello et al. 2008) to 35.6% (Swanson et al. 2010). Also noises from MoM and MoP bearings have been reported (Jarrett et al. 2009, Bernasek et al. 2011), but only a few studies have reported the influence of noises on PROs and health-related quality of life (Restrepo et al. 2010, Sexton et al. 2011).

We therefore conducted a nationwide cross-sectional questionnaire survey in a cohort of patients registered in the Danish Hip Arthroplasty Registry (DHR). We examined the association between CoC, MoM, and MoP bearings and both generic and disease-specific PROs. Furthermore, we examined the prevalence and types of noises from the 3 types of bearings and the association of noises with postoperative PROs. We hypothesized that there was no difference in PRO for patients with different types of bearings.

PATIENTS AND METHODS

Approximately 5.6 million inhabitants live in Denmark. Every Danish citizen has a unique, 10-digit civil registration number, which allows unambiguous linkage between Danish medical and demographic databases (Frank 2000).

Data sources

The DHR, founded in 1995 (Lucht 2000), is a nationwide, population-based clinical database containing prospectively collected data on primary THAs and revisions. The DHR was validated in 2004 (Pedersen et al. 2004) and a validation process is carried out every year in relation to the annual report. Furthermore, the DHR has a coverage of 100% since all orthopaedic departments and private clinics report to the registry. Thus, 28 orthopaedic departments and 16 private clinics reported data on 9,410 primary THAs and 1,366 revisions in 2014 (Danish Hip Arthroplasty Registry 2015). The completeness of the DHR has been about 95% for both

primary procedures and revisions during the last many years compared to the National Patient Registry (NPR), which is considered the gold standard as departments are reimbursed from the authorities when reporting to the NPR.

The Civil Registration System (CRS) was established in 1968 (Pedersen et al. 2006). The CRS contains data on all changes in vital status for the entire Danish population, including changes in address, date of emigration, and date of death. The CRS also includes information whether persons have protection against inquiry from researchers or not.

The NPR was established in 1977 and contains data on all admissions and discharges from Danish hospitals, including diagnoses and surgical procedure codes. Since 1994, diagnoses have been classified according to the Danish version of the International Classification of Diseases, tenth edition. Based on data from the NPR, the Charlson comorbidity index (CCI) using 10 years history of hospitalization was determined at the time of receiving PROs (Charlson et al. 1987, Thygesen et al. 2011). The CCI is composed of 19 major disease categories each weighted with 0, 1, 2, 3, or 6 points. The index score is provided by the sum of these weights, and patients were classified according to 3 levels of comorbidity: low-index (individuals with a score of 0 prior to the time of receiving PROs), moderate-index (individuals with 1 or 2 points), and high-index (individuals with more than 2 points) (Groot et al. 2003).

Study population

The study population consisted of patients having stemmed THA with CoC, MoM or MoP bearings operated for primary OA, femoral head osteonecrosis, inflammatory arthritis, and sequelae from childhood hip disorder. In MoP bearings, the polyethylene could be either ultra-high-molecular-weight polyethylene or highly cross-linked. A flow chart of definition of the study population is presented in Figure 1.

In the DHR, registration of type of bearings started in 2002. From the DHR, we identified all patients with CoC bearings who had undergone primary THA from January 1, 2002 to December 31, 2009, with no registered revisions in the DHR and alive at the time of May 31, 2012. Each CoC patients were matched on sex, year of birth, and year of surgery to 1 control patient with MoM and MoP bearings. Controls had to fulfill the same inclusion criteria as CoC patients. When a patient received bilateral THA only the first was eligible in this study due to the statistical assumption of independent observations. Patients were excluded if they had protection against inquiry from researchers, unknown address or have received hip resurfacing arthroplasty and dual mobility acetabular systems due to the different prosthetic/mobility concept and thereby prognosis.

In total, 3,770 patients were eligible for the study and received PROs. Patients who send back answered PROs were classified as responders (n=3,089). Patients were classified as non-responders, if they returned unanswered PROs (n=31), or if they did not send back the PROs (n=505). Due to possible delay of registration of revision in the DHR or revision surgery after May 31, 2012, 145 patients answered that they had undergone revision surgery and were therefore excluded.

PROs

At November 1, 2012, a complete questionnaire including a return addressed and pre-paid envelope was mailed in paper form to the patient. The questionnaire comprised an introduction letter with printed signatures from all authors, disease-specific and generic PROs, and questions about noises from the THA. In the introduction letter it was clearly pointed out, that the questionnaire should be answered on the basis of the left or right THA in the case that the patient might have bilateral THA. Also questions about background data such as height and weight were included in the questionnaire. Due to the possible delay of registration of revision

data in the DHR, patients were asked if they had had revision surgery in the specific THA. If necessary, 1 reminder letter was sent. Returned questionnaires were scanned electronically using a validated automated forms-processing technique (Paulsen et al. 2012a).

HOOS. The hip disability and osteoarthritis outcome score (*HOOS*) (Nilsdotter et al. 2003) is disease-specific and was constructed by adding dimensions concerning sport and recreation function and hip-related quality of life to the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (Bellamy et al. 1988). HOOS includes five subscales: pain, other symptoms, activities of daily living, sport and recreation function, and hip related quality of life. It is a validated instrument (Klassbo et al. 2003, Nilsdotter et al. 2003) and is recommended for evaluating patients with hip OA undergoing non-surgical treatment and surgical interventions such as THA (Thorborg et al. 2010). For each subscale a score between 0 and 100 is calculated (100 indicating no symptoms and 0 indicating extreme symptoms). The subscale score can be calculated if at least 50% of items in the subscale have been answered (HOOS scoring instructions available at http://www.koos.nu/index.html).

EQ-5D-3L. The EuroQol EQ-5D-3L is a generic, standardized, reliable and validated instrument used for measure of quality of life and is applicable to a wide range of health conditions and treatments (The EuroQol Group 1990, Brooks 1996). The EQ-5D-3L describes the health-related quality of life from a social perspective (EQ-5D index) and from the patient's perspective (EQ visual analogue scale (VAS)). The EQ-5D index is determined from five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, and the patient choses 1 of 3 levels of severity for each dimension: no problems, some/moderate problems, and extreme problems. Based on the time trade-off method (Dolan et al. 1996), a value set ranging from -0.624 to 1, where 1 describes full health and 0 represents being dead, constitutes the Danish culture-adjusted EQ-5D index (Wittrup-Jensen et al. 2009). The EQ VAS is determined when the

patients on a thermometer scale ranging from 0 ("worst imaginable") to 100 ("best imaginable") value their current state of health.

UCLA activity score. University of California, Los Angeles (UCLA) activity score is disease-specific and has 10 descriptive activity levels ranging from wholly inactive and dependent on others (level 1), to moderate activities such as unlimited housework and shopping (level 6), to regular participation in impact sports such as jogging or tennis (level 10) (Amstutz et al. 1984). The UCLA activity score is found to be the most appropriate scale for assessment of physical activity levels in patients undergoing total joint replacement (Naal et al. 2009).

Information on noises. We asked all patients if they had experienced noises from the THA. If this was confirmed, patients were asked to characterize the noises as squeaking, creaking, grating, clicking, or other. Furthermore, patients were asked to answer questions about onset (time after surgery at which the noises started), frequency (daily, weekly, more seldom than weekly), audibility (whether noises could be heard only by the patient or by others), activities triggering the noises (rising from a chair, sitting down, bending, walking, walking up or down the steps, climbing a high step, or other activity), and personal impact (to what degree noises led to reduced physical function and hindered being together with other people). The questions about noises were developed through the test phase based on 18 patients randomly selected among patients admitted to Department of Orthopaedic Surgery, Vejle Hospital, Denmark for primary THA surgery. Furthermore, 3 patients who had undergone revision of their CoC THA due to noises tested the questions.

Statistical analyses

Characteristics of the study population, response rate for every item, the rate of discarded subscale scores, and characteristics of noises from the THA were calculated as proportions. Chi-

square test was used to compare proportions between groups. Comparison between responders and non-responders was carried out by prevalence proportion ratios (PPR). Time period from surgery to onset of noises from the THA was presented as median and interquartile range (IQR) and compared by Kruskal-Wallis test due to skewness. Univariate linear regression was used to compute and compare mean values of age, time since index surgery when receiving PROs, and BMI between the 3 bearing groups. Multivariate linear regression was used to assess and compare mean values of PRO subscale scores between the bearing groups. Adjustments in the multivariate linear models were made for the categorical variables sex, diagnosis, CCI, year of surgery, fixation and femoral head size as categorized in Table 2. Adjustment for the continuous variables age and BMI were performed by restricted cubic splines to allow for a non-linear dependency of PRO subscale scores and each variable. Due to the large study population, 5 knots placed at the 0.05, 0.275, 0.5, 0.725, and 0.95 percentiles were used on the splines (Harrell Jr. 2001). All estimates are presented with 95% confidence intervals (CI). To adjust for departure of normality of the outcomes in the regression analyses, all 95% CI was based on bootstraps with 100 samplings with replacement at the patient level. In all analyses, MoP was considered the standard bearings and therefore used as reference. A p-value below 0.05 was considered significant, and a mean difference including 95% CI different from 0 indicates a statistical significant finding with the 5% significant level. Statistical analyses were carried out by using the Stata Statistical Software, Release 14.1, College Station, TX: Stata Corporation.

Ethics

This study was approved by the Danish Data Protection Agency (j.no. 2010-41-4926) and by the Statens Serum Institut for the delivery of data from the NPR (FSEID 00000467).

RESULTS

Non-responders vs. responders

The response rate was 85% (3,089 of 3,625). Compared to responders, non-responders were younger, less likely to be diagnosed with OA, but more likely to have comorbidity. Furthermore, fewer non-responders had cementless and more had cemented THA, and fewer had CoC and more had MoP bearings compared to responders (Table 1).

Description of the study population

In the study population (n=3,089), 45% received CoC, 17% MoM, and 38% MoP THA. There was a similar distribution of sex within the 3 bearing groups. Patients with CoC and MoM bearings were significantly younger than patients with MoP bearings, and patients with MoM bearings had significantly lower BMI than patients with MoP bearings. No significant difference in BMI level was found for patients with CoC and MoP bearings. More patients with MoM bearings were diagnosed with OA than patients with MoP and CoC bearings, and patients with MoP bearings had more comorbidity than patients with the other bearings. During the period from 2002 to 2005, 15% of patients with MoM bearings had their THA implanted, whereas 56% of patients with CoC and 55% of patients with MoP bearings underwent surgery during the same period. For 2006 to 2009, the percentages were 85%, 44%, and 45% for MoM, CoC, and MoP bearings, respectively. The majority of patients in the all 3 bearing groups received cementless THA. The majority of patients with MoP bearings had femoral head sizes of 28 mm or smaller, whereas the majority of patients with CoC bearings had 32 mm femoral heads, and patients with MoM bearings mainly had femoral head sizes of 36 mm or larger. Mean follow-up was similar in the CoC and MoP groups, but mean follow-up was shorter in the MoM group compared to the MoP group (Tables 2 and 3).

Missing items and subscales

Except from the HOOS item A6 about difficulties when "Walking on flat surface" that had a higher proportion of missing answer in the MoP group, no difference in the proportion of missing items in HOOS, EQ-5D index, EQ VAS, and UCLA activity score between the 3 bearing groups was found (Appendix tables 1-3). The proportion of discarded subscale scores and BMI was low, and there was no difference between the bearing groups (Table 4).

Comparison of subscale scores between bearing groups

For HOOS Symptoms, the adjusted mean score was significantly lower for the CoC group compared to the MoP group (adjusted mean difference (aMD) -2.3 (95% CI, -4.1 to -0.5)). No other stastistical significant adjusted differences were found for the other HOOS subscales, EQ-5D index, EQ-5D VAS, or UCLA activity score when comparing the CoC and MoM groups to the MoP group (Table 5).

Noises

27% of patients with CoC, 29% of patients with MoM, and 12% of patients with MoP bearings had experienced noises from the THA. Patients with CoC THA mainly experienced clicking and creaking noises, whereas patients with MoM and MoP bearings mainly experienced clicking, grating, and creaking noises. Half of the patients were not able to indicate how long after surgery noises were experienced for the first time. Median onset of noises after surgery was 10 months for CoC, 0 months for MoM, and 5 months for MoP bearings (p=0.016). Of patients with noises from the THA, 33-47% experienced noises daily or weekly, and 4-12% indicated that the noises always were audible to other persons. Noises were mainly present when bending in patients with CoC and MoM bearings and when walking in patients with MoP bearings. In 36%-47% of patients, noises from the THA led to some degree of reduction in physical activity, and 6-16%

indicated that noises from the THA to some degree hindered being together with other people (Table 6).

Stratified analyses for the 3 types of bearings with and without noises showed significantly lower adjusted mean scores of all HOOS subscales, EQ-5D index, and EQ-5D VAS for patients experiencing noises from the CoC, MoM or MoP THA compared to patients having MoP THA without noises. For all subscales, the aMD was largest for MoP THA with noises. Only for the ULCA activity score, no difference was found for CoC and MoM THA with noises compared to MoP THA without noises, but patients having MoP THA with noises had significantly lower mean UCLA activity scores when compared to patients having MoP THA without noises. No significant aMD was found for any subscale for the CoC or MoM groups without noises compared to the MoP group without noises (Table 7).

DISCUSSION

In this population-based cross-sectional questionnaire survey we found no significant difference in mean scores in the 5 HOOS subscales, EQ-5D index, EQ VAS, or UCLA activity score between patients with CoC, MoM, and MoP THA after 5-7 years follow-up. Patients with MoP THA experienced less self-reported noises compared with MoM and CoC THA patients. Patients with noises irrespective of bearing had significantly lower subscale scores compared to MoP THA patients without noises.

Comparison of the main findings to other studies

In a study from the Swedish Hip Arthroplasty Register, the mean EQ-5D index 6 years after index surgery was 0.75 (standard deviation 0.27) among 4962 patients, which is slightly lower than observed in our study for all bearing groups after a mean follow-up of 5.1 years for MoM and 6.9

years for CoC and MoP bearings. Similarly, the EQ VAS after 6 years was lower in the Swedish study (Lindgren et al. 2014). The differences might be caused by the differences in follow-up, a greater proportion of females and higher mean age in the Swedish study.

In a cross-sectional study from a Swiss hospital-based cohort including patients who underwent elective primary THA and hip resurfacing, the mean ULCA activity score was 5.7 and 5.5 5 and 10 years after primary surgery (Lubbeke et al. 2014), respectively, which is similar to our findings after mean follow-up of 5.1 (for MoM THA) and 6.9 (for CoC and MoP THA) years. In contrast to our study, the Swiss study included both THA and hip resurfacings, but it has been shown that there is no significant difference in the rate of return to sport according to the type of operation (Wylde et al. 2008).

In January 2012 the Danish Broadcasting Corporation started a series of news about the adverse events and risks of having MoM bearings, and the negative publicity continued in the Danish media throughout the spring 2012. For this study, the questionnaire was mailed to the patients at November 1, 2012. Although increased risk of revision has been found for MoM (Varnum et al. 2015b), no differences in PROs were found for MoM compared to MoP THA. One explanation of this might be that patients are not revised due to functional impairment or pain but more likely due to concerns of having a MoM THA, elevated metal ion levels, or radiological findings such as pseudotumors.

Noises

We found a prevalence of noises from CoC THA of 27%, which is lower than the prevalence of 33% reported by Jarrett et al. (2009) whereas for MoM bearings, the prevalence of noises of 29% in our study was higher than the reported prevalence of squeaking of 1.5% (Bernasek et al. 2011). The prevalence of noises from MoP THA in our study was threefold the earlier reported

prevalence of 4% (Jarrett et al. 2009). Noises from THA have been described in particular for CoC bearings as “squeaking”, “clickling”, “grating”, “grinds”, “pops”, and “snaps”(Keurentjes et al. 2008, Jarrett et al. 2009). In contrast, noises from MoP THAs were reported as “clicks” (Jarrett et al. 2009), and in our study the clicking noise was most prevalent in patients with MoP bearings. Satisfaction or PROs was described in several studies on squeaking CoC THA. Sexton et al. (2011) found that a squeaking THA was not associated with a significant difference in patient satisfaction or Harris hip score (HHS). Other authors reported no significant difference in HHS, SF-36 or WOMAC between patients with and without squeaking CoC THAs (Restrepo et al. 2010). These reports are in contrast to our findings.

Paulsen et al. estimated the minimal clinically important improvement (MCII) and patient-acceptable symptom state (PASS) of 3 HOOS subscales, EQ-5D index, and EQ VAS 1 year postoperatively. The MCII and PASS were 24 and 91 for HOOS Pain, 23 and 88 for HOOS Sport, 17 and 83 for HOOS QoL, 0.31 and 0.92 for EQ-5D index, and 23 and 85 for EQ VAS, respectively (Paulsen et al. 2014). In our study, the maximal adjusted mean difference in subscale score exceeded MCII for HOOS QoL for noisy MoP compared to silent MoP, and only the crude mean of HOOS Pain, HOOS QoL and EQ-5D index for silent THAs almost reached values for PASS, whereas PRO scores for noisy THAs were lower. This indicates that THAs with noises may not only have a statistical but also a clinical significance when compared to silent THA. In contrast, the significantly lower adjusted mean difference for HOOS Symptoms of -2.3 for the CoC compared to the MoP group in general may not be considered as clinically relevant.

Methodological considerations

The strengths of this study included the nationwide population-based design. The registers providing data to our study have a documented overall good validity (Andersen et al. 1999, Pedersen et al. 2004, Pedersen et al. 2006). Furthermore, the PROs used in the study are all well

validated (Brooks 1996, Nilsdotter et al. 2003, Naal et al. 2009, Thorborg et al. 2009, Wittrup-Jensen et al. 2009, Paulsen et al. 2012b, Paulsen et al. 2014). This, together with the high response rate, increased the generalizability of the results.

Our study also has several limitations. Since the response rate was slightly dependent on bearing type, we might have introduced selection bias in our study. Also the question about onset of noises from the THA might be influenced by recall bias. Although the questions about noises from the THA had been tested before administration, the questions were not psychometrically validated, and no retests were performed before administration.

In order to reduce the confounding effects of sex, age, and follow-up, patients with MoM and MoP THA were matched to patients with CoC THA on sex, year of birth, and year of surgery. As it was impossible to identify a unique match among patients with MoM and MoP bearings for all patients with CoC THA, some patients with MoM and MoP THA were controls for more than 1 patient with CoC THA. To maintain the matched design, 2 responders with 2 different bearings should have been excluded, if their unique match with the third bearings was a non-responder. This would have reduced the study-population substantially. Therefore, when performing the regression analyses the matching was ignored and instead, adjustments for sex, age, and follow-up were performed to account for these confounders. There might still be the possibility of residual confounding as we have no information of the patient's preoperative function, smoking habits, civil status, educational level, or income.

Quality of PRO data depends on the proportion of missing data. Missing data were managed in accordance with the specifications in the manual for each PRO, and the amount of missing data were lower than seen in previous studies among Danish THA patients (Paulsen et al. 2012b).

The very low proportion of missing data in our study would not influence our results substantially.

Conclusion

In this nation-wide population-based cross-sectional study we found no significant difference in mean scores in the 5 HOOS subscales, EQ-5D index, EQ VAS, or UCLA activity score between patients with CoC, MoM, and MoP THA after mean follow-up of 6.9, 5.1, and 6.9 years, respectively. There were significantly lower mean subscale scores for all types of bearings and subscales when comparing noisy THA to silent MoP THA, except for patients having noisy CoC and MoM THA who had similar mean UCLA activity scores as patients with silent MoP THA. The most unfavorable PRO scores were found for noisy MoP THA, which may have a clinical significance.

CONTRIBUTIONS

CV, ABP, PKA, and SO designed the study protocol. CV and ABP collected the data. Analyses were planned by CV, ABP, PKA, and SO and were carried out by CV. CV wrote the initial draft of the manuscript, which was critically revised by CV, ABP, PKA, and SO.

SOURCE OF FUNDING

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Figure 1. Flow chart showing patients in the study population.

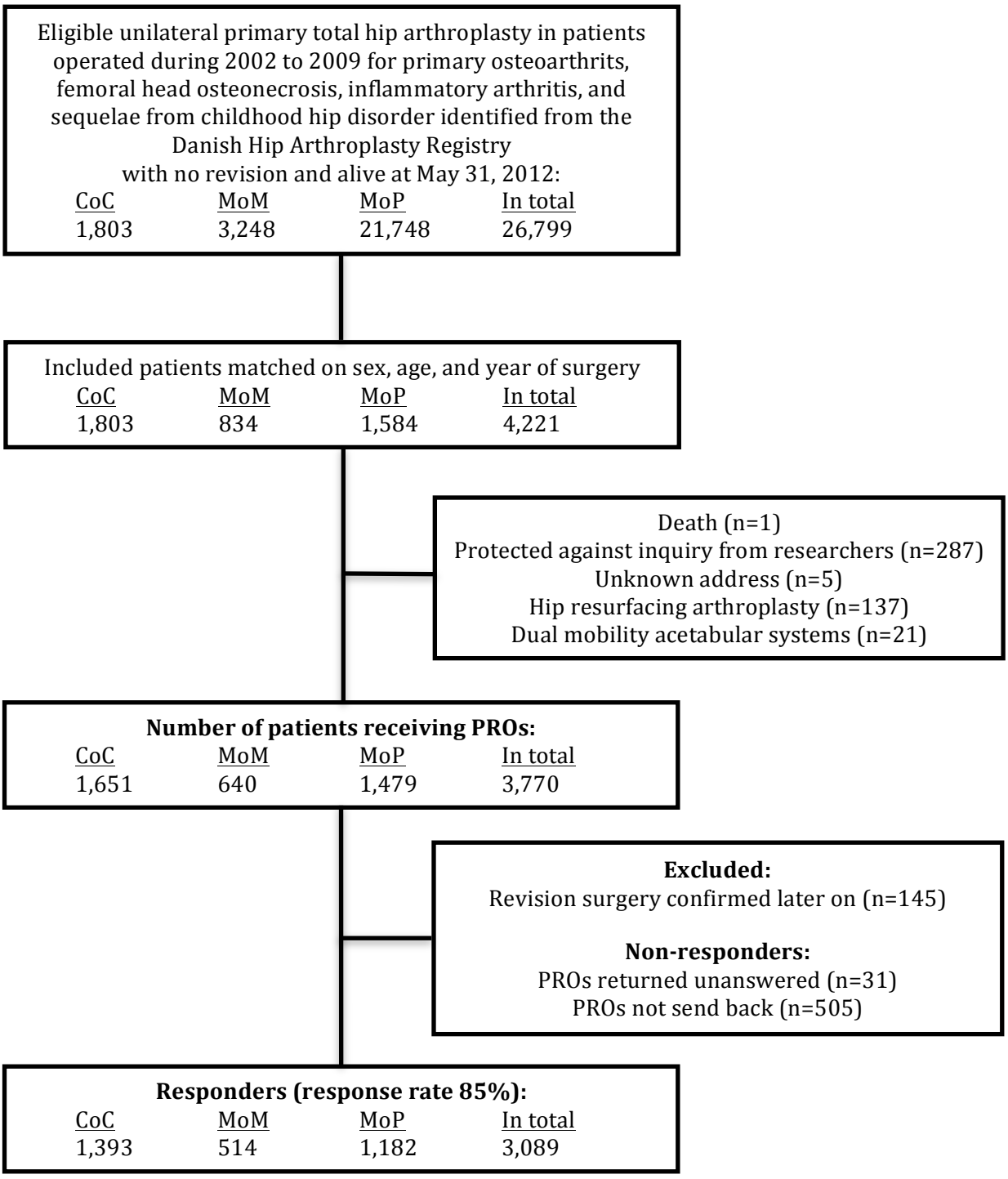

Table 1. Characteristics of non-responders and responders. Values represent numbers of patients and percentages (%) within each group and prevalence-proportion ratio (PPR), non-responders vs. responders, with 95% confidence interval (95% CI).

	Non-responders n=536	Responders n=3,089	PPR (95% CI)
Percent of total	15	85	
Sex			
Female	251 (47)	1,394 (45)	1.04 (0.94 to 1.14)
Male	285 (53)	1,695 (55)	0.97 (0.89 to 1.06)
Age groups when receiving questionnaire (years)			
≤49	70 (13)	175 (6)	2.31 (1.77 to 2.99)
50-69	305 (57)	1,769 (57)	0.99 (0.92 to 1.08)
≥70	161 (30)	1,145 (37)	0.81 (0.71 to 0.93)
Diagnosis			
Primary OA	425 (79)	2,685 (87)	0.91 (0.87 to 0.95)
Other	111 (21)	404 (13)	1.58 (1.31 to 1.91)
Charlson co-morbidity index when receiving questionnaire at November 1, 2012			
Low (%)	246 (46)	1,783 (58)	0.80 (0.72 to 0.88)
Medium (%)	195 (36)	994 (32)	1.13 (1.00 to 1.28)
High (%)	95 (18)	312 (10)	1.75 (1.42 to 2.17)
Year of surgery			
2002-2003	88 (16)	507 (16)	1.00 (0.81 to 1.23)
2004-2005	153 (29)	999 (32)	0.88 (0.76 to 1.02)
2006-2007	137 (26)	820 (27)	0.96 (0.82 to 1.13)
2008-2009	158 (29)	763 (25)	1.19 (1.03 to 1.38)
Fixation			

Cementless (%)	425 (79)	2,607 (85)	0.94 (0.90 to 0.98)
Cemented (%)	60 (11)	226 (7)	1.53 (1.17 to 2.00)
Hybrid (%)	51 (10)	256 (8)	1.15 (0.86 to 1.53)
Femoral head size (mm)			
≤28	252 (47)	1,369 (44)	1.06 (0.96 to 1.17)
32	132 (25)	915 (30)	0.83 (0.71 to 0.97)
≥36	152 (28)	805 (26)	1.09 (0.94 to 1.26)
Bearings			
Ceramic-on-ceramic (%)	200 (37)	1,393 (45)	0.83 (0.74 to 0.93)
Metal-on-metal (%)	101 (19)	514 (17)	1.13 (0.93 to 1.37)
Metal-on-polyethylene (%)	235 (44)	1,182 (38)	1.15 (1.03 to 1.27)

Table 2. Demographics of patients classified as responders and having ceramic-on-ceramic (CoC), metal-on-metal (MoM) and metal-on-polyethylene (MoP) total hip arthroplasty. Values represent numbers of patients and percentages (%) within each group.

	CoC n=1,393	MoM n=514	MoP n=1,182	p-value
Sex				0.682
Female	639 (46)	233 (45)	522 (44)	
Male	754 (54)	281 (55)	660 (56)	
Age groups when receiving questionnaire (years)				0.001
≤49	97 (7)	38 (7)	40 (3)	
50-69	789 (57)	298 (58)	682 (58)	
≥70	507 (36)	178 (35)	460 (39)	
Diagnosis				0.022
Primary OA	1,191 (86)	464 (90)	1,030 (87)	
Other	202 (14)	50 (10)	152 (13)	
Charlson co-morbidity index when receiving questionnaire				0.001
Low	837 (60)	315 (61)	631 (53)	
Medium	423 (30)	160 (31)	411 (35)	
High	133 (10)	39 (8)	140 (12)	
Year of surgery				<0.001
2002-2003	267 (19)	7 (1)	233 (20)	
2004-2005	515 (37)	71 (14)	413 (35)	
2006-2007	321 (23)	213 (42)	286 (24)	
2008-2009	290 (21)	223 (43)	250 (21)	

Fixation				<0.001
Cementless	1,351 (97)	422 (82)	834 (71)	
Cemented	0 (0)	2 (0)	224 (19)	
Hybrid	42 (3)	90 (18)	124 (10)	
Femoral head size (mm)				<0.001
≤28	471 (34)	23 (4)	875 (74)	
32	713 (51)	8 (2)	194 (16)	
≥36	209 (15)	483 (94)	113 (10)	

Table 3. Association between patients having total hip arthroplasty with ceramic-on-ceramic (CoC), metal-on-metal (MoM) and metal-on-polyethylene (MoP) bearings, crude mean values, and crude mean differences of age, BMI, and follow-up with 95% confidence intervals.

	CoC n=1,393	MoM n=514	MoP n=1,182
Age when receiving questionnaire			
Mean	65.7 (65.2 to 66.2)	65.5 (64.7 to 66.2)	67.3 (66.9 to 67.8)
Mean difference	-1.6 (-2.3 to -1.0)	-1.9 (-2.7 to -1.0)	0 (ref.)
BMI			
Mean	28.1 (27.4 to 28.7)	27.4 (27.1 to 27.7)	28.2 (27.8 to 28.6)
Mean difference	-0.11 (-0.92 to 0.71)	-0.76 (-1.25 to -0.27)	0 (ref.)
Follow-up (time from index surgery to receipt of questionnaire)			
Mean	6.9 (6.8 to 7.0)	5.1 (5.0 to 5.3)	6.9 (6.8 to 7.0)
Mean difference	0.01 (-0.17 to 0.19)	-1.74 (-1.90 to -1.58)	0 (ref.)

Table 4. Distribution of discarded subscale scores and BMI due to missing items for patients with ceramic-on-ceramic (CoC), metal-on-metal (MoM) and metal-on-polyethylene (MoP) total hip arthroplasty and comparison of the proportion of kept and discarded subscales and BMI. Values represent numbers and percentage of patients within each bearing group.

	CoC	MoM	MoP	p-value
HOOS Symptoms	14 (1)	4 (1)	15 (1)	0.63
HOOS Pain	19 (1)	4 (1)	16 (1)	0.56
HOOS ADL	10 (1)	3 (1)	11 (1)	0.71
HOOS Sport	28 (2)	7 (1)	28 (2)	0.40
HOOS QoL	12 (1)	3 (1)	14 (1)	0.46
EQ-5D index	37 (3)	11 (2)	24 (2)	0.55
EQ VAS	82 (6)	28 (5)	65 (6)	0.89
UCLA activity score	32 (2)	5 (1)	24 (2)	0.18
BMI	41 (3)	16 (3)	38 (3)	0.92

Table 5. Association between patients having total hip arthroplasty with ceramic-on-ceramic (CoC), metal-on-metal (MoM) and metal-on-polyethylene (MoP) bearings, mean values, and mean differences of PRO subscales with 95% confidence intervals (95% CI).

		CoC (95% CI)	MoM (95% CI)	MoP (95% CI)
HOOS Symptoms				
Mean	Crude	84.4 (83.5 to 85.3)	85.2 (83.8 to 86.7)	85.9 (84.9 to 86.9)
	Adjusted	78.2 (56.3 to 100.2)	79.2 (56.6 to 101.7)	80.6 (58.2 to 102.9)
Mean difference	Crude	-1.51 (-2.82 to -0.20)	-0.68 (-2.49 to 1.13)	0 (ref.)
	Adjusted	-2.31 (-4.10 to -0.52)	-1.40 (-3.60 to 0.79)	0 (ref.)
HOOS Pain				
Mean	Crude	88.4 (87.4 to 89.5)	89.3 (87.8 to 90.8)	88.7 (87.7 to 89.7)
	Adjusted	78.1 (55.1 to 101.0)	79.0 (55.8 to 102.3)	78.8 (55.4 to 102.1)
Mean difference	Crude	-0.22 (-1.64 to 1.20)	0.62 (-1.22 to 2.46)	0 (ref.)
	Adjusted	-0.70 (-2.34 to 0.94)	0.29 (-2.05 to 2.63)	0 (ref.)
HOOS ADL				
Mean	Crude	85.0 (83.9 to 86.0)	86.3 (84.6 to 88.0)	85.2 (84.1 to 86.2)
	Adjusted	83.7 (58.5 to 108.8)	83.9 (59.0 to 108.9)	84.7 (59.2 to 110.2)
Mean difference	Crude	-0.20 (-1.67 to 1.26)	1.14 (-0.77 to 3.05)	0 (ref.)
	Adjusted	-1.04 (-2.93 to 0.85)	-0.80 (-3.39 to 1.80)	0 (ref.)
HOOS Sport				
Mean	Crude	71.5 (70.1 to 72.9)	74.5 (72.1 to 76.9)	70.9 (69.2 to 72.6)
	Adjusted	75.6 (42.6 to 108.6)	75.6 (42.7 to 108.4)	76.4 (43.1 to 109.7)
Mean difference	Crude	0.64 (-1.53 to 2.82)	3.63 (0.74 to 6.51)	0 (ref.)
	Adjusted	-0.74 (-3.41 to 1.92)	-0.79 (-4.93 to 3.36)	0 (ref.)
HOOS QoL				
Mean	Crude	77.5 (76.2 to 78.8)	77.9 (76.1 to 79.7)	78.2 (76.8 to 79.6)
	Adjusted	55.9 (26.8 to 85.0)	55.8 (27.2 to 85.6)	56.4 (27.2 to 85.6)

Mean difference	Crude	-0.70 (-2.57 to 1.17)	-0.30 (-2.66 to 2.06)	0 (ref.)
	Adjusted	-0.52 (-2.87 to 1.83)	-0.56 (-4.26 to 3.13)	0 (ref.)
EQ-5D index				
Mean	Crude	0.872 (0.864 to 0.880)	0.870 (0.856 to 0.884)	0.865 (0.855 to 0.876)
	Adjusted	0.797 (0.542 to 1.052)	0.787 (0.528 to 1.047)	0.797 (0.540 to 1.053)
Mean difference	Crude	0.006 (-0.006 to 0.019)	0.005 (-0.013 to 0.022)	0 (ref.)
	Adjusted	0.000 (-0.015 to 0.015)	-0.009 (-0.036 to 0.018)	0 (ref.)
EQ VAS				
Mean	Crude	77.6 (76.5 to 78.7)	77.9 (76.2 to 79.7)	76.4 (75.2 to 77.6)
	Adjusted	64.2 (38.9 to 89.4)	62.6 (36.9 to 88.2)	64.4 (39.3 to 89.5)
Mean difference	Crude	1.20 (-0.31 to 2.71)	1.49 (-0.64 to 3.62)	0 (ref.)
	Adjusted	-0.09 (-1.85 to 1.45)	-1.83 (-4.84 to 1.18)	0 (ref.)
UCLA activity score				
Mean	Crude	6.40 (6.30 to 6.50)	6.61 (6.45 to 6.77)	6.17 (6.07 to 6.28)
	Adjusted	6.01 (3.56 to 8.47)	5.88 (3.47 to 8.29)	5.91 (3.44 to 8.38)
Mean difference	Crude	0.22 (0.08 to 0.37)	0.44 (0.25 to 0.62)	0 (ref.)
	Adjusted	0.10 (-0.07 to 0.28)	-0.03 (-0.30 to 0.24)	0 (ref.)

Table 6. Prevalence and characteristics type of noises from total hip arthroplasties with ceramic-on-ceramic (CoC), metal-on-metal (MoM) and metal-on-polyethylene (MoP) total hip arthroplasty. Values represent numbers of patients and percentages (%) within each group.

	CoC	MoM	MoP	p-value
Noise experienced				<0.001[2]
- yes	383 (27)	147 (29)	146 (12)	
- no	925 (67)	345 (67)	977 (83)	
- missing	85 (6)	22 (4)	59 (5)	
Squeaking noise experienced[1]	71 (19)	7 (5)	2 (1)	<0.001[2]
Creaking noise experienced[1]	160 (42)	30 (20)	26 (18)	<0.001[2]
Grating noise experienced[1]	114 (30)	30 (20)	28 (19)	0.013[2]
Clicking noise experienced[1]	168 (44)	95 (65)	96 (66)	<0.001[2]
Other noise experienced[1]	37 (10)	19 (13)	26 (18)	0.035[2]
Time period from surgery to beginning of noise				
- median (IQR) months	10 (0-48)	0 (0-12)	5 (0-40)	0.024[3]
- unknown[1]	191 (50)	76 (52)	76 (52)	
- missing[1]	61 (16)	28 (19)	31 (21)	
Noise experienced[1]				0.097[2]
- daily	103 (27)	32 (22)	27 (18)	
- weekly	76 (20)	34 (22)	22 (15)	
- more seldom than weekly	152 (40)	55 (38)	68 (47)	
- missing	52 (13)	26 (18)	29 (20)	
Noise can be heard[1]				<0.001[2]
- only by the patient	177 (46)	92 (62)	74 (51)	
- from time to time by others	112 (29)	23 (16)	30 (20)	

- always by others	44 (12)	6 (4)	13 (9)	
- missing	50 (13)	26 (18)	29 (20)	
Noise experienced when				
- rising from a chair[1]	89 (23)	28 (19)	34 (23)	0.557[2]
- sitting down[1]	44 (11)	14 (10)	14 (10)	0.722[2]
- bending[1]	194 (51)	60 (41)	42 (29)	<0.001[2]
- walking[1]	109 (28)	40 (27)	58 (40)	0.025[2]
- walking up or down the steps[1]	83 (22)	28 (19)	37 (25)	0.423[2]
- climbing a high step[1]	96 (25)	38 (26)	33 (23)	0.788[2]
- other activity[1]	135 (35)	54 (37)	45 (31)	0.525[2]
To what degree lead noises from the THA to reduced physical activity?[1]				0.431[2]
- none	207 (54)	74 (50)	63 (43)	
- mild	76 (20)	32 (22)	32 (22)	
- moderate	41 (11)	14 (9)	23 (16)	
- severe	19 (5)	6 (4)	12 (8)	
- extreme	3 (1)	1 (1)	1 (1)	
- missing	37 (9)	20 (14)	15 (10)	
To what degree hindered noises from the THA being together with other people?[1]				0.018[2]
- none	312 (81)	118 (80)	106 (73)	
- mild	26 (7)	5 (4)	12 (8)	
- moderate	8 (2)	1 (1)	8 (5)	
- severe	2 (1)	2 (1)	4 (3)	
- extreme	0 (0)	0 (0)	0 (0)	

- missing	35 (9)	21 (14)	16 (11)	

[1]Percent of patients having experienced noises from the THA within the same bearing group

[2]Chi-square test

[3]Kruskal-Wallis test

Table 7. Association between experience of noise from total hip arthroplasty (THA) with ceramic-on-ceramic (CoC), metal-on-metal (MoM) and metal-on-polyethylene (MoP) bearings, mean values, and mean differences of PROM subscales with 95% confidence intervals (95% CI).

		Noise experienced from THA			No noise experienced from THA		
		CoC (95% CI)	MoM (95% CI)	MoP (95% CI)	CoC (95% CI)	MoM (95% CI)	MoP (95% CI)
HOOS Symptoms							
Mean	Crude	75.5 (73.6 to 77.5)	77.0 (73.3 to 80.6)	71.6 (68.0 to 75.2)	88.1 (87.1 to 89.2)	89.4 (87.8 to 91.0)	88.4 (87.4 to 89.3)
	Adjusted	72.5 (51.0 to 94.0)	74.1 (51.9 to 96.3)	70.1 (48.6 to 91.5)	84.7 (63.5 to 105.9)	85.9 (63.9 to 107.8)	86.1 (64.8 to 107.4)
Mean difference	Crude	-12.9 (-14.9 to -10.8)	-11.4 (-15.2 to -7.65)	-16.8 (-20.6 to -13.0)	-0.25 (-1.57 to 1.08)	1.03 (-0.89 to 2.94)	0 (ref.)
	Adjusted	-13.6 (-15.8 to -11.4)	-12.0 (-16.2 to -7.83)	-16.1 (-20.0 to -12.2)	-1.39 (-3.07 to 0.28)	-0.24 (-3.20 to 2.72)	0 (ref.)
HOOS Pain							
Mean	Crude	83.4 (81.6 to 85.2)	85.6 (82.5 to 88.8)	76.7 (72.6 to 80.8)	90.8 (89.7 to 91.9)	91.3 (89.7 to 92.9)	90.7 (89.9 to 91.6)
	Adjusted	73.7 (51.5 to 96.0)	76.4 (54.5 to 98.3)	68.1 (45.3 to 90.9)	80.8 (58.8 to 102.8)	81.5 (59.2 to 103.8)	81.5 (59.4 to 103.6)
Mean difference	Crude	-7.33 (-9.21 to -5.45)	-5.11 (-8.31 to -1.90)	-14.0 (-18.1 to -9.97)	0.04 (-1.29 to 1.37)	0.56 (-1.32 to 2.45)	0 (ref.)
	Adjusted	-7.79 (-10.0 to -5.59)	-5.11 (-8.56 to -1.67)	-13.4 (-17.5 to -9.37)	-0.71 (-2.33 to 0.91)	-0.04 (-2.56 to 2.48)	0 (ref.)
HOOS ADL							
Mean	Crude	80.2 (78.1 to 82.2)	81.9 (78.5 to 85.4)	73.2 (69.5 to 77.0)	87.3 (86.2 to 88.4)	88.8 (87.1 to 90.6)	87.4 (86.4 to 88.5)
	Adjusted	77.2 (53.6 to 100.4)	78.0 (54.5 to 101.5)	72.0 (48.2 to 95.8)	84.4 (61.1 to 107.7)	84.9 (61.0 to 108.8)	85.6 (62.1 to 109.0)
Mean difference	Crude	-7.29 (-9.63 to -4.95)	-5.52 (-9.19 to -1.84)	-14.2 (-18.3 to -10.1)	-0.13 (-1.60 to 1.33)	1.38 (-0.55 to 3.30)	0 (ref.)
	Adjusted	-8.53 (-11.2 to -5.89)	-7.58 (-11.8 to -3.40)	-13.6 (-17.9 to -9.27)	-1.14 (-3.01 to 0.73)	-0.66 (-3.48 to 2.15)	0 (ref.)
HOOS Sport							
Mean	Crude	64.6 (61.4 to 67.8)	66.9 (62.4 to 71.3)	52.8 (47.3 to 58.3)	74.9 (73.3 to 76.5)	78.4 (75.5 to 81.2)	74.0 (72.2 to 75.8)
	Adjusted	67.0 (35.6 to 98.3)	66.7 (35.0 to 98.4)	58.7 (27.0 to 90.3)	77.5 (46.5 to 108.6)	78.4 (46.8 to 110.0)	78.3 (47.2 to 109.4)
Mean difference	Crude	-9.45 (-13.0 to -5.94)	-7.16 (-11.8 to -2.47)	-21.2 (-26.9 to -15.5)	0.88 (-1.47 to 3.23)	4.36 (0.95 to 7.77)	0 (ref.)
	Adjusted	-11.3 (-15.6 to -7.13)	-11.6 (-17.8 to -5.44)	-19.7 (-25.4 to -13.9)	-0.79 (-3.34 to 1.76)	0.13 (-4.23 to 4.49)	0 (ref.)

HOOS QoL							
Mean	Crude	69.0 (66.3 to 71.8)	68.9 (64.6 to 73.2)	61.1 (56.6 to 65.6)	81.1 (79.7 to 82.6)	82.3 (80.2 to 84.4)	81.2 (79.9 to 82.5)
	Adjusted	49.6 (18.3 to 80.9)	49.2 (17.3 to 81.1)	42.3 (10.7 to 73.9)	61.1 (30.1 to 93.1)	61.6 (30.1 to 93.1)	61.4 (30.2 to 92.6)
Mean difference	Crude	-12.1 (-15.0 to -9.24)	-12.3 (-16.8 to -7.76)	-20.1 (-24.6 to -15.5)	-0.06 (-1.74 to -1.61)	1.13 (-1.28 to -3.53)	0 (ref.)
	Adjusted	-11.8 (-14.7 to -8.94)	-12.2 (-17.3 to -7.10)	-19.1 (-24.0 to -14.3)	-0.27 (-2.36 to 1.82)	0.18 (-4.01 to 4.37)	0 (ref.)
EQ-5D index							
Mean	Crude	0.825 (0.800 to 0.850)	0.816 (0.786 to 0.847)	0.771 (0.741 to 0.801)	0.892 (0.881 to 0.902)	0.894 (0.878 to 0.910)	0.883 (0.872 to 0.895)
	Adjusted	0.739 (0.488 to 0.989)	0.727 (0.484 to 0.970)	0.692 (0.446 to 0.938)	0.801 (0.554 to 1.049)	0.796 (0.546 to 1.045)	0.800 (0.549 to 1.052)
Mean difference	Crude	-0.059 (-0.085 to -0.032)	-0.067 (-0.100 to -0.034)	-0.113 (-0.144 to -0.081)	0.008 (-0.008 to 0.024)	0.011 (-0.009 to 0.030)	0 (ref.)
	Adjusted	-0.061 (-0.088 to -0.035)	-0.073 (-0.117 to -0.030)	-0.108 (-0.137 to -0.079)	0.001 (-0.016 to 0.019)	-0.005 (-0.033 to 0.024)	0 (ref.)
EQ VAS							
Mean	Crude	74.7 (72.5 to 76.9)	75.0 (71.3 to 78.6)	67.9 (63.7 to 71.9)	79.0 (77.7 to 80.2)	79.3 (77.2 to 81.3)	77.8 (76.5 to 79.1)
	Adjusted	60.7 (37.2 to 84.3)	59.0 (34.3 to 83.7)	55.9 (31.0 to 80.7)	64.9 (41.0 to 88.8)	63.7 (39.4 to 88.1)	65.3 (41.4 to 89.2)
Mean difference	Crude	-3.07 (-5.80 to –0.38)	-2.81 (-6.63 to 1.01)	-9.99 (-14.5 to -5.51)	1.19 (-0.75 to 3.13)	1.49 (-0.98 to 3.96)	0 (ref.)
	Adjusted	-4.56 (-7.20 to -1.92)	-6.29 (-9.72 to -2.87)	-9.44 (-13.5 to -5.38)	-0.40 (-2.38 to 1.58)	-1.56 (-4.66 to 1.54)	0 (ref.)
UCLA activity score							
Mean	Crude	6.34 (6.11 to 6.57)	6.41 (6.10 to 6.73)	5.73 (5.40 to 6.06)	6.43 (6.31 to 6.56)	6.68 (6.45 to 6.92)	6.26 (6.13 to 6.39)
	Adjusted	5.75 (3.51 to 7.99)	5.43 (3.12 to 7.74)	5.30 (3.07 to 7.54)	5.90 (3.70 to 8.10)	5.79 (3.51 to 8.08)	5.87 (3.66 to 8.07)
Mean difference	Crude	0.08 (-0.20 to 0.35)	0.16 (-0.16 to 0.47)	-0.53 (-0.89 to -0.17)	0.17 (-0.02 to 0.36)	0.42 (0.16 to 0.68)	0 (ref.)
	Adjusted	-0.12 (-0.38 to 0.15)	-0.44 (-0.88 to 0.00)	-0.56 (-0.88 to -0.25)	0.03 (-0.16 to 0.22)	-0.08 (-0.41 to 0.26)	0 (ref.)

Appendix table 1. HOOS items for responders having ceramic-on-ceramic (CoC), metal-on-metal (MoM) and metal-on-polyethylene (MoP) total hip arthroplasty and comparison of the proportion of answered and unanswered items. Values represent numbers and percentage of patients within each bearing group.

	CoC n=1,393	MoM n=514	MoP n=1,182	p-value
S1. Do you feel grinding, hear clicking or any other type of noise from your hip?				
Never	737 (53)	268 (52)	767 (65)	
Rarely	256 (18)	103 (20)	186 (16)	
Sometimes	252 (18)	104 (20)	139 (12)	
Often	99 (7)	24 (5)	51 (4)	
Always	35 (3)	10 (2)	22 (2)	
Missing	14 (1)	5 (1)	17 (1)	0.54
S2. Difficulties spreading legs wide apart				
None	886 (64)	343 (67)	769 (65)	
Mild	244 (17)	90 (18)	204 (17)	
Moderate	176 (13)	59 (11)	137 (11)	
Severe	43 (3)	11 (2)	44 (4)	
Extreme	23 (2)	6 (1)	10 (1)	
Missing	21 (1)	5 (1)	18 (2)	0.64
S3. Difficulties to stride out when walking				
None	990 (71)	381 (74)	869 (74)	
Mild	199 (14)	64 (12)	133 (11)	
Moderate	133 (10)	45 (9)	111 (9)	

Severe	39 (3)	14 (3)	40 (4)	
Extreme	16 (1)	6 (1)	13 (1)	
Missing	16 (1)	4 (1)	16 (1)	0.60
S4. How severe is your hip joint stiffness after first wakening in the morning?				
None	826 (59)	298 (58)	689 (59)	
Mild	357 (26)	134 (26)	298 (25)	
Moderate	124 (9)	46 (9)	110 (9)	
Severe	55 (4)	16 (3)	52 (4)	
Extreme	8 (0)	7 (1)	6 (1)	
Missing	23 (2)	13 (3)	27 (2)	0.36
S5. How severe is your hip stiffness after sitting, lying or resting later in the day?				
None	808 (58)	309 (60)	684 (58)	
Mild	380 (28)	132 (25)	311 (26)	
Moderate	127 (9)	50 (10)	119 (10)	
Severe	58 (4)	15 (3)	48 (4)	
Extreme	4 (0)	3 (1)	3 (0)	
Missing	16 (1)	5 (1)	17 (2)	0.68
P1. How often is your hip painful?				
Never	824 (59)	305 (59)	702 (59)	
Monthly	203 (15)	83 (16)	163 (14)	
Weekly	106 (8)	50 (10)	84 (7)	
Daily	105 (7)	39 (8)	107 (9)	
Always	32 (2)	4 (1)	21 (2)	

Missing	123 (9)	33 (6)	105 (9)	0.19
P2. Straightening your hip fully				
None	1,082 (78)	405 (79)	922 (78)	
Mild	181 (13)	59 (11)	130 (11)	
Moderate	78 (5)	37 (7)	87 (8)	
Severe	24 (2)	4 (1)	16 (1)	
Extreme	2 (0)	3 (1)	3 (0)	
Missing	26 (2)	6 (1)	24 (2)	0.46
P3. Bending your hip fully				
None	953 (68)	357 (69)	804 (68)	
Mild	247 (18)	85 (17)	202 (17)	
Moderate	125 (9)	51 (10)	104 (9)	
Severe	33 (2)	9 (2)	36 (3)	
Extreme	7 (1)	5 (1)	12 (1)	
Missing	28 (2)	7 (1)	24 (2)	0.61
P4. Walking on a flat surface				
None	1,099 (79)	409 (80)	942 (80)	
Mild	146 (10)	58 (11)	118 (10)	
Moderate	95 (7)	31 (6)	79 (6)	
Severe	17 (1)	8 (2)	13 (1)	
Extreme	7 (1)	1 (0)	8 (1)	
Missing	29 (2)	7 (1)	22 (2)	0.59
P5. Going up or down stairs				
None	831 (60)	320 (62)	714 (60)	
Mild	273 (19)	110 (21)	239 (20)	

Moderate	183 (13)	54 (11)	133 (11)	
Severe	58 (4)	19 (4)	54 (5)	
Extreme	24 (2)	5 (1)	19 (2)	
Missing	24 (2)	6 (1)	23 (2)	0.53
P6. At night while in bed				
None	1,072 (77)	400 (78)	921 (78)	
Mild	158 (11)	62 (12)	131 (11)	
Moderate	103 (7)	36 (7)	76 (6)	
Severe	30 (2)	8 (2)	25 (2)	
Extreme	7 (1)	2 (0)	11 (1)	
Missing	23 (2)	6 (1)	18 (2)	0.75
P7. Sitting or lying				
None	991 (71)	385 (75)	866 (73)	
Mild	227 (16)	82 (16)	186 (16)	
Moderate	121 (9)	33 (6)	80 (7)	
Severe	28 (2)	9 (2)	25 (2)	
Extreme	4 (0)	1 (0)	5 (0)	
Missing	22 (2)	4 (1)	20 (2)	0.34
P8. Standing upright				
None	926 (67)	356 (69)	815 (69)	
Mild	264 (19)	95 (19)	201 (17)	
Moderate	118 (8)	42 (8)	90 (7)	
Severe	43 (3)	10 (2)	35 (3)	
Extreme	14 (1)	2 (0)	8 (1)	
Missing	28 (2)	9 (2)	33 (3)	0.29

P9. Walking on a hard surface (asphalt, concrete, etc.)				
None	972 (70)	357 (69)	823 (69)	
Mild	219 (16)	93 (18)	186 (16)	
Moderate	129 (9)	44 (9)	106 (9)	
Severe	40 (3)	13 (3)	34 (3)	
Extreme	14 (1)	2 (0)	8 (1)	
Missing	19 (1)	5 (1)	25 (2)	0.15
P10. Walking on an uneven surface				
None	787 (57)	300 (58)	662 (56)	
Mild	306 (22)	120 (24)	274 (23)	
Moderate	171 (12)	62 (12)	146 (13)	
Severe	89 (6)	21 (4)	63 (5)	
Extreme	16 (1)	3 (1)	16 (1)	
Missing	24 (2)	7 (1)	21 (2)	0.82
A1. Descending stairs				
None	916 (66)	371 (72)	803 (68)	
Mild	260 (19)	87 (17)	219 (18)	
Moderate	138 (10)	34 (6)	93 (8)	
Severe	50 (3)	14 (3)	42 (4)	
Extreme	15 (1)	5 (1)	12 (1)	
Missing	14 (1)	3 (1)	13 (1)	0.60
A2. Ascending stairs				
None	840 (60)	334 (65)	730 (62)	
Mild	301 (22)	105 (20)	242 (20)	
Moderate	147 (10)	42 (8)	126 (11)	

Severe	68 (5)	21 (4)	48 (4)	
Extreme	23 (2)	9 (2)	20 (2)	
Missing	14 (1)	3 (1)	16 (1)	0.35
A3. Rising from sitting				
None	892 (64)	330 (64)	757 (64)	
Mild	281 (20)	113 (22)	251 (21)	
Moderate	142 (10)	44 (8)	100 (9)	
Severe	55 (4)	21 (4)	51 (4)	
Extreme	9 (1)	3 (1)	9 (1)	
Missing	14 (1)	3 (1)	14 (1)	0.52
A4. Standing				
None	939 (67)	360 (70)	830 (70)	
Mild	260 (19)	91 (18)	190 (16)	
Moderate	115 (8)	44 (8)	97 (8)	
Severe	48 (4)	14 (3)	34 (3)	
Extreme	17 (1)	2 (0)	14 (1)	
Missing	14 (1)	3 (1)	17 (2)	0.27
A5. Bending to the floor/pick up an object				
None	750 (54)	274 (53)	641 (54)	
Mild	334 (24)	133 (26)	268 (23)	
Moderate	175 (13)	67 (13)	139 (12)	
Severe	85 (6)	25 (5)	72 (6)	
Extreme	35 (2)	11 (2)	43 (3)	
Missing	14 (1)	4 (1)	19 (2)	0.24
A6. Walking on a flat surface				

None	1,089 (78)	399 (78)	926 (78)	
Mild	171 (12)	70 (14)	144 (12)	
Moderate	92 (7)	34 (6)	77 (7)	
Severe	23 (2)	7 (1)	11 (1)	
Extreme	7 (0)	1 (0)	4 (0)	
Missing	11 (1)	3 (1)	20 (2)	0.04
A7. Getting in/out of car				
None	743 (53)	300 (58)	636 (54)	
Mild	357 (25)	122 (24)	295 (25)	
Moderate	191 (14)	61 (12)	151 (13)	
Severe	65 (5)	20 (4)	58 (5)	
Extreme	25 (2)	8 (1)	24 (2)	
Missing	12 (1)	3 (1)	18 (1)	0.13
A8. Going shopping				
None	1,004 (72)	380 (74)	864 (73)	
Mild	198 (14)	64 (12)	124 (10)	
Moderate	113 (8)	47 (9)	113 (10)	
Severe	39 (3)	13 (3)	44 (4)	
Extreme	23 (2)	3 (1)	14 (1)	
Missing	16 (1)	7 (1)	23 (2)	0.24
A9. Putting on socks/stockings				
None	713 (51)	265 (52)	611 (52)	
Mild	341 (24)	126 (24)	274 (23)	
Moderate	195 (14)	68 (13)	134 (11)	
Severe	78 (6)	27 (5)	95 (8)	

Extreme	49 (4)	17 (3)	49 (4)	
Missing	17 (1)	11 (2)	19 (2)	0.33
A10. Rising from bed				
None	1,032 (74)	374 (73)	847 (72)	
Mild	201 (14)	79 (15)	179 (15)	
Moderate	117 (8)	40 (8)	101 (8)	
Severe	26 (2)	10 (2)	28 (2)	
Extreme	7 (1)	5 (1)	9 (1)	
Missing	10 (1)	6 (1)	18 (2)	0.15
A11. Taking off socks/stockings				
None	780 (56)	300 (58)	680 (58)	
Mild	325 (23)	116 (23)	255 (21)	
Moderate	186 (13)	61 (12)	128 (11)	
Severe	49 (4)	21 (4)	58 (5)	
Extreme	40 (3)	12 (2)	42 (3)	
Missing	13 (1)	4 (1)	19 (2)	0.19
A12. Lying in bed (turning over, maintaining hip position)				
None	836 (60)	321 (62)	720 (61)	
Mild	308 (22)	111 (22)	253 (22)	
Moderate	156 (11)	52 (10)	122 (10)	
Severe	52 (4)	18 (3)	52 (4)	
Extreme	17 (1)	3 (1)	14 (1)	
Missing	24 (2)	9 (2)	21 (2)	1.00
A13. Getting in/out of bath				
None	1,038 (74)	378 (74)	880 (75)	

Mild	181 (13)	71 (14)	153 (13)	
Moderate	89 (6)	38 (7)	63 (5)	
Severe	21 (2)	6 (1)	24 (2)	
Extreme	7 (1)	4 (1)	13 (1)	
Missing	57 (4)	17 (3)	49 (4)	0.69
A14. Sitting				
None	1,027 (74)	384 (75)	871 (74)	
Mild	220 (16)	77 (15)	186 (16)	
Moderate	97 (7)	34 (6)	78 (6)	
Severe	24 (2)	9 (2)	22 (2)	
Extreme	8 (0)	1 (0)	2 (0)	
Missing	17 (1)	9 (2)	23 (2)	0.32
A15. Getting on/off toilet				
None	991 (71)	363 (71)	836 (71)	
Mild	225 (16)	84 (16)	199 (17)	
Moderate	120 (9)	38 (7)	94 (8)	
Severe	28 (2)	19 (4)	29 (2)	
Extreme	10 (1)	2 (0)	6 (0)	
Missing	19 (1)	8 (2)	18 (2)	0.93
A16. Heavy domestic duties (moving heavy boxes, scrubbing floors, etc)				
None	602 (43)	231 (45)	513 (43)	
Mild	346 (25)	116 (22)	274 (23)	
Moderate	195 (14)	75 (15)	174 (15)	
Severe	107 (8)	31 (6)	91 (8)	

Extreme	67 (5)	24 (5)	59 (5)	
Missing	76 (5)	37 (7)	71 (6)	0.36
A17. Light domestic duties (cooking, dusting, etc)				
None	1,050 (75)	385 (75)	892 (75)	
Mild	175 (13)	65 (13)	141 (12)	
Moderate	109 (8)	42 (8)	107 (9)	
Severe	21 (2)	8 (1)	10 (1)	
Extreme	7 (0)	3 (1)	9 (1)	
Missing	31 (2)	11 (2)	23 (2)	0.88
SP1. Squatting				
None	562 (40)	205 (40)	474 (40)	
Mild	258 (19)	123 (24)	224 (19)	
Moderate	213 (15)	79 (15)	135 (11)	
Severe	160 (12)	53 (11)	144 (12)	
Extreme	159 (11)	42 (8)	161 (14)	
Missing	41 (3)	12 (2)	44 (4)	0.27
SP2. Running				
None	455 (33)	171 (33)	368 (31)	
Mild	221 (16)	101 (20)	209 (18)	
Moderate	242 (17)	98 (19)	185 (16)	
Severe	187 (13)	57 (11)	159 (13)	
Extreme	231 (17)	66 (13)	199 (17)	
Missing	57 (4)	21 (4)	62 (5)	0.33
SP3. Twisting/pivoting on loaded leg				
None	769 (55)	313 (61)	641 (54)	

Mild	252 (18)	77 (15)	205 (17)	
Moderate	170 (12)	70 (13)	147 (13)	
Severe	93 (7)	19 (4)	86 (7)	
Extreme	71 (5)	25 (5)	68 (6)	
Missing	38 (3)	10 (2)	35 (3)	0.49
SP4. Walking on uneven surface				
None	767 (55)	304 (59)	655 (55)	
Mild	326 (23)	111 (22)	239 (20)	
Moderate	151 (11)	56 (11)	162 (14)	
Severe	85 (6)	26 (5)	65 (6)	
Extreme	39 (3)	9 (2)	33 (3)	
Missing	25 (2)	8 (1)	28 (2)	0.44
Q1. How often are you aware of your hip problem?				
Never	651 (47)	224 (44)	592 (50)	
Monthly	251 (18)	117 (23)	182 (16)	
Weekly	145 (10)	55 (11)	105 (9)	
Daily	247 (18)	95 (18)	205 (17)	
Constantly	77 (5)	17 (3)	70 (6)	
Missing	22 (2)	6 (1)	28 (2)	0.16
Q2. Have you modified your life style to avoid activities potentially damaging to your hip?				
Not at all	595 (43)	214 (41)	498 (42)	
Mildly	411 (29)	164 (32)	375 (32)	
Moderately	185 (13)	61 (12)	126 (11)	
Severely	147 (11)	60 (12)	135 (11)	

Totally	38 (3)	10 (2)	29 (2)	
Missing	17 (1)	5 (1)	19 (2)	0.52
Q3. How much are you troubled with lack of confidence in your hip?				
Not at all	820 (59)	294 (57)	714 (60)	
Mildly	352 (25)	149 (29)	284 (24)	
Moderately	111 (8)	40 (8)	86 (7)	
Severely	76 (6)	22 (4)	67 (6)	
Extremely	19 (1)	5 (1)	18 (2)	
Missing	15 (1)	4 (1)	13 (1)	0.82
Q4. In general, how much difficulty do you have with your hip?				
None	669 (48)	244 (48)	605 (51)	
Mild	431 (31)	170 (33)	332 (28)	
Moderate	193 (14)	69 (13)	160 (14)	
Severe	58 (4)	21 (4)	52 (4)	
Extreme	28 (2)	7 (1)	19 (2)	
Missing	14 (1)	3 (1)	14 (1)	0.52

Appendix table 2. EQ-5D dimensions and EQ VAS for responders having ceramic-on-ceramic (CoC), metal-on-metal (MoM) and metal-on-polyethylene (MoP) total hip arthroplasty and comparison of the proportion of answered and unanswered items. Values represent numbers and percentage of patients within each bearing group.

	CoC n=1,393	MoM n=512	MoP n=1,177	p-value
EQ-5D index				
Mobility				
No problems (%)	1,085 (78)	419 (82)	938 (79)	
Some problems (%)	284 (20)	88 (17)	225 (19)	
Confined to bed (%)	2 (0)	1 (0)	6 (1)	
Missing (%)	22 (2)	6 (1)	13 (1)	0.54
Self-Care				
No problems (%)	1,213 (87)	452 (88)	1,021 (86)	
Some problems (%)	153 (11)	52 (10)	138 (12)	
Unable (%)	4 (0)	3 (1)	9 (1)	
Missing (%)	23 (2)	7 (1)	14 (1)	0.60
Usual Activities				
No problems (%)	927 (66)	351 (68)	802 (68)	
Some problems (%)	404 (29)	142 (27)	323 (27)	
Unable (%)	36 (3)	13 (3)	44 (4)	
Missing (%)	26 (2)	8 (2)	13 (1)	0.29
Pain/Discomfort				
None (%)	899 (65)	327 (63)	745 (63)	
Moderate (%)	434 (31)	168 (33)	401 (34)	

Extreme (%)	35 (2)	10 (2)	25 (2)	
Missing (%)	25 (2)	9 (2)	11 (1)	0.16
Anxiety/Depression				
None (%)	1,198 (86)	433 (84)	1,015 (86)	
Moderate (%)	154 (11)	66 (13)	140 (12)	
Extreme (%)	10 (1)	7 (1)	8 (1)	
Missing (%)	31 (2)	8 (2)	19 (1)	0.43
EQ VAS				
0	12 (1)	8 (2)	9 (1)	
1-25	20 (1)	5 (1)	17 (1)	
26-50	153 (11)	38 (7)	137 (12)	
51-75	282 (20)	124 (24)	292 (25)	
75-99	710 (51)	267 (52)	556 (47)	
100	134 (10)	44 (9)	106 (9)	
Missing	82 (6)	28 (5)	65 (5)	0.90

Appendix table 3. UCLA activityscore for responders having ceramic-on-ceramic (CoC), metal-on-metal (MoM) and metal-on-polyethylene (MoP) total hip arthroplasty and comparison of the proportion of answered and unanswered items. Values represent numbers and percentage of patients within each bearing group.

	CoC n=1,393	MoM n=512	MoP n=1,177	p-value
1. Wholly inactive: dependent on others; cannot leave residence	3 (0)	0 (0)	3 (0)	
2. Mostly inactive: restricted to minimal activities of daily living	23 (2)	5 (1)	17 (1)	
3. Sometimes participate in mild activities, such as walking, limited housework, and limited shopping	98 (7)	39 (8)	113 (10)	
4. Regularly participate in mild activities	144 (10)	49 (9)	149 (13)	
5. Sometimes participate in moderate activities, such as swimming and unlimited housework or shopping	166 (12)	50 (10)	156 (13)	
6. Regularly participate in moderate activities	225 (16)	87 (17)	185 (16)	
7. Regularly participate in active events, such as bicycling	369 (27)	128 (25)	284 (24)	
8. Regularly participate in very active events, such as golf	87 (6)	37 (7)	59 (5)	
9. Sometimes participate in impact sports such as jogging, tennis, skiing, acrobatics, ballet, heavy labor, or backpacking	127 (9)	62 (12)	92 (8)	
10. Regularly participate in impact sports	119 (9)	52 (10)	100 (8)	
Missing	32 (2)	5 (1)	24 (2)	0.18

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12. APPENDIX

Questionnaire (aim III)

«navn» «co»
«adresse» «sted»
«postnrby»

Odense den 25.10.2012

Videnskabelig undersøgelse af hoftefunktion og livskvalitet efter indsættelse af hofteprotese

Du har fået indsat en kunstig hofteprotese, og vi er i gang med en stor spørgeskemaundersøgelse, som omhandler hoftefunktion og livskvalitet efter din hofteoperation. 5.730 patienter vil blive spurgt om deltagelse i undersøgelsen, og enhver besvarelse af spørgeskemaet har stor betydning for det endelige resultat.

Det samlede resultat af vores spørgeskemaundersøgelse vil bringe ny viden til gavn for fremtidige patienter. Resultatet forventes offentliggjort på kongresser i Danmark og udlandet samt forventes trykt i nationale og internationale tidsskrifter.

Spørgsmålene i spørgeskemaet tager ca. 15 minutter at besvare, og vi beder om, at du først gennemlæser siden "Sådan udfyldes spørgeskemaerne" og efterfølgende besvarer alle spørgsmål.

Spørgsmålene omhandler hofteprotesen på «side» side.

Spørgeskemaet sendes retur i vedlagt svarkuvert, hvor portoen er betalt. Hvis vi ikke har modtaget dit udfyldte spørgeskema indenfor ca. 4 uger, vil vi tillade os at sende dig en påmindelse om udfyldelse af spørgeskemaet. Vi er klar over, at nogle patienter har modtaget lignende spørgeskema tidligere, men vi kan ikke genbruge svarene og beder derfor om din forståelse for nødvendigheden af at besvare spørgsmålene endnu en gang.

Projektetsgennemførelse er godkendt af Datatilsynet og Sundhedsstyrelsen, som endvidere har leveret relevante data fra Sundhedsregistrene.

Vi siger mange tak for din deltagelse i vores spørgeskemaundersøgelse.

Med venlig hilsen

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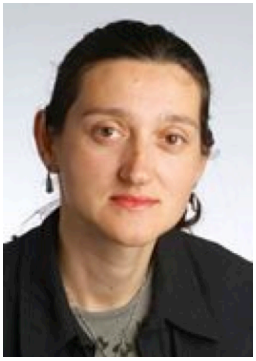


Sådan udfyldes spørgeskemaerne

- Læs teksten/vejledningen på de forskellige spørgeskemaer.
- Hvis der er spørgsmål, hvor dit svar ikke helt passer til svarmulighederne, skal du sætte kryds ved det svar, der passer **bedst** til din situation.
- Der skal kun sættes **ét** kryds per spørgsmål.
- Det er vigtigt for undersøgelsen, at **alle** spørgsmålene besvares.
- Skulle et spørgeskema blive borte eller ødelagt, kan du få tilsendt et nyt ved at kontakte 1. reservelæge Claus Varnum på telefon 7940 5779 mellem kl. 14.45-15.15 eller ved at sende en e-mail til: Claus.Varnum@slb.regionsyddanmark.dk.
- Det er vigtigt at bruge en kuglepen, der skriver mørkeblåt eller anden mørk farve, når skemaet udfyldes.
- Sæt tydeligt kryds indenfor feltet.
- Hvis et felt er udfyldt forkert, skal **hele** feltet skraveres, og krydset sættes i det rigtige felt.
- Svarene bliver skannet ind på en computer, så kryds skal være nemme at tolke, som vist i nedenstående eksempler.

Eksempler på angivelser af afkrydsning	**RIGTIGT**	**FORKERT**
Sæt tydeligt kryds **indenfor** feltet. Kryds eller tal må **ikke** ramme kanten rundt om feltet		
Hvis et felt er udfyldt forkert, skal **HELE** feltet skraveres, og krydset sættes i det rigtige felt.		

Vigtige oplysninger

1. Hvad er din nuværende højde? (Skal skrives i cm, f.eks. 167 cm)	☐☐☐ cm

2. Hvad er din nuværende vægt? (Skal skrives i hele tal, f.eks. 68 kg)	☐☐☐ kg

	Ja	Nej
3. Er du blevet opereret igen i din **«side»** hofte med fjernelse eller udskiftning af en eller flere protesedele efter isættelsen af hofteprotesen?	☐	☐

HOOS
Spørgeskemaer til patienter med hofteproblemer

Vejledning: Dette spørgeskema indeholder spørgsmål om, hvordan din hofte fungerer. Svarene skal hjælpe os til at følge med i hvordan du har det, og hvor godt du klarer dig i hverdagen.
Du skal besvare spørgsmålene ved at sætte kryds i de svar, der passer bedst på dig. Du må kun sætte ét kryds ved hvert spørgsmål. Du skal besvare ALLE spørgsmål. Hvis du er i tvivl om hvad du skal svare, er det vigtigt at du alligevel sætter kryds i den svar-boks, der føles mest rigtig.

Symptomer
Tænk på de **symptomer** og det besvær du har haft i forhold til din hofte i løbet af **den sidste uge**, når du besvarer de næste spørgsmål.

S1	**Har du murren i hoften, hørt klik eller andre lyde fra hoften?**	Aldrig	Sjældent	Ind imellem	Ofte	Altid
		☐	☐	☐	☐	☐
S2	**Har du problemer med at få benene langt ud til siden?**	Ingen	Lette	Moderate	Store	Meget store
		☐	☐	☐	☐	☐
S3	**Har du problemer med at tage skridtet fuldt ud, når du går?**	Ingen	Lette	Moderate	Store	Meget store
		☐	☐	☐	☐	☐

Stivhed
Følgende spørgsmål handler om **stivhed i hofteleddet**. Stivhed medfører besvær med at komme i gang eller øget modstand, når du bevæger hoften. **Angiv i hvor høj grad du har oplevet stivhed i hoften i løbet af den sidste uge.**

S4	**Hvor stiv er du i din hofte, når du lige er vågnet om morgenen?**	Slet ikke	Lidt	Moderat	Meget	Ekstremt
		☐	☐	☐	☐	☐
S5	**Hvor stiv er du i din hofte senere på dagen, efter at du har siddet eller ligget og hvilet?**	Slet ikke	Lidt	Moderat	Meget	Ekstremt
		☐	☐	☐	☐	☐

Smerter

P1 Hvor ofte har du ondt i hoften?	Aldrig	Hver måned	Hver uge	Hver dag	Altid
	☐	☐	☐	☐	☐

Følgende spørgsmål handler om hvor mange smerter du har haft i hoften i løbet af **den sidste uge.**
Angiv graden af smerter du har oplevet i følgende situationer?

	Ingen	Let	Moderat	Stærk	Meget stærk
P2 Rette hoften helt ud	☐	☐	☐	☐	☐
P3 Bøje hoften helt	☐	☐	☐	☐	☐
P4 Gå på jævnt underlag	☐	☐	☐	☐	☐
P5 Gå op eller ned ad trapper	☐	☐	☐	☐	☐
P6 Om natten, når du ligger ned (smerter, som forstyrrer din søvn)	☐	☐	☐	☐	☐
P7 Sidde eller ligge	☐	☐	☐	☐	☐
P8 Stående	☐	☐	☐	☐	☐
P9 Gå på hårdt underlag, fx asfalt eller fliser	☐	☐	☐	☐	☐
P10 Gå på ujævnt underlag	☐	☐	☐	☐	☐

Fysisk funktion
Følgende spørgsmål handler om din fysiske funktion. **Angiv hvilken grad af besvær du har haft under følgende aktiviteter i løbet af den sidste uge, på grund af problemer med din hofte**.

		Ingen	Let	Moderat	Stor	Meget stor
A1	**Gå ned ad trapper**	☐	☐	☐	☐	☐
A2	**Gå op ad trapper**	☐	☐	☐	☐	☐
A3	**Rejse sig fra siddende**	☐	☐	☐	☐	☐
A4	**Stå stille**	☐	☐	☐	☐	☐
A5	**Bøje sig ned, fx for at samle noget op fra gulvet**	☐	☐	☐	☐	☐
A6	**Gå på jævnt underlag**	☐	☐	☐	☐	☐
A7	**Stige ind/ud af en bil**	☐	☐	☐	☐	☐
A8	**Handle ind/gå på indkøb**	☐	☐	☐	☐	☐
A9	**Tage strømper på**	☐	☐	☐	☐	☐
A10	**Stå ud af sengen**	☐	☐	☐	☐	☐
A11	**Tage strømper af**	☐	☐	☐	☐	☐

		Ingen	Let	Moderat	Stor	Meget stor
A12	**Ligge i sengen (vende sig eller have hoften i samme stilling i lang tid)**	☐	☐	☐	☐	☐
A13	**Stige ind og ud af brusebad/badekar**	☐	☐	☐	☐	☐
A14	**Sidde**	☐	☐	☐	☐	☐
A15	**Sætte sig og rejse sig fra toilettet**	☐	☐	☐	☐	☐
A16	**Udføre tungt husarbejde (vaske gulv, støvsuge, bære øl/sodavandskasser o.lign.)**	☐	☐	☐	☐	☐
A17	**Udføre let husarbejde (lave mad, tørre støv af o.lign.)**	☐	☐	☐	☐	☐

Funktion, sport og fritid
Følgende spørgsmål handler om din fysiske formåen. **Angiv hvilken grad af besvær du har haft under følgende aktiviteter i løbet af den sidste uge, på grund af problemer med din hofte.**

		Ingen	Let	Moderat	Stor	Meget stor
SP1	**Sidde på hug**	☐	☐	☐	☐	☐
SP2	**Løbe**	☐	☐	☐	☐	☐
SP3	**Vride/dreje kroppen, når du står på benet**	☐	☐	☐	☐	☐
SP4	**Gå på ujævnt underlag**	☐	☐	☐	☐	☐

Livskvalitet

Q1	**Hvor ofte bliver du mindet om dine problemer med hoften?**	Aldrig	Hver måned	Hver uge	Hver dag	Altid
		☐	☐	☐	☐	☐
Q2	**Har du ændret din måde at leve på for at undgå at belaste hoften?**	Slet ikke	Noget	Moderat	I stor udstrækning	Totalt
		☐	☐	☐	☐	☐
Q3	**I hvor høj grad kan du stole på din hofte?**	Fuldt ud	I stor udstrækning	Moderat	Til en vis grad	Slet ikke
		☐	☐	☐	☐	☐
Q4	**Hvor store problemer har du generelt med din hofte?**	Ingen	Små	Moderate	Store	Meget store
		☐	☐	☐	☐	☐

EQ-5D
Helbredsspørgeskema

Angiv, ved at sætte kryds i én af kasserne i hver gruppe, hvilke udsagn, der bedst beskriver din helbredstilstand i dag.

Bevægelighed

Jeg har ingen problemer med at gå omkring	
Jeg har nogle problemer med at gå omkring	
Jeg er bundet til sengen	

Personlig pleje

Jeg har ingen problemer med min personlige pleje	
Jeg har nogle problemer med at vaske mig eller klæde mig på	
Jeg kan ikke vaske mig eller klæde mig på	

Sædvanlige aktiviteter *(fx. arbejde, studie, husarbejde, familie- eller fritidsaktiviteter)*

Jeg har ingen problemer med at udføre mine sædvanlige aktiviteter	
Jeg har nogle problemer med at udføre mine sædvanlige aktiviteter	
Jeg kan ikke udføre mine sædvanlige aktiviteter	

Smerter/ubehag

Jeg har ingen smerter eller ubehag	
Jeg har moderate smerter eller ubehag	
Jeg har ekstreme smerter eller ubehag	

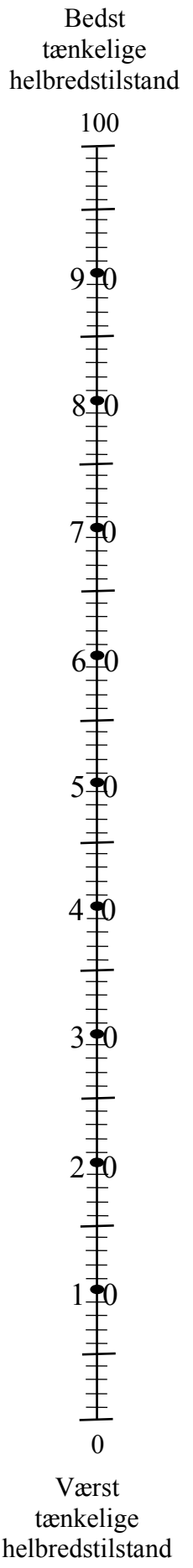
Angst/depression

Jeg er ikke ængstelig eller deprimeret	
Jeg er moderat ængstelig eller deprimeret	
Jeg er ekstremt ængstelig eller deprimeret	

For at hjælpe folk med at sige, hvor god eller dårlig en helbredstilstand er, har vi tegnet en skala (næsten ligesom et termometer), hvor den bedste helbredstilstand du kan forestille dig er markeret med 100, og den værste helbredstilstand du kan forestille dig er markeret med 0.

Vi beder dig angive på denne skala, hvor godt eller dårligt du mener dit eget helbred er i dag. Angiv dette ved at tegne en streg fra kassen nedenfor til et hvilket som helst punkt på skalaen, der viser, hvor god eller dårlig din helbredstilstand er i dag.

Din egen helbredstilstand i dag



UCLA aktivitetsscore

Afkryds det felt, der bedst beskriver dit aktuelle aktivitetsniveau (sæt kun ét kryds).

1. Fuldstændig inaktiv, afhængig af andre og kan ikke forlade bopælen	☐
2. For det meste inaktiv eller begrænset til et minimum af dagligdags aktiviteter	☐
3. Deltager ind imellem i lette aktiviteter som gang, begrænset husligt arbejde og begrænsede indkøbsaktiviteter	☐
4. Deltager jævnligt i lette aktiviteter	☐
5. Deltager ind imellem i moderate aktiviteter som svømning eller kan deltage i ubegrænset husligt arbejde eller ubegrænsede indkøbsaktiviteter	☐
6. Deltager jævnligt i moderate aktiviteter	☐
7. Deltager jævnligt i aktiviteter som cykling	☐
8. Deltager jævnligt i aktiviteter som golf	☐
9. Deltager ind imellem i aktiviteter med høj intensitet som løb, tennis, skiløb, akrobatik, ballet, hårdt fysisk arbejde eller vandreture	☐
10. Deltager jævnligt i aktiviteter med høj intensitet	☐

Spørgeskema om lyde fra hofteprotese

1. Er der/har der været lyde fra den opererede hofte? Sæt kun ét kryds.

Ja (besvar venligst resten af spørgeskemaet)	☐
Nej (du er nu færdig med udfyldelse af spørgeskemaet)	☐

2. Er/var lyden(e) pibende? Sæt kun ét kryds.

Ja	☐
Nej	☐

3. Er/var lyden(e) knirkende? Sæt kun ét kryds.

Ja	☐
Nej	☐

4. Er/var lyden(e) skurrende? Sæt kun ét kryds.

Ja	☐
Nej	☐

5. Er/var lyden(e) klikkende? Sæt kun ét kryds.

Ja	☐
Nej	☐

6. Er/var lyden(e) andet end ovenstående? Sæt kun ét kryds.

Ja	
Nej	
Hvis ja, beskriv:	

Hvis du oplever/har oplevet flere forskellige lyde fra den opererede hofte, bedes du besvare nedenstående spørgsmål ud fra den mest fremtrædende lyd.

7. Hvornår begyndte lyden?

Inden for en måned efter operationen?	Ja	
	Nej	
Hvis NEJ, angiv venligst hvor mange måneder efter operationen lyden begyndte		
Ved ikke		

8. Hvor ofte er/var lyden til stede? Sæt kun ét kryds.

Mindst en gang dagligt	
Mindst en gang ugentligt	
Sjældnere end en gang ugentligt	

9. Hvor høj er/var lyden? Sæt kun ét kryds.

Kan kun høres af dig selv	
Kan af og til høres af andre	
Kan altid høres af andre	

10. Kommer/kom lyden, når du rejser/rejste dig fra en stol? Sæt kun ét kryds.

Ja	☐
Nej	☐

11. Kommer/kom lyden, når du sætter/satte dig ned? Sæt kun ét kryds.

Ja	☐
Nej	☐

12. Kommer/kom lyden, når du bøjer/bøjede dig fremover? Sæt kun ét kryds.

Ja	☐
Nej	☐

13. Kommer/kom lyden, når du går/gik? Sæt kun ét kryds.

Ja	☐
Nej	☐

14. Kommer/kom lyden, når du går/gik på trapper? Sæt kun ét kryds.

Ja	☐
Nej	☐

15. Kommer/kom lyden, når du træder/trådte op på et højt trin? Sæt kun ét kryds.

Ja	☐
Nej	☐

16. Kommer/kom lyden ved anden aktivitet? Sæt kun ét kryds.

Ja	
Nej	
Hvis ja, beskriv:	

17. Har lyden fra din hofte bevirket, at du er/var mindre fysisk aktiv? Sæt kun ét kryds.

Slet ikke	
Lidt	
Moderat	
Meget	
Ekstremt	

18. Har lyden fra din hofte hæmmet dit samvær med andre mennesker? Sæt kun ét kryds.

Slet ikke	
Lidt	
Moderat	
Meget	
Ekstremt	

Tak for din besvarelse