Studies based on the Danish Hip Arthroplasty Registry

PhD thesis

Alma Bečić Pedersen

Faculty of Health Sciences

University of Aarhus, Denmark, 2006

Department of Clinical Epidemiology, Aarhus University Hospital

Report no. 20

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Department of Orthopedics, Aarhus University Hospital
Department of Clinical Epidemiology, Aarhus University Hospital
Department of Orthopedics, Odense University Hospital

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Supervisors

Ulf Lucht, MD, DMSc
Department of Orthopaedics
Aarhus University Hospital, Denmark

Søren Paaske Johnsen MD, PhD
Department of Clinical Epidemiology
Aarhus University Hospital, Denmark

Kjeld Søballe, Professor, MD, DMSc
Department of Orthopaedics
Aarhus University Hospital, Denmark;

Søren Overgaard, Professor, MD, DMSc
Department of Orthopaedics
Odense University Hospital, Denmark

Evaluation committee

Anders Odgaard, Lecturer, MD, DMSc
Department of Orthopaedics
Aarhus University Hospital, Denmark

Torben Jørgensen, Lecturer, Chief of the Center, MD, DMSc
Research Center for Prevention and Health
Glostrup Hospital, Denmark

Ove Furnes, MD, PhD
Department of Orthopaedics
Haukeland Universitetssygehus, Bergen, Norway

Preface

This PhD thesis is based on studies carried out during my employment at the Department of Clinical Epidemiology and the Department of Orthopedics, Aarhus University Hospital, University of Aarhus, in the period 2002-2005.

I am deeply indebted to a number of persons who have made this work possible. First of all, I wish to express my sincere gratitude to my supervisors Ulf Lucht, Søren Overgaard, and Kjeld Søballe for their valuable and skilful guidance, discussion, and support in the field of orthopedic surgery. I am especially grateful to my supervisor Søren Paaske Johnsen for his great engagement in my daily work, enthusiasm, and patience, and wonderful way of advising me throughout the research period.

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I. Alma B. Pedersen, Søren P. Johnsen, Søren Overgaard, Kjeld Søballe, Henrik T. Sørensen, Ulf Lucht. Registration in the Danish Hip Arthroplasty Registry. Completeness of total hip arthroplasties and positive predictive value of registered diagnosis and postoperative complications. Acta Orthop Scand 2004; 75 (4):434-441.

II. Alma B. Pedersen, Søren P. Johnsen, Søren Overgaard, Kjeld Søballe, Henrik T. Sørensen, Ulf Lucht. Total hip arthroplasty in Denmark. Incidence of primary operations and revisions during 1996-2002 and estimated future demands. Acta Orthopaedica 2005; 76 (2): 182-189.

III. Alma B. Pedersen, Søren P. Johnsen, Søren Overgaard, Kjeld Søballe, Henrik T. Sørensen, Ulf Lucht. Regional variation in incidence of primary total hip arthroplasties and revisions in Denmark, 1996-2002. Acta Orthopaedica 2005; 76 (6): 815-822.

IV. Alma B. Pedersen, Søren P. Johnsen, Søren Overgaard, Kjeld Søballe, Henrik T. Sørensen, Ulf Lucht. Patient-related predictors of short and long term implant failure after primary total hip arthroplasty. A nationwide Danish follow-up study with 36 984 patients. Submitted.

Abbreviations

DHR	Danish Hip Arthroplasty Registry
THA	Total hip arthroplasty
ICD	International Classification of Diseases
CI	Confidence Interval
IR	Incidence rate
IRR	Incidence rate ratio
OA	Osteoarthritis

CONTENTS

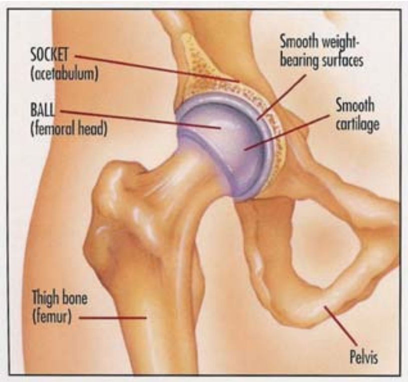
1. INTRODUCTION

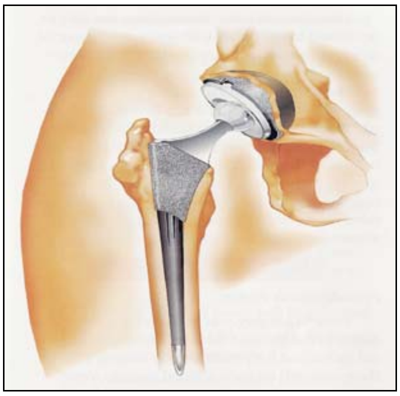
1.1. Clinical background

1.1.1. THA history and aim

A total hip arthroplasty (THA) is a surgical procedure which involves surgical removal of diseased cartilage and bone of the femoral head and acetabulum, and replacing them with a artificial ball joint, which includes a stem inserted into the femur bone with a ball on the top and an artificial socket with plastic liner inside, acetabulum (1) (Figure 1). The artificial ball, stem and socket are referred to as the "prosthesis" or “arthroplasty”.

Figure 1. Total hip arthroplasty





The history of THA started in 1925 with the invention of the “mould arthroplasty” by Marius Smith-Petersen from Boston, Massachusetts. He moulded a piece of glass into the shape of a hollow hemisphere and fitted it over the ball of a patient’s hip joint. Because the glass was very fragile, he later experimented with other materials, including plastic and steel (2). During the 1940’s, “mould arthroplasty” was the preferred method of treatment for osteoarthritis. However, “mould arthroplasty” was not a suitable treatment for all patients with arthritic hip deformities, as many patients still complained of pain and limited hip movement. Subsequently, Frederick R. Thomsen from New York and Austin T. Moore from South Carolina separately introduced a new type of hip arthroplasty, called hemiarthroplasty (3) which solved the problem of the arthritic femoral head by replacing it with a metal ball. The acetabulum was not replaced. Hemiarthroplasty was however, also associated with a number of problems, including destruction of the normal acetabulum surface and pain because of early loosening of the implant. This led to the development of total hip arthroplasty in 1960 by John Charnley from England (4;5). He replaced the acetabulum component with polyethylene, whereas the femoral component was made of metal. His further achievements were to use methyl-methacrylate bone cement for fixation of both components, and the development of the concept of low-friction arthroplasty (4), using a 22 mm-diameter femoral head to reduce the contact area and subsequent friction, and introduction of clean-air operating technique to reduce the risk of infection during the surgery (6).The Charnley prosthesis is still one of the most frequently used (7;8).

The aims of the THA treatment are relief of pain and improvement of function and quality of life, and THA has proved to be successful in achieving those goals (9-11). THA is usually considered following the failure of other treatments, such as pain medication, osteosynthesis, osteotomy, or hemiarthroplasty.

Primary osteoarthritis is the most common diagnosis for primary THA (75%) (7). When none of the other diagnoses below listed are present, patient is assigned diagnoses primary osteoarthritis. Other diagnoses for primary THA include a fresh fracture of the proximal femur, late sequelae from a fracture of the proximal femur, fracture of the acetabulum, traumatic hip dislocation, atraumatic necrosis of femoral head, rheumatoid arthritis, Mb. Bechterew, congenital hip dislocation, Mb. Calve-Legg-Perthes, epiphysiolysis, and acetabular dysplasia.

1.1.2. Literature search

We used the Medline Database for the literature search. The keywords in the aim I were ”arthroplasty, replacement, hip” in combination with “validity”, “data quality”, “hip registry”, “predictive value”. The following keywords were used for aim II and III: ”arthroplasty, replacement, hip” combined with “epidemiology”, “statistics and numerical data”, “incidence”, “utilization”, “variation”, and “geographic”. For the aim IV, we used ”arthroplasty, replacement, hip” combined with “risk factors”, “prognosis”, and “predictor” as the keywords. Moreover, the reference lists of relevant articles, mostly based on data from the national databases, were reviewed. Thus, the literature search was not based on systematically review of literature.

1.1.3. Incidence rates of THA procedures

Due to the improvements in the surgical technique and the increasing number of elderly people in most Western populations, the annual number of THA procedures has risen steadily worldwide during the last decades (8;12-17). However, there are substantial differences between the reported THA incidence rates in Europe, United States, Canada, and Australia (18). Recent studies on incidence rates of primary THA are presented in Table 1. A number of factors have been proposed as possible reasons for the variation in incidence rates, including differences in age and sex distribution of the studied populations, variation in the proportion of patients with osteoarthritis, and comparison of different study periods (18;19). Table 1 shows that less than half of the studies have presented age-adjusted incidence rates.

Although THA surgery, together with other forms of major joint surgery, is among the most resource-demanding areas within Western health care systems (20), it appears to be both a cost-utility and a cost-effective procedure (9;21;22). Several cost analyses have been done in the field of THA surgery. The results are usually expressed as costs per Quality Adjusted Life Years (QALY) based on use of well-established health measurement scales to assess quality of life and functional status after the procedure. The patients achieved quality of life within all parameters of the various health measurement scales, and the QALY gained was maintained during a 5 year follow-up period (9;22). The costs-effectiveness of THA, including acute hospital costs, physician costs, and post-acute care rehabilitation costs, compared with cost-effectiveness of conservative management, including the physician, medication, and custodial care costs due to functional and social dependency, are approximately $4,600 per QALY gained (21).

Table 1. Recent studies on incidence rates (IR) of primary THA.

Authors	Country	Study period	Age	Annual IR per 100,000	Indication for primary THA	Age standardized
Ingvarsson (23)	Iceland	1992-1996	All	114*	OA†	No
Ingvarsson (19)	Iceland Sweden	1992-1996 1992-1996	> 49	319 209	OA OA	Yes Yes
Ostendorf et al. (15)	Netherlands	1986 1997	All	71 112	All	No
Puolakka et al. (16)	Finland	1999	All	93	All	No
Hoaglund et al. (24)	United States (San Francisco)	1984-1988	All	7.3* Chinese 75.5* White	All	Yes
Mahomed et al. (14)	United States	1995-1996	> 65	164-295‡	All§	No
Peterson et al. (25)	United States	1988	> 65	194-883‡	All§	Yes
Madhok et al. (26)	United States (Olmsted County)	1969-1974 1987-1990	All	49* 60*	All	Yes
Wells et al. (17)	Australian	1994 1998	> 30	51 61	OA	No
Alibhai et al. (27)	Canada (Alberta)	1991-1992 1996-1997	All	72 85	All	Yes
Bourne et al. (28)	Canada	1998-1999	> 65	190-440‡	All	Yes
Herberts et al. (29)	Sweden	1991-1995	All	108-125‖	All	No
Havelin et al. (12)	Norway	1988-1998	All	120*	All	No
Dunsmuir et al. (30)	Scotland	1991-1993	All	66.9* urban area 85.6* rural area	All	No
Birrell et al. (31)	England	1996	All	87	All	Yes
Overgaard et al. (32)	Denmark	1988-1990	All	86* women 78* men	All	No

* Overall IR
† Primary osteoarthritis; ‡ In different regions; § Fracture excluded; ‖ Variation during the study period.

It has, however, been suggested that the future needs for THA may exceed the current capacity for THA procedures (13;31). The projected number of primary THAs in England has been estimated to increase with 40% in year 2026 compared to 1996, based on the projected population change alone (31). Likewise, the needs for primary THA for osteoarthritis in Iceland have been estimated to increase with approximately 36% from 1996 to 2015 (23). In 1992, the total number of primary THAs in Denmark in the year 2000 was estimated at 4,461 (32), based on population forecast; However, in reality 5,474 primary THAs were done in 2000 (33).

Estimations of the future incidence of primary THA procedures may be indicative for the number of revisions. Thus, the absolute number of patients needing revision is likely to increase as a consequence of the increasing number of patients requiring primary THA. The costs of a revision in Denmark are more than three times higher than the costs of a primary THA according to the National Danish Diagnosis Related Groups (DRG) system, used by the government as the method to distribute economical sources to hospitals depending on the surgical activities (34).

A number of studies have indicated that the incidence rates of THA procedures vary between different types of hospitals (*e.g.,* university, central, and local) (8), and geographical regions, even within small areas (17;18;27). Regional variations in incidence rates have also been found for numerous other surgical procedures, including lower extremity revascularization, spinal surgery, radical and transurethral prostatectomy, coronary artery bypass grafting, mastectomy, knee arthroplasty, angioplasty, and cataract surgery (17;35-37), and also for a number of chronic medical diseases (38). A number of factors have been suggested to be associated with the variation of the utilization patterns of medical care in general. The factors included differences in occurrence of illness in the underlying populations, differences in patient preferences, variations in the effectiveness of the offered treatment and care, differences in the medical decision making, or differences in the availability of healthcare resources in the units which have been compared (39) (Table 2).

Table 2. Factors which may possible be associated with variation in the utilization of medical care.

Patient related	
	Age
	Sex
	Illness
	Patient preferences
Physician related	
	Number of physicians
	Medical decision making
Healthcare system related	
	Availability of resources
	Flexibility in relation to allocation of resources
	Spending

In theory, any differences in the health of the underlying populations should be reflected by the resources available in corresponding health care units. However, although differences in health appear to be substantial between different populations, they still explain only one third of the variation in the healthcare expenditure in United States (39). Moreover, experiences from the US have also confirmed that although treatment choice should rely on the decisions made by informed patients based on thorough information from the physicians; they are in practice, often delegated to the physicians. However, there are substantial differences among physicians concerning decision making, even in areas with strong evidence of efficacy of the treatment (40). Furthermore, according to information from the Dartmouth Atlas of Health Care project in the US, increased expenditure is not necessarily associated with increased use of the health care services (41).

In order to improve the quality and efficiency, the healthcare system in Denmark has undergone a marked change over the last few years. This change began with the introduction of the principle of free hospital choice for all patients in 1993, and was followed by a reduction in the number of somatic hospitals from 90 to 60, and a decrease in the average length of hospital stays from 6.7 to 5.1 between 1990 and 2002 (42). In recent years, considerable effort has been channelled into developing and implementing clinical guidelines based on scientific and clinical evidence in order to improve the quality of treatment and care, and to ensure shared decision making both among surgeons, and between surgeon and patient.

Denmark is divided into 14 counties and one municipality. There is a system of partial fiscal equalisation between the various counties and municipalities that removes 45% of the difference between the municipal figure and the national average. As a result of this system, 80% of the differences in fiscal resources between the counties are removed. Further, Denmark is considered one of the European countries with the lowest poverty rate, which is largely because of the redistribution of incomes (43). Thus, in theory, fiscal resources should have minor impact on utilization rates of medical care in Denmark.

1.1.4. Outcomes of THA

The performance of the THA can be measured in different ways, including for instance the occurrence of postoperative complications or the implant failure rate. There are a number of complications which can occur in the immediate postoperative period, such as superficial and deep infection, haematoma, wound rupture, one or several hip dislocations, fracture or fissure of femur, deep vein thrombosis, paralysis of peroneal nerve, pain in the hip, or leg length difference. According to annual reports from the hip replacement clinical databases in the Scandinavian countries, the frequency of postoperative complications has increased in the last five years by 20-80% (44-46). Although a patient may have sustained one of the postoperative complications, it is not necessarily the reason for implant failure and subsequent revision. The term "implant failure" is used when a part of or the whole implant is removed or exchanged. Aseptic loosening, with or without osteolysis of the femur and/or the acetabulum component, is the main cause of revision (7). Other reasons for revision include deep infection, dislocation, femoral fracture, pain, osteolyses/granuloma formation, implant failure, and a number of miscellaneous reasons. The overall failure rates have been reported to vary between 5-20 %, 5-15 years after primary surgery and depend on many factors including cause of failure, implant type or fixation, and data source (47;48).

A number of patient and surgery related factors have been proposed to be associated with the risk of implant failure (Table 3). Although the majority of the suggested factors are able to predict implant failure, they are not all necessarily the direct cause of failure.

The primary focus of the existing studies has been overall implant failure 5-15 years after primary THA, whereas data on short-term implant failure are sparse.

Table 3. Predictors of implant failure

Patient related	
	Age
	Sex
	Comorbidity
	Smoking
	Medication at follow-up
	Alcohol intake
	Height
	Weight
	Diagnosis for primary THA
Surgery related	
	Antibiotic prophylactic treatment
	A revision of opposite hip
	The time between right and left primary THA
	Type of bone cement
	Pulsatile lavage
	Proximal femoral seal
	Distal femoral plug
	Non steroid antiinflamatory drugs treatment
	Femoral head size
	Surgeon volume
	Particular implant component
	Year of the primary THA
	Duration of surgery
	Fixation technique

Patient related predictors of implant failure

In relation to implant failure due to any reason, younger age and males have consistently been found to be associated with increased overall risk after 5, 10, 15, or 20 years of follow-up (8;16;49-51). Higher Charlson comorbidity index (over 2) have also been associated with increased overall risk of implant failure due to any reason during the median follow-up time of 47 months (52). In addition, being a former heavy smoker was associated with an increased overall risk of implant failure due to any reason compared with non-smokers, even when controlling for a number of patient- and surgery-related factors (53). Moreover, use of systemic steroids and local pulmonary steroids at the time of the primary operation, as well as antibiotics for at least one month after primary surgery have been associated with an increased overall risk of implant failure due to any reason (53).

In relation to implant failure due to specific causes, alcohol intake has been associated with an increased overall risk of implant failure due to dislocation (53). Finally, increasing body mass index was found not to be associated with an overall risk of implant failure due to any reason, although subanalyses showed that increasing weight can be a predictor of implant failure among males older that 67 years who were taller than 1.77 cm (53).

Surgery related predictors of implant failure

A number of surgery related factors have been shown to be important predictors of implant failure. Use of antibiotic prophylactic treatment systemically 4 times on the day of surgery in combination with antibiotic in bone cement (54) has been associated with a decreased risk of overall implant failure due to any reason. Revision of the opposite THA was found to be a strong predictor of overall implant failure due to any reason for the remaining THA (55). Further, the time period of more than two years between first and second primary THA in the same patient was found to be a predictor of increased implant failure in the first primary THA compared with patients who sustained only first primary THA (55).

Regarding implant failure due to aseptic loosening, others found that the use of CMW1, CMW3 and Boneloc bone cement for implant fixation (56;57) was associated with an increased overall risk of implant failure. In contrast, the use of pulsatile lavage, proximal femoral seal, and distal femoral plug in cementing fixation technique (47) have been associated with a decreased risk of implant failure due to aseptic loosening. Recently, treatment with non steroid antiinflamatory drugs in the early period after uncemented primary THA was suggested to be associated with an increased risk of implant failure due to aseptic loosening (58). Other surgery related factors, including low-volume surgeons, long operating times, particular implant components, and year of the primary THA have also been associated with an increased overall risk of implant failure (8;52;59) due to any reason or aseptic loosening. Moreover, the use of 28 mm femoral head size (60) has been associated with an increased risk of implant failure due to dislocation.

Some of these predictors, including diagnosis for primary THA (49;53), and type of implant or fixation technique (47;49;61;62), have not been consistently associated with a risk of implant failure. This could possibly be related to the use of different length of follow-up in the published studies; however, it is unclear whether the impact of the specific predictive factors is the same during the entire follow-up period. Studies among other patient groups, *e.g.,* patients with breast cancer, lymphomas and soft tissue sarcoma (63-65), have suggested that many predictors of treatment outcome may often be time-dependent, *e.g.,* in breast cancer, a positive steroid hormone status is initially a positive predictive factor, which becomes a negative factor for metastases after 3-5 years of follow-up. Less is known about possible time-dependence of predictors for THA outcome.

Many other factors than those identified in the literature may be potential predictors of implant failure, thus based on studies of other outcomes after THA, as patient's mortality or quality of life, but they suffer from lack of documentation. These potential predictors include ethnicity, waiting time for the surgery, hospital volume, physical activity of the patient, further medication, education status of patient, marital status, rehabilitation programs, and patient's expectations before surgery.

1.2. Use of clinical databases in THA research

Determination of implant efficacy, *i.e.,* the extent to which an implant produces a beneficial result under ideal conditions, can in theory best be studied in a randomized clinical trial. Randomized clinical trials remain the gold standard for the design of clinical research and when appropriate, practically, and ethically, they should be used. Nevertheless, randomized clinical trials have several limitations if the outcome is implant failure/survival. Trials often reflect the performance of a specific implant used at a specific hospital, or even by a specific surgeon. These studies may therefore often be influenced by possible performance bias and impaired generalization (66). Moreover, randomized clinical trials in the field of THA surgery are expensive and have a late feedback as 10 to 15 years follow-up is usually required.

For practical purposes, effectiveness, *i.e.,* the extent to which THA fulfills its objectives in routine clinical settings, may be a more relevant measure than efficacy. Observational studies play a central role in the assessment of effectiveness, as these studies can be based on information from the everyday clinical practice. Observational studies are usually based on analytical methods, such as cohort and case-control study designs. Retrospective case series, which have been widely used

within orthopedic surgery, are a specific category of observational studies and may be helpful. They are however, often limited by the lack of generalization and a reference group.
Analytical observational studies have the possibility of drawing the study population from clinical databases, which have previously been proposed to be an important tool for organizing and monitoring THA service (67). The use of the clinical databases in THA research have a number of advantages: 1) timely and early dissemination of information on outcome of THA surgery; 2) large sample sizes of various patients and surgeons performing THA provides high precision of estimates and ensures generalization; 3) costs of observational studies based on clinical databases can be considerably reduced; 4) collection of information in clinical databases are done prospectively and therefore independently of the outcomes in the study of interest, reducing both selection and information bias. Use of clinical databases can contribute to quality improvement of THA outcome through continuous feedback to the participating departments and enables comparison of results, *e.g.,* implant failure between different departments.

However, it is also essential to be aware of the limitations of clinical databases, including the THA databases. The data collection and quality of the data entered into the database are not controlled by researcher and can be difficult to validate. Incomplete registration of patients, *e.g.,* patients with a high risk of failure, or specific variables or insufficient quality of the registered data may cause biases, which may have strong implications for the usability of a clinical database. Different methods have been described for evaluating the completeness and data quality of clinical databases (68).

1.3. THA clinical databases

Detailed data on the use of THA in everyday clinical practice are important for planning, prediction of prognosis, monitoring, quality improvement, and research (69). Such data can be obtained from properly designed clinical databases. A number of clinical databases on THA have been initiated in recent years in several countries, including Sweden, Norway, Finland, Australia, Romania, Scotland, England and Wales, New Zealand and Canada (8) (Table 4). Initiatives are also currently undertaken in the United States for establishing a national joint replacement clinical database (48). Furthermore, the feasibility of establishing an International Society of Arthroplasty Registries has been explored over the last few years. In Europe, efforts have been started to develop a European Arthroplasty Register. The aims of the international clinical databases on THA are to provide a network for established and developing registries in order to facilitate cooperation and distribution of information about both practical experiences and specific clinical findings, and to encourage collaborative activities. Further, the ease by which comparisons are made between different national clinical databases would be enhanced by the use of a standardized terminology and standardization of the statistical analyses, *e.g.*, developing common definitions and terms combined with use of those terms when constructing and reporting from the databases.

Table 4. National clinical databases on joint replacement.

Country	Established in year	Joints included	Other data	Participative departments or surgeons	Public vs. private hospitals	Website
Denmark	1995	Total hip*	Revision, postoperative complications	52 (100%)	+/+	www.dhr.dk
Finland	1980	Total hip, knee, elbow and shoulder	Revision, postoperative complications	80 (?)	?	www.nam.fi/english/
Norway	1987	Total hip and knee, shoulder, elbow, wrist, ankle, finger, toe, spine, unicondylar knee	Revision	70 (100%)	+/+	www.haukeland.no/nrl/
Sweden	1979	Total hip	Revision	80 (100%)	+/+	www.jru.orthop.gu.se/
Romania	2001	Total hip, knee, shoulder, ankle, spine, fractures, tumors	Revision	69 (?)	+/?	www.rne.ro/public/situatii_eng.php
Scotland	1999	Total hip, knee, shoulder, elbow, finder, wrist, thumb, toe, ankle	Revision, postoperative complications	15 (100%)	+/-	www.show.scot.nhs.uk/arthro/index.htm
England and Wales	2003	Total hip and knee	Revision	384 (94%)	+/+	www.njrcentre.org.uk/
Australia	1998	Total and partial hip and knee, unicondylar knee,	Revision	294 (100%)	+/+	www.dmac.adelaide.edu.au/aoanjrr/index.jsp
Canada	2001	Total hip and knee	Revision	72% of all hip and knee surgeons	+/?	http://secure.cihi.ca/cihiweb/dispPage.jsp?cw_page=services_cjrr_e
New Zealand	1999	Total hip, knee, shoulder, ankle, elbow	Revision	62 (?)	+/+	www.cdhb.govt.nz/NJR/

* From January 1, 2006 Danish Hip Arthroplasty Registry is expected to merge with the Danish Knee Arthroplasty Registry, the Danish Shoulder Arthroplasty Registry, the Danish Ganz Registry, and the Danish Artificial Cruciate Ligaments Registry into the Danish Common Orthopedic Registry.

1.4. Conclusions

Although crucial for the use of clinical databases, the literature provides only sparse information on the data quality among the existing THA clinical databases. The DHR has existed for almost 10 years and the questions concerning data quality and usability of the register in clinical and research settings remain unanswered.

Existing studies have indicated that the incidence of THA procedures is increasing worldwide and that the demands are not yet met. However, concerns about methodological aspects of most of the existing studies, including a lack of age-standardization and clinical details make it difficult to draw firm conclusions. In order to predict the coming need for THA procedures, organize the healthcare system and allocate the necessary resources in time it is necessary to estimate the incidence of THA in the context of the changing population demographics.

Geographical variations in incidence rates of THA have been reported in a number of populations. Less is known about the possible existence of such variation in a tax-financed healthcare system. Furthermore, there is still a lack of data on the possible factors associated with these variations.

A number of factors have been proposed as predictors of THA implant failure. However, to the best of our knowledge, the possible time-dependence of these predictors has not previously been examined.

2. AIMS OF THESIS

The aims of this thesis were:

I. To examine the validity of the data in the Danish Hip Arthroplasty Registry, including the registration completeness of THA procedures and the quality of the registered data, and its usability for study op the THA epidemiology.

II. To estimate the IRs of primary THAs and revisions in Denmark in the period 1996-2002, and the expected needs for primary THA in Denmark in the coming decades.

III. To examine the existence of regional variation in the IRs of THA procedures in Denmark in the period 1996-2002, and further to examine the role of patient- and healthcare system-related factors in relation to any variation.

IV. To assess whether the effect of potential predictors for THA failure, including sex, age, diagnoses for primary THA, and comorbidity vary during the short and long term follow-up after primary THA surgery.

3. MATERIALS AND METHODS

3.1. Data sources

3.1.1. The Danish healthcare system

The Danish healthcare system provides tax-supported health care for all inhabitants and free access to general practitioners and hospitals. Through the use of a civil registry number, which is unique to every Danish citizen and encodes sex and date of birth, a complete hospital discharge history can be established for each individual, and unambiguous linkages between population-based registers can be made.

In the Danish healthcare system, the responsibility for financing, planning, running, and management of hospitals lies within 14 counties and one municipality. The Danish healthcare service provides free medical care, including both emergency and other admissions to hospitals and outpatients clinics, after referral from the general practitioner. More than 95% of the patients are registered with one general practitioner of their choice. After referral from the general practitioner, patients have free hospital choice in the entire country, which also includes some of the private hospitals. Approximately 28% of the population is covered by private health insurance in addition to the general public insurance (42). The private health insurance is generally used for elective surgical or medical treatment in private hospitals in order to avoid waiting lists on public hospitals.

3.1.2. The Danish Hip Arthroplasty Registry (Aims I, II, III and IV)

The Danish Hip Arthroplasty Registry was initiated by The Danish Orthopaedic Society January 1, 1995 (7). The objective of the register is to examine the epidemiology of THA procedures including both primary operations and revisions in Denmark, and to facilitate continuous improvement of hip replacement surgery outcomes on both a local and national level. In order to fulfil this objective, detailed clinical data on all primary THAs, revisions, and follow-up examinations in Denmark are prospectively collected. All currently active orthopedic departments in Denmark (n=45) report to the register, including 4 departments located at private hospitals. The registered data include pre, peri and postoperative data. The data are collected using a standardized form. The following preoperative data are registered: the civil registry number, the laterality of the affected hip, previous surgery on the same hip, primary diagnosis, hospital code, and function, according to Charnley (70).

In addition, departments can register the Harris Hip Score (71) as a measure of hip function and the patient's mobility before surgery. The perioperative data include: date of the surgery, the surgeon's code number (which is not registered centrally), type of operation gowns and theatre, use of antibiotic and antithrombotic prophylactic treatment, type of anesthesia, prophylaxis against ectopic bone formation, duration of surgery, surgical approach and method, trochanteric osteotomy, type of acetabular component and fixation, type of femoral component and fixation, transplantation of bone to acetabulum and/or femur, perioperative complications, material and diameter of the prosthetic femoral head, and material and type of liner. In case of revision, defined as exchange of a part or the whole prosthesis or removal of the prosthesis, the following data are registered: cause of revision, previous surgery, extent of revision, the number of earlier revisions, and classification of bone loss related to revision of acetabular and/or femoral component. The perioperative data is filled in by the operating surgeon immediately after the surgery. The postoperative data, including the civil registry number, the laterality of hip, date of the latest surgery, date of follow-up examination, status at the follow-up examination, hospital code, function according to Charnley, postoperative complications, patient's own assessment of the satisfaction with the surgery, and Harris Hip Score, are registered at the follow-up examination. Because of lack of general guidelines about the use and timing of follow-up examinations, patients can be followed for only few months or several years after THA, depending on the specific hospital's protocol.
The registry publishes annual reports, which have been published on the Registry website http://www.dhr.dk since 2004.

3.1.3. The Danish National Registry of Patients (Aims I and IV)

The Danish National Registry of Patients (72) is an administrative nationwide public registry which covers all discharges from somatic hospitals in Denmark since January 1, 1977. The registry data include the civil registry number (unique for Denmark with possibility of data linkage), the dates of admission and discharge, the surgical procedures performed, and up to 20 diagnoses for every discharge, classified according to the Danish version of the International Classification of Diseases, eighth (ICD-8 from 1977 until 1993) and tenth edition (ICD-10 since 1994). All discharge diagnoses are assigned by the physician who discharges the patient.

3.1.4. The Central Personal Registry (Aims III and IV)

By using the civil registry number, which is unique and encodes gender and date of birth, of every Danish citizen, the Central Personal Registry stores electronic records of all changes in vital status and migration for the entire Danish population, including changes in address, date of emigration, and the date of death since 1968 (69).

3.1.5. The StatBank Denmark (Aims II and III)

The StatBank Denmark contains detailed statistical information on the Danish society, including information about the population size by each calendar year, estimates of the population size for the coming years, or county-specific data on population density and Gross Domestic Product (73).

3.1.6. Medical records and radiographs (Aim I)

For aim I, medical records and preoperative radiographs of the hip and pelvis from a randomly selected sample of patients registered in the Danish Hip Arthroplasty Registry, were retrieved and reviewed by a single physician (ABP), using a detailed standardized form (Appendix 12.1 and 12.2.) designed in close collaboration with 3 consultants with extensive experience in the field of hip surgery (UL, KS, SO). The criteria used to define the presence of diagnoses and postoperative complications were also established in collaboration with these consultants and in accordance with existing literature (74-77). All cases with an uncertain diagnosis based on the available information were discussed with the consultants.

3.1.7. Other data sources

For aim I, data on hospital costs for both primary THA and revision were retrieved from the website of the Danish National Board of Health (34) on July 24, 2003.

For aim II and III, data on the European Standard Population (divided into 18 age groups) were retrieved from the website of the Surveillance Epidemiology and End Results within SEER*Stat (78) on September 10, 2003. The website has been changed since and the Standard European Population is now available from the Surveillance Epidemiology and End Results within SEER*Stat (79) (website accessed July 6, 2005).

For aim II, data on waiting time for THA procedures from 1996 to 2002 were retrieved from the website of the Danish National Board of Health (80) on July 24, 2003.

For aim III, data on county-specific hospitals costs per capita were retrieved from the website of the Association of County Councils (81) accessed on July 24, 2003.

For aim III, data on the number of orthopedic surgeons per county were obtained from the Danish Medical Association in the middle of each calendar year. The Danish Medical Association was established on September 1, 1857. Approximately 94% of all Danish doctors are members of the association.

3.2. Outcomes

The outcome in aim I was the validity of the data in the Danish Hip Arthroplasty Registry, including the registration completeness of THA procedures and the quality of the registered data. The registration completeness of THA procedures was defined as the proportion of individuals in the target population that appear in the registry database (82). We assessed the registration completeness for the primary THAs and revisions using the Danish National Registry of Patients as an independent reference source. The comparison was made on an individual level (through the civil registry number). We assessed the quality of the data in the DHR by focusing on aspects which are of major importance when studying and comparing outcomes of THA surgery, *i.e*., the diagnoses for primary THA of the patients and the development of postoperative complications.

We first assessed the positive predictive value of the registered data, *i.e.,* the proportion of cases in the DHR with a given characteristic that "truly" had this attribute (68). The positive predictive value is the indirect measure of the specificity, in the settings where specificity can not be estimated directly. In our study, the positive predictive value of the diagnoses for primary THA was the proportion of patients fulfilling the criteria for having the particular diagnosis in the total group of registered patients with that diagnosis. The positive predictive value of the postoperative complications was the probability of having postoperative complications given a registration in the DHR. Calculation of the positive predictive value relied on review of retrieved medical records and radiographs as a reference.

Further, we assessed the sensitivity and specificity of the registration of postoperative complications in the DHR. The sensitivity is an expression of a test's ability to correctly classify patients, with a specific characteristic of interest (83). A sensitive test leads to few false negative results and will rarely miss patients with the characteristic of interest. The sensitivity of the registration of postoperative complications during follow-up was therefore defined as the proportion of patients with postoperative complications, who were registered in DHR with a postoperative complication. The specificity is an expression of a test's ability to classify patients, not having a specific characteristic of interest, correctly (83). A specific test leads to few false positive results and will rarely misclassify patients with the characteristic of interest. The specificity of the registration of postoperative complications during follow-up was defined as the proportion of patients without postoperative complications, who were registered in DHR as not having a postoperative complication.

In aim II and III, the outcome was the incidence rate (IR) of THA procedures in relation to sex, age, diagnoses, hospital type, and county of residence, as well as expected future IRs of THA procedures. We also estimated the Incidence rate ratio (IRR) as a measure of the relative change in IRs of THA procedures during the period 1996-2002.

The outcome in aim IV was defined as time to failure, *i.e.,* first revision of any causes involving removal or exchange of a part of or the whole implant. Aseptic loosening, with or without osteolysis of the femur and/or the acetabulum component, is in general the main cause of revision (7) and occurs most frequently years after primary THA. Other reasons for revision include deep infection, dislocation, femoral fracture, pain, osteolyses/granuloma formation, implant failure, and a group of miscellaneous reasons. The miscellaneous group is not clearly defined and may include acetabulum fracture, fracture of the femur or acetabulum component, fracture of liner, polyethylene wear, and acetabulum component dislocation. Any of the above mentioned reasons for revision were per definition included as an outcome in this study. The association between the possible patient-related predictors and the time to implant failure was described by the IRR for each predictor.

3.3. Study population

In the aim I of registration completeness the study population comprised of all persons in Denmark who underwent THA procedures during the period from January 1, 1995 until December 31, 2000. We identified 27,076 and 27,757 patients with THA procedures registered in the DHR and the Danish National Registry of Patients, respectively.
In the aim I of the positive predictive value of diagnosis for the primary THA the study population included stratified samples of 100 randomly selected patients from each of the 6 categories of THA diagnoses registered in DHR. Medical records and preoperative radiographs could be retrieved for 76.5% (459/600) of the patients. In the aim I of the positive predictive value for postoperative complications, 100 randomly selected patients with follow-up examinations were included. Medical records could be retrieved for 89.0% (89/100) of these patients.

In the aim II and III, the study population included the Danish population older than 10 years of age. Of those, 37,144 persons underwent primary THA procedure (87.1% of the initial 42,624) and 6,446 persons underwent revision (86.1% of the initial 7,489) during the period from January 1, 1996 through December 31, 2002.

In the aim IV, a total of 36,984 primary THA patients registered in the DHR between 1 January 1995 and 30 June 2003 were available as the study population.

3.4. Data analyses

3.4.1. Aim I

The completeness was calculated as a proportion. The numerator contained the number of patients who had sustained primary THA or revision registered in both the DHR and the Danish National Registry of Patients. The denominator consisted of the total number of patients who had sustained primary THA or revision registered in the Danish National Registry of Patients.
We assessed the registration completeness of primary THAs and revisions in the DHR in combination and separately. Furthermore, we examined the completeness for the entire DHR, as well as according to sex, age, type of hospital and hospital volume of THA.

A capture-recapture analysis was performed afterwards to estimate the number of cases not registered in either the DHR or the Danish National Registry of Patients (84) (Table 5).

Table 5. Capture-recapture analysis: two source model.

DHR	Danish National Registry of Patients		
	Registered cases	Non-registered cases	
Registered cases	a	b	a+b
Non-registered cases	c	d	c+d
	a+c	b+d	

If P_1 (a/a+b) is estimate of the registration completeness of the Danish National Registry of Patients and P_2 (a/a+c) is estimate of the registration completeness of the DHR, then $P_{1,2}$ is estimate of the registration completeness of the Danish National Registry of Patients and the DHR together, and can be calculated as $1-(1-P_1) * (1-P_2)$. The expected number of cases with a THA procedure performed in Denmark during the study period (N) is calculated as $(a+b+c)/P_{1,2}$. Finally, the number of cases not registered in the DHR or the Danish National Registry of Patients (d) can be estimated as N-(a+b+c).

The positive predictive value of the registered diagnoses for primary THA was also calculated as a proportion. The numerator contained the number of patients confirmed with a specific diagnosis after review of the medical records and preoperative radiographs using the diagnosis criteria, previously established as the gold standard. The denominator contained the total number of patients from our random sample with the specific diagnosis.

The sensitivity of the registration of postoperative complications during follow-up was calculated as the number of patients with a postoperative complication listed in their medical records and registered with a postoperative complication in the DHR, divided by the total number of patients in our random sample with postoperative complications listed in their medical records.

The specificity of the registration of postoperative complications during follow-up was calculated as the number of patients without any registered postoperative complications in the DHR and with no postoperative complications identified after review of the medical records, divided by the total number of patients in our random sample without any postoperative complications in the medical records.

We relied on the normal approximation of the binominal distribution to estimate confidence intervals and compare proportions.

3.4.2. Aim II and III

Incidence rates according to age, sex, primary diagnoses, and hospital type

We standardized all IRs according to the age and sex distribution of a standard population. We used both direct and indirect methods of standardization. The direct method was used to estimate age and sex-specific IRs of primary THAs and revisions adjusted to the Danish population in 1996 or the European Standard population. The indirect method was used to estimate IRRs as an expression of the relative change in IRs of primary THAs or revisions in the years 1996–2002 compared with IRs in the reference category.

The annual overall IRs of primary THAs or revisions were estimated as followed; the numerator contained the number of patients undergoing primary THA or revision by calendar year. The denominator consisted of the total number of persons in Denmark older than 10 years of age by calendar year. The IRs were all given annually by 100,000 inhabitants, with 95% CI as a measure of statistical precision. Poisson regression was used to estimate IRR, using the year 1996 as the reference.

Incidence rates according to county of residence

First we estimated the unadjusted average IRs of primary THAs or revisions as follows; the numerator contained the total number of patients undergoing THA or revision between 1996 and 2002 in the specific county. The denominator contained the total number of persons by the specific county during the entire period 1996-2002.

Secondly, the average IRs were standardized according to the total average age and sex distribution of the Copenhagen Hospital Cooperation (H:S) between 1996 and 2002, which was the county with the lowest unadjusted IRs.

Thirdly, we examined whether regional variation in the IRs of primary THA and revision were associated with different patient- and healthcare system-related factors. As patient-related data, we included the county-specific proportion of patients with primary arthrosis, the Harris Hip Score (HHS) before surgery, and population density (number of inhabitants per square meter). The healthcare system-related data included the county-specific Gross Domestic Product, hospital costs per capita, and the number of the orthopedic surgeons per 100,000 inhabitants. These associations were described by regression coefficients derived from linear regression analyses.

Fourthly, we performed a multivariate linear regression analysis including all the examined factors in the model.

The coefficients of variation were used to describe the size of the variation of the examined factors and IRs among the counties. We calculated the coefficient of variation for all the factors examined and IRs by dividing the standard deviation with the mean value of the specific factor or IR.

Predictions for the years 2010, 2015, and 2020

Based on two different scenarios, we estimated the future demands for primary THA in Denmark using the age-specific IRs of primary THAs for year 2002 as a reference: A) with the expected changes in the age distribution of the population; and B) with the combined effect of the expected changes in the age distribution of the population and a continued relatively annual age and sex - specific increase in the age-standardized IRs (based on the development in the period 1996-2002). In scenario A, the predicted number of primary THAs in 2010 ($A_{2010\,(total)}$) was estimated as a sum of products between the age and sex-specific IRs of primary THA in 2002 and the predicted population in 2010. 95% CIs of IRs were estimated as $eks\left[\ln\left(\frac{A_{2010(total)}}{POP_{2010(total)}}\right) \pm \left(\frac{1.96}{\sqrt{A_{2010(total)}}}\right)\right]$.

In scenario B, the predicted number of primary THAs in 2010 ($B_{2010\,(total)}$) was estimated as a sum of products between the IRs of primary THA in 2002, the predicted population in 2010, and the trend (the continued relatively annual age and sex- specific increase of the IRs) for five age groups for both males and females. 95% CIs of IRs were estimated as

$eks\left[\ln\left(\frac{B_{2010\,(total)}}{POP_{2010(total)}}\right) \pm \left(\frac{1.96}{\sqrt{B_{2010(total)}}}\right) \pm \sqrt{y * SE}\right]$, where y is the number of years since 2002, and SE is the Standard Error of the trend seen between 1996 and 2002.

The predicted numbers of primary THAs and corresponding IRs and 95% CI for the years 2015 and 2020 were estimated in the same way, except that specific age distributions and trends were used in IRs for years 2015 and 2020, respectively.

3.4.3. Aim IV

We used the Cox proportional hazards analysis to examine the time-dependent association between possible patient related predictors and the time to implant failure.

The possible predictors examined in this study included sex, age, diagnosis for primary THA, and comorbidity. Comorbidity at the time of surgery for each patient based on the complete hospitalization history was assessed by computing the widely used comorbidity index developed by Charlson et al. (85), which was originally developed and validated for the prediction of short- and long-term mortality among patients admitted to departments of internal medicine (86). The Charlson index includes 19 major disease categories which were translated into corresponding ICD-8 and ICD-10 codes, similar to the precious approaches by Deyo et al. (87). We divided the patients into three levels: index low (0); index medium (1-2); and index high (> 2).

Follow-up started on the day of primary THA and ended on the day of revision, death, emigration, or 30 June 2003, whichever came first. The follow-up period after primary THA was divided into three time windows: 1) from 0 to 30 days and 2) from 31 day to 6 months as short term follow-up; and 3) the remaining long term follow-up time extending from 6 months to 8.6 years after primary THA.

We estimated both crude IRRs, and IRRs mutually adjusted for the possible predictors and non-patient related covariates previously reported to be associated with implant failure, *i.e.* fixation technique of implant and hospital type (44;61).

4. MAIN RESULTS

4.1. Aim I: The data validity in the DHR

The registration completeness for primary THA and/or revisions

The overall registration completeness for primary THAs and/or revisions in the DHR was 94.1% (95% CI: 93.9-94.4) (Table 6.). The registration completeness of primary THAs and revision was 93.9% (95% CI: 93.6-94.2) and 81.4% (95% CI: 80.2-82.6), respectively. When we excluded hemiarthroplasty patients from the analyses, 549 cases were misclassified in the Danish National Registry of Patients as revisions, and correctly classified in the DHR as primary THAs, and the registration completeness of revision in DHR was 90.1% (95% CI: 89.1-91.0).

We found no relevant differences in the overall registration completeness according to sex and age. The registration completeness for primary THAs and /or revisions was lower at university hospitals compared with other hospitals (Table 6).

Table 6. The degree of completeness of registration in the DHR of primary THAs and/or revisions (absolute numbers in parentheses) according to sex, age, and hospital type.

	Degree of completeness	
	% (N)	95% CI (%)
Overall	94.1 (26,129/27,757)	93.9 – 94.4
Male	95.1 (11,099/11,665)	94.7 – 95.5
Female	93.5 (15,004/16,047)	93.1 – 93.9
Age < 50	95.6 (1,814/1,896)	94.6 – 96.5
Age >=50 and <70	95.1 (11,076/11,641)	94.6 – 95.4
Age >=70	92.9 (13,210/14,212)	92.5 – 93.4
University hospitals	90.7 (5,309/5,851)	90.0 – 91.5
Other hospitals	94.8 (20,780/21,906)	94.3 – 95.0

There was a trend towards a lower registration completeness with decreasing hospital volume ($P<0.05$ based on chi^2 test) (Table 7). Registration completeness for hospitals that performed less than 300 THA procedures during the study period (n=5) was found to be 70.8% (95% CI: 68.3-73.2).

Table 7. The degree of completeness of registration in the DHR of primary THAs and/or revisions (absolute numbers in parentheses) according to hospital volume.

Hospital volume	Degree of completeness	
	% (N)	95% CI (%)
Low	86.7 (5,080/5,859)	85.8 - 87.6
Middle	91.7 (11,958/13,045)	91.2 – 92.1
High	95.8 (8,489/8,853)	95.5 – 96.3

The registration completeness of revisions was lower in females (77.6%, 95% CI: 75.9-79.3) compared with males (86.2%, 95% CI: 84.5-87.7), and for patients older than 70 years age (77.5%, 95% CI: 75.7-79.2) compared with patients between 50-70 years (85.1%, 95% CI: 83.2-86.8) and patients less than 50 years age (88.5%, 95% CI: 84.8-91.5). Further, the registration completeness of revisions was lower for patients whose surgery was performed in low- volume hospitals (60.7%, 95% CI: 56.7-64.6) compared with middle- (79.1%, 95% CI: 77.3-80.8) and high- volume hospitals (85.6%, 95% CI: 83.7-87.4). However, there was no difference in registration completeness of revisions between university and other type of hospitals (80.7%, 95% CI: 78.7-82.6 vs. 81.0%, 95% CI: 79.4-82.5).

The capture-recapture analyses revealed 57 cases, which were not registered in the DHR nor in the Danish National Registry of Patients. A total of 947 cases were registered in the DHR, but not in the Danish National Registry of Patients.

The positive predictive value of the registered data

The overall positive predictive value of the diagnoses for primary THA was 84.3% (95% CI: 80.6-87.5) after review of both medical records and preoperative radiographs.

The positive predictive value differed slightly between the diagnoses; the primary osteoarthritis was confirmed in 84.6 % of the cases (95 % CI: 74.7-91.8). Sequelae after trauma and atraumatic necrosis of the femoral head were confirmed in 95.0 % (95 % CI: 87.7-98.6) and 98.7 % of the cases (95 % CI: 93.2-99.9), respectively. The inflammatory diseases and the hip disorders in childhood were confirmed in 100 % (95 % CI: 94.9-100) and 89.7 % of the cases (95 % CI: 80.8-95.5), respectively (Table 8).

In contrast, the positive predictive value for fresh fractures of the proximal femur was low, with confirmation of the diagnosis in only 30.1 % of the cases (95 % CI: 19.9-42.0) (Table 8).

Table 8. Positive predictive value of diagnoses registered in the Danish Hip Arthroplasty Registry.*

Diagnosis recorded in DHR	Total N(%)	Verified	PPV(%)	95% CI
Primary osteoarthritis	78 (100)	66	84.6	74.7 – 91.8
Fresh fracture of proximal femur	73 (100)	22	30.1	19.9 – 42.0
Sequelae after trauma				
Late sequelae from fracture of proximal femur	70 (100)	67	95.7	88.0 – 99.1
Fracture of acetabulum	8 (100)	7	87.5	47.4 – 99.7
Traumatic hip dislocation	2 (100)	2	100	15.8 – 100
Atraumatic necrosis of femoral head	80 (100)	79	98.7	93.2 – 99.9
Inflammatory diseases				
Rheumatoid arthritis	63 (100)	63	100	94.3 – 100
Mb. Bechterew	7 (100)	7	100	59.0 – 100
Hip disorders in childhood				
Congenital hip dislocation	31 (100)	29	93.6	78.6 – 99.2
Mb. Calve-Legg-Perthes	10 (100)	9	90.0	55.5 – 99.7
Epiphysiolysis	11 (100)	11	100	71.5 – 100
Acetabular dysplasia	26 (100)	21	80.8	60.6 – 93.4

* based on both medical records and preoperative radiographs.
PPV =positive predictive value.

The positive predictive value for all postoperative complications was 76.0 % (95 % CI: 64.7-85.1), whereas the positive predictive value of the specific postoperative complications was 66.7 % (95 % CI: 52.5-78.9).

The sensitivity and specificity of the registration of postoperative complications during follow-up was 90.5 % (95 % CI: 80.4-96.4) and 30.8 % (95 % CI: 14.3-51.8), respectively.

4.2. Aim II: IRs of primary THAs and revision, and future demands

For primary THAs, the overall annual IR increased from 100.5 (95% CI: 97.6-103.5) in 1996 to 131.1 (95% CI: 128.3-134.9) in 2002 per 100,000 inhabitants resulting in an IRR of 1.3 (95% CI: 1.3-1.4) when comparing 2002 with 1996. For revisions, the annual IRs increased from 19.2 (95% CI: 17.9-20.5) to 20.7 (95% CI: 19.4-22.1) per 100,000 inhabitants in the same period resulting in an IRR of 1.1 (95% CI: 0.9-1.4) (Standardized to the Danish population in 1996).

Females and males were found to have a similar relative increase in IRs of primary THAs (IRR 1.3, 95% CI: 1.1-1.5 for males and 1.3, 95% CI: 1.1-1.4 for females) and revisions (IRR 1.1, 95% CI: 0.9-1.3 for both sexes). Age-specific IRs of primary THAs (Table 9) and revision increased with increasing age for both sexes. Further, increases in age-specific IRs of primary THA were also seen during the period 1996-2002. Regarding age-specific IRs of revision, we found a small reduction in the age group between 10-49 years (IRR 0.9, 95% CI: 0.6-1.2), increase among persons aged 50-59 years (IRR 1.2, 95% CI: 0.9-1.4), 70-79 years (IRR 1.1, 95% CI: 1.0-1.3), and person older than 80 years (IRR 1.2, 95% CI: 1.0-1.5), and no change among patients aged 60-69 years (IRR of 1.0, 95% CI: 0.9-1.2).

Table 9. Annual age- and sex-specific incidence rates (IRs) of primary THA per 100,000 inhabitants in Denmark 1996-2002.

Age group (year) male	1996	1997	1998	1999	2000	2001	2002
10-49	11.7	12.0	12.1	12.6	11.8	11.7	14.1
50-59	88.7	92.2	106.9	109.8	113.6	116.8	135.7
60-69	273,9	280.9	273.7	318.2	310.1	303.9	346.7
70-79	416,3	413.9	405.4	406.5	495.1	440.4	513.5
>=80	337.1	320.8	331.8	352.1	351.7	373.4	368.6

Age group (year) female	1996	1997	1998	1999	2000	2001	2002
10-49	9.3	10.5	9.9	10.5	9.1	8.9	10.7
50-59	97.4	97.1	94.7	102.3	109.3	110.5	129.3
60-69	300.8	311.1	337.9	354.1	351.2	360.7	389.1
70-79	491.6	536.3	542.2	563.6	545.2	603.6	678.1
>=80	325.8	389.1	405.6	368.4	395.5	414.4	459.1

In relation to diagnoses for primary THA, increase in IRs of primary THA was found for primary osteoarthritis, atraumatic necrosis of femoral head, late sequelae from fracture of proximal femur, and hip disorders in childhood, whereas a decrease in IRs was found for patients with rheumatoid arthritis (Table 10).

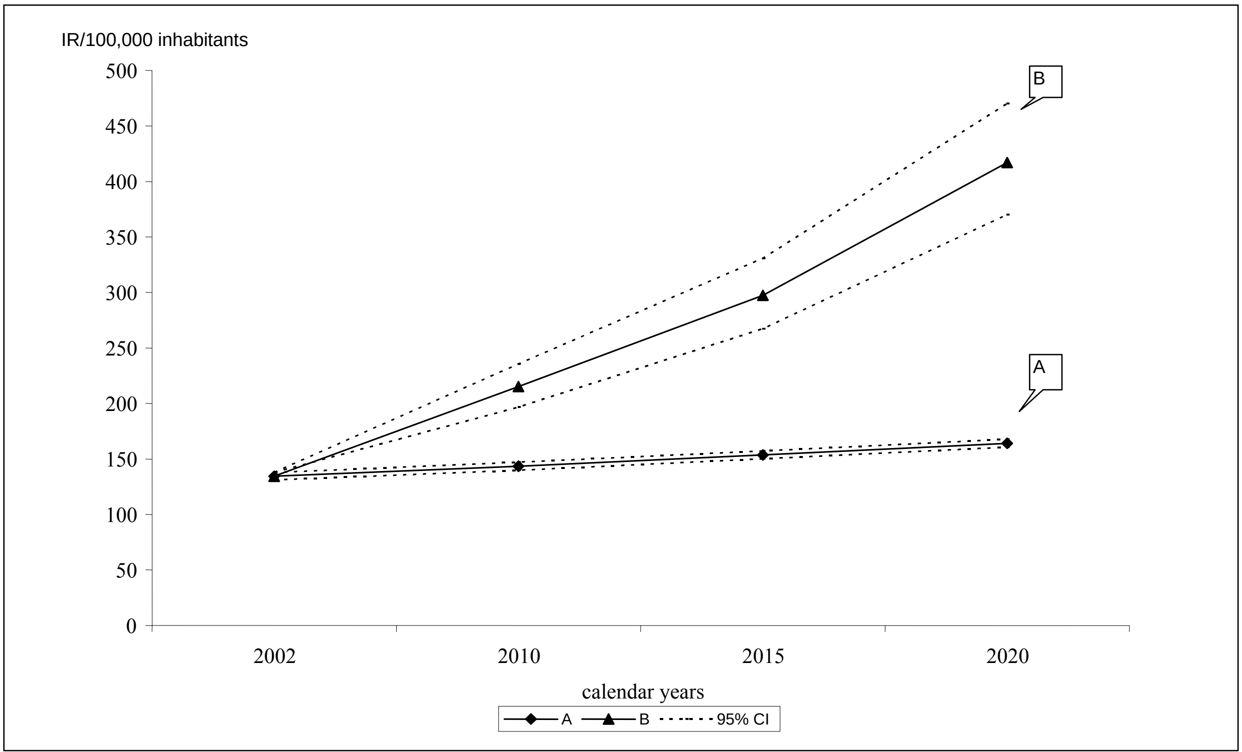
Table 10. Estimates of incidence rates and incidence rate ratios between 1996 and 2002 according to different diagnosis in patients undergoing primary THA (Poisson regression).

Diagnosis	IR* of primary THA 1996	IR of primary THA 2002	IRR† (95% CI) 1996-2002
Primary osteoarthritis	65.6	89.8	1.4 (1.3-1.4)
Rheumatoid arthritis	3.1	2.1	0.7 (0.6-0.9)
Atrumatic necrosis of femoral head	2.7	2.9	1.1 (0.9-1.4)
Late sequelae from fracture of proximal femur	8.5	9.7	1.1 (1.0-1.3)
Hip disorders in childhood	2.9	3.9	1.3 (1.1-1.6)

* Incidence rate per 100,000 inhabitants standardized to The European Standard population.
† Incidence rate ratio.

Based on the expected changes in the age distribution of the population, the IRs were estimated to increase continually from 2002 corresponding to an increase of 7% in 2010, 14% in 2015, and 22% in 2020. Based on changes in the age distribution combined with a continued annual age- and sex-specific increase in the age-standardized IRs of primary THA of the same magnitude as the average annual increase observed in the period 1996-2002, increases in IRs of 60%, 121%, and 210% in 2010, 2015, and 2020, respectively, can be expected when compared with 2002 (Figure 2).

Figure 2. Expected incidence rates (IRs) of primary THAs in Denmark, year 2010, 2015, 2020 based on constant age-specific IRs of primary THAs (2002). A, with expected changes in the age distribution. B, with the expected changes in the age distribution combined with the continued annual age and sex specific increase in the standardized IRs of primary THA from 1996-2002.



4.3. Aim III: Regional variation in the IRs of primary THAs and revisions

We found an increase in IRs of primary THAs at both university (IRR 1.1, 95% CI: 0.9-1.3) and other hospitals (IRR 1.4, 95% CI: 1.3-1.4) during the study period. Further, IRs of revisions at other hospitals increased in the same period as well; the IRR was 1.3 (95% CI: 1.1-1.5), whereas IRs of revisions at university hospitals dropped (IRR 0.7, 95% CI: 0.4- 1.0) (Table 11).

At private hospitals, IRs of primary THA were unchanged; whereas IRs of revision at private hospitals increased in the same period, providing an IRR of 2.0 (95% CI: 1.5-2.3) when comparing 2002 with 1996.

Table 11. Hospital-specific incidences rates (IR) of primary total hip arthroplasty (THA) and revision per 100,000 person years, standardized according to the European Standard Population, 1996-2002.

Hospital type	1996	1997	1998	1999	2000	2001	2002
University hospitals							
Primary THA	15.0	13.9	13.8	15.7	15.4	14.1	16.5
Revision	6.2	6.3	6.0	5.6	5.5	4.9	4.5
Other hospitals							
Primary THA	71.6	76.5	78.9	81.7	83.6	86.2	96.9
Revision	10.1	10.2	10.3	11.0	10.8	12.2	12.8

Unadjusted average IRs of primary THAs showed substantial variation among the counties, providing the unadjusted IRRs between 1.1 (95% CI: 1.0-1.1) and 1.8 (95% CI: 1.6-2.0) in different counties compared with H:S county. Age- and sex-standardization of county-specific IRs of primary THAs resulted in a reduction of the regional variation, as the adjusted IRRs varied now between 1.1 (95% CI: 1.0-1.1) and 1.4 (95% CI: 1.3-1.6) (Table 12.).

Unadjusted average IRs of revisions also showed regional variations, which remained after age- and sex-standardization (Table 12).

Three factors, including the number of orthopedic surgeons per 100,000 inhabitants, population density, and the GDP per capita appeared to be associated with regional variation in IRs of primary THA in the univariate regression analyses. However, these associations disappeared when we mutually adjusted for all six factors. Further, no association was found between the number of orthopedic surgeons per 100,000 inhabitants, proportion of patients with primary arthrosis, HHS, population density, hospitals' costs per capita, and GDP per capita and regional variations in IRs of revisions (Table 13).

Table 12. Incidence rate ratio (IRR) of primary total hip arthroplasty (THA) and revision for each Danish county compared with Copenhagen Hospital Cooperation (H:S) (Poisson regression).

		Primary THA			Revision		
Counties	Person years	THA (n)	Crude IRR (95% CI*)	Adjusted IRR† (95% CI)	Revision (n)	Crude IRR (95% CI)	Adjusted IRR (95% CI)
H:S	3,644,182	3,163	1.0 (ref.)	1.0 (ref.)	796	1.0 (ref.)	1.0 (ref.)
Copenhagen county	3,725,886	4,072	1.3 (1.2-1.3)	1.1 (1.1-1.2)	667	0.8 (0.7-0.9)	0.8 (0.7-0.8)
Frederiksborg	2,199,387	2,526	1.3 (1.3-1.4)	1.3 (1.2-1.3)	547	1.1 (1.0-1.3)	1.2 (1.1-1.3)
Roskilde	1,394,380	1,475	1.2 (1.1-1.3)	1.3 (1.2-1.4)	237	0.8 (0.8-0.9)	0.8 (0.7-1.0)
West Zealand	1,801,941	2,294	1.5 (1.4-1.5)	1.3 (1.2-1.4)	390	1.0 (0.9-1.1)	0.9 (0.8-1.0)
Stor Stroem	1,597,433	2,346	1.7 (1.6-1.8)	1.4 (1.3-1.4)	389	1.1 (1.0-1.3)	0.9 (0.8-1.1)
Bornholm	276,087	431	1.8 (1.6-2.0)	1.4 (1.3-1.6)	83	1.4 (1.1-1.7)	1.1 (0.9-1.4)
Funen	2,891,186	3,766	1.5 (1.4-1.6)	1.3 (1.3-1.4)	497	0.8 (0.7-0.9)	0.7 (0.6-0.8)
South Jutland	1,545,866	2,174	1.6 (1.5-1.7)	1.4 (1.3-1.5)	272	0.8 (0.7-0.9)	0.7 (0.6-0.8)
Ribe	1,354,561	1,652	1.4 (1.3-1.5)	1.3 (1.3-1.4)	425	1.4 (1.3-1.6)	1.4 (1.2-1.6)
Vejle	2,106,678	2,342	1.3 (1.2-1.4)	1.2 (1.0-1.3)	417	0.9 (0.8-1.0)	0.9 (0.8-1.0)
Rinkjøbing	1,651,990	1,887	1.3 (1.2-1.4)	1.3 (1.2-1.3)	376	1.0 (0.9-1.2)	1.0 (0.9-1.2)
Aarhus	3,865,611	3,594	1.1 (1.0-1.1)	1.1 (1.0-1.1)	584	0.9 (0.8-1.0)	0.8 (0.7-0.8)
Viborg	1,419,522	1,690	1.4 (1.3-1.5)	1.2 (1.1-1.3)	218	0.7 (0.6-0.8)	0.6 (0.5-0.7)
North Jutland	3,020,018	3,557	1.4 (1.3-1.4)	1.2 (1.1-1.3)	485	0.7 (0.6-0.8)	0.8 (0.6-0.8)

* 95% confidence interval

† Adjusted for age and gender

Table 13. Characteristics of the possible factors associated with regional variation in the age and gender standardized incidence rates of primary total hip arthroplasty (factors are expressed on average between 1995 -2002 per county).

Factor	Mean (range)	Coefficient of variation (%)	Unadjusted Regression coefficient (95 % CI)†	Adjusted Regression coefficient (95 % CI)‡
The number of orthopedic surgeons per 100,000 inhabitants	8.2 (4.9-11.6)	20	-4.132 (-7.519 ; -0.745)	-3.091 (-8.824; 2.641)
Harris Hip Score	41.5 (22.5-45.1)	10	-0.837 (-2.040 ; 0.366)	-0.041 (-1.505; 1.422)
Proportion of patients with primary osteoarthritis	77.5 (68.3-83.9)	5	1.552 (-0.015 ; 3.119)	0.927 (-1.155; 3.009)
Population density*	640.2 (56.2-6944.4)	275	-0.004 (-0.007 ; -0.001)	0.003 (-0.006; 0.012)
Gross Domestic Product per capita	209.5 (159.5-364.0)	25	-0.164 (-0.252 ; -0.076)	-0.157 (-0.390; 0.076)
Hospitals costs per capita	6860.5 (6462.5-7272.3)	4	0.024 (-0.0005 ;0.048)	0.005 (-0.021; 0.031)

* Number of inhabitants per square meter
† Based on univariate linear regression
‡ Based on multiple linear regression

4.4. Aim IV: Predictors of short and long term implant failure after primary THA

Possible predictors for implant failure 0-30 days after primary THA (Table 14)

Being a male was associated with an increased IRR for failure of any cause of 1.4 (95 % CI; 1.1-1.9) after adjustment for comorbidity, age, diagnosis for primary THA, fixation technique and hospital type. There was a tendency of increased adjusted IRR for failure with increasing age (p=0.036 based on chi^2 test).

A number of diagnoses for primary THA, including sequelae after trauma, avascular necrosis, and pediatric diseases were associated with increased IRR for failure compared with primary osteoarthritis. Finally, a high comorbidity index score was found to be a strong predictor of THA failure compared with a low comorbidity index score, with an adjusted IRR for failure of 2.3 (95% CI; 1.6-3.5).

Table 14. Predictors of implant failure from any causes 0-30 days after primary total hip arthroplasty.

	Patients (n)	Revisions (n)	Crude IRR* (95 % CI)	Adjusted IRR† (95 % CI)
Sex				
Female	21,707	93	**1.0 (ref.)**	**1.0 (ref.)**
Male	15,277	93	1.4 (1.1-1.9)	1.5 (1.1-2.0)
Age Groups (years)				
10-49	2,226	20	2.1 (1.3-3.6)	1.0 (0.6-1.8)
50-59	5,360	32	1.4 (0.9-2.2)	1.0 (0.6-1.6)
60-69	10,597	45	**1.0 (ref.)**	**1.0 (ref.)**
70-79	13,067	58	1.1 (0.7-1.6)	1.3 (0.9-1.9)
>=80	5,734	31	1.3 (0.8-2.0)	1.6 (1.0-2.6)
Diagnoses				
Primary osteoarthritis	27,942	113	**1.0 (ref.)**	**1.0 (ref.)**
Sequelae after trauma	5,285	35	1.7 (1.1-2.4)	1.6 (1.1-2.4)
Avascular necrosis	1,093	16	3.6 (2.2-6.1)	2.9 (1.7-5.0)
Rheumatoid arthritis	925	5	1.3 (0.6-3.3)	1.3 (0.5-3.3)
Pediatric diseases	1,101	13	2.9 (1.7-5.2)	2.6 (1.4-4.8)
Other diagnoses	638	4	1.6 (0.6-4.2)	1.4 (0.5-3.8)
Charlson Comorbidity Index				
Index, low (0)	27,148	131	**1.0 (ref.)**	**1.0 (ref.)**
Index, medium (1-2)	7,288	25	0.7 (0.5-1.1)	0.7 (0.5-1.1)
Index, high (>2)	2,548	30	2.4 (1.6-3.6)	2.3 (1.6-3.5)

* Incidence rate ratio as measure of relative risk of implant failure

† IRR mutually adjusted for other patient-related predictors, fixation technique

Possible predictors for implant failure 31 day – 6 months after primary THA (Table 15)

No clear differences in failure rate regarding sex and age were evident in this time window. Diagnoses such as sequelae after trauma, avascular necrosis, and other diagnoses were all associated with an increased IRR for failure compared with primary osteoarthritis. A high comorbidity index score was also a strong predictor of THA failure in this time window, with an adjusted IRR of 3.0 (95% CI; 2.1-4.5) compared with a low comorbidity index score.

Table 15. Predictors of implant failure from any causes 31 day- 6 months after primary total hip arthroplasty.

	Patients (n)	Revisions (n)	Crude IRR* (95 % CI)	Adjusted IRR† (95 % CI)
Sex				
Female	21,502	101	**1.0 (ref.)**	**1.0 (ref.)**
Male	15,083	74	1.0 (0.8-1.4)	1.2 (0.9-1.6)
Age Groups (years)				
10-49	2,204	9	0.8 (0.4-1.7)	0.5 (0.2-1.1)
50-59	5,312	20	0.8 (0.5-1.3)	0.6 (0.4-1.1)
60-69	10,537	52	**1.0 (ref.)**	**1.0 (ref.)**
70-79	12,937	67	1.1 (0.7-1.5)	1.1 (0.8-1.6)
>=80	5,595	27	1.0 (0.6-1.8)	0.9 (0.6-1.5)
Diagnoses				
Primary osteoarthritis	27,716	102	**1.0 (ref.)**	**1.0 (ref.)**
Sequelae after trauma	5,167	53	2.8 (2.0-4.0)	2.8 (2.0-4.0)
Avascular necrosis	1,073	9	2.3 (1.2-4.5)	2.3 (1.1-4.6)
Rheumatoid arthritis	915	2	0.6 (0.2-2.4)	0.6 (0.1-2.3)
Pediatric diseases	1,087	4	1.0 (0.4-2.7)	1.9 (0.4-3.3)
Other diagnoses	627	5	2.2 (0.9-5.5)	2.4 (1.0-5.9)
Charlson Comorbidity Index				
Index, low (0)	26,865	115	**1.0 (ref.)**	**1.0 (ref.)**
Index, medium (1-2)	7,210	24	0.8 (0.5-1.2)	0.7 (0.5-1.2)
Index, high (>2)	2,510	36	3.4 (2.3-4.9)	3.0 (2.1-4.5)

* Incidence rate ratio as measure of relative risk of implant failure

† IRR mutually adjusted for other patient-related predictors, fixation technique and hospital type.

Possible predictors for implant failure 6 months – 8.6 years after primary THA (Table 16)

Male gender remained a predictor for THA failure. In contrast to the short term time window, younger age *i.e.,* patients aged 10-49 and 50-59 years, appeared to be associated with an increased risk of THA failure. Age between 70-79 years and age 80 years and more were associated with a reduced adjusted IRR for failure compared with age between 60-69 years.

There were no evident differences in risk estimates regarding the diagnoses for primary THA. A medium comorbidity index score was associated with reduced adjusted IRR for failure, whereas a high comorbidity index score was again strongly associated with increased adjusted IRR for failure compared with a low comorbidity index score.

Table 16. Predictors of implant failure from any causes 6 months – 8.6 years after primary total hip arthroplasty.

	Patients (n)	Revisions (n)	Crude IRR* (95 % CI)	Adjusted IRR† (95 % CI)
Sex				
Female	20,666	417	**1.0 (ref.)**	**1.0 (ref.)**
Male	14,502	353	1.2 (1.1-1.4)	1.2 (1.0-1.4)
Age Groups (years)				
10-49	2,122	78	1.5 (1.2-1.9)	1.7 (1.3-2.3)
50-59	5,137	142	1.2 (1.0-1.5)	1.3 (1.0-1.6)
60-69	10,173	238	**1.0 (ref.)**	**1.0 (ref.)**
70-79	12,423	243	0.9 (0.7-1.0)	0.9 (0.7-1.0)
>=80	5,313	69	0.6 (0.5-0.8)	0.6 (0.5-0.8)
Diagnoses				
Primary osteoarthritis	26,804	583	**1.0 (ref.)**	**1.0 (ref.)**
Sequelae after trauma	4,850	97	1.0 (0.8-1.2)	1.0 (0.8-1.2)
Avascular necrosis	1,030	27	1.2 (0.8-1.8)	0.9 (0.6-1.3)
Rheumatoid arthritis	882	24	1.1 (0.8-1.7)	0.9 (0.6-1.3)
Pediatric diseases	1,048	30	1.2 (0.9-1.8)	1.0 (0.6-1.4)
Other diagnoses	554	9	0.8 (0.4-1.5)	0.6 (0.3-1.2)
Charlson Comorbidity Index				
Index, low (0)	25,672	478	**1.0 (ref.)**	**1.0 (ref.)**
Index, medium (1-2)	7,081	122	0.7 (0.6-0.8)	0.7 (0.6-0.8)
Index, high (>2)	2,415	170	2.8 (2.4-3.4)	2.8 (2.3-3.3)

* Incidence rate ratio as measure of relative risk of implant failure

† IRR mutually adjusted for other patient-related predictors, fixation technique and hospital type.

5. METHODOLOGICAL CONSIDERATIONS

The interpretation of our study findings is dependent on a critical evaluation of the strengths and limitations of the specific studies. The results from any analytical epidemiological study can be affected by several types of errors. The errors can appear as systematic errors, including selection bias, information bias, and confounding, and as random error or chance, which pertain to the statistical precision of the estimates. However, because of the somewhat atypical study designs used to study Aims I-III, a thorough schematic discussion of these possible types of errors for all studies is not relevant.

5.1. Aim I: The data validity in the DHR

We used data from the Danish National Registry of Patients as a reference in the analysis of registration completeness. Several validation studies of the nationwide and population-based Danish National Registry of Patients have been undertaken showing a moderate-to-high completeness of administratively collected hospital discharge data on a number of different diagnoses and procedures (72;88;89). However, we did identify 947 patients in the DHR that were not registered in the Danish National Registry of Patients, indicating that the Danish National Registry of Patients is not a perfect reference. Additional analyses disclosed no association between patients who are not registered in the Danish National Registry of Patients and the type of THA surgery (primary THA or revision), sex, age, and hospital type or volume.
Further, the unique civil registry number facilitated unambiguous individual level record linkage between the DHR and the Danish National Registry of Patients.
Information bias in the analysis of registration completeness may have occurred because of misclassification of the registered THA procedures in the DHR or the Danish National Registry of Patients. However, registration of data in the DHR and the Danish National Registry of Patients occurs systematically and independently of each other or of any later research and therefore any misclassification is probably non-differential. We experienced a non-differential misclassification of patients, where primary THAs had been incorrectly classified as revisions and revisions that had been classified as primary THAs, in both the DHR and the Danish National Registry of Patients. To the best of our knowledge, the predictive value of THA procedures in the Danish National Registry of Patients has not previously been examined.

The analyses of the positive predictive value of data registered in the DHR were based on randomly selected stratified samples of patients. The retrieval of both medical records and radiographs was 76.5% and selection problems can therefore not be entirely excluded. In the additional analyses, however, we found no indication that the positive predictive value was different among patients where the medical records and radiographs could not be retrieved. There was no systematic pattern among the missing records and radiographs with respect to patient characteristics or hospital types. The risk of information bias in the analyses of positive predictive values was reduced by use of a standardized form for systematic reviews of medical records and preoperative radiographs. The reviews were conducted without knowledge of the diagnoses for primary THA registered in the DHR. Detailed clinical information was available from the medical records and preoperative radiographs, thus making it possible to diagnose according to internationally accepted criteria.

The calculation of the positive predictive value for some of the specific diagnoses, as well as sensitivity and specificity of the registration of postoperative complications during follow-up was based on a relatively small number of patients. These findings should therefore be interpreted with caution.

5.2. Aim II and III: IRs of primary THAs and revision, future demands, and regional variation

Analyses of IRs included all registered THA cases in the population-based DHR. The overall risk of selection bias was probably therefore of minor importance due to overall high registration completeness of THA procedures found in the Aim I.
However, a registration completeness of revision in the DHR (81%) might have caused selection bias if it is related to a particular sex, age, diagnoses for primary THA, hospital type, or specific county. When studying Aim I, we found differences in the registration completeness of revisions according to sex and age. Caution is therefore necessary when comparing the IRs of females in relation to males, and the IR of patients allocated to different age groups.

Furthermore, registration completeness according to different counties has not been examined before and possible selection bias can therefore also not be entirely excluded. We were not able to examine the registration completeness according to diagnoses for primary THA in the Aim I due to discrepancy in coding between the classification used in the DHR and the ICD-system used in the Danish National Registry of Patients. Thus, IRs for primary THA according to different diagnoses might not have been based on all incident cases and therefore not entirely accurate.

Moreover, registration completeness could have changed over time and subsequently affect IRR estimates, if the changes are associated with sex, age, or diagnoses for primary THA, or if these changes vary between sex, different age groups or diagnoses.

Further, misclassification of primary THA and revision in the DHR in relation to gender, age, diagnoses for primary THA, hospital and county-specific IRs was low and not systematically related to the different patient groups, hospitals, or counties.

The information from the StatBank Denmark is based on population registers, which are regularly updated from the Central Personal Registry. Further, to reduce the risk of information bias, data were drawn from the StatBank Denmark by the same person, in the same manner on several occasions.

We included a number of covariates in the multivariate linear regression analyses, which could be associated with regional variation in IRs (Aim III). Most of the covariates included in the linear regression analyses were not available on an individual level (except for HHS). It was therefore only possible to conduct the linear regression analyses on a county (group) level and the examined factors could not be adjusted for in the Poisson regression analyses.
Preoperative HHS, which was included as one of the independent factors in the multivariate regression analyses, was only available for 72.2% of the patients. However, additional analyses disclosed no systematic pattern in the distribution of patients without registered HHS across the different hospital types or counties. Further, HHS is the questionnaire administrated by the surgeon and thus can introduce the possibility of surgeon bias. We can not be certain whether eventual surgeon bias was associated with certain hospitals or counties, and subsequently have had an influence on the association estimation achieved from the regression analyses.

Misclassification may possible also have influenced our analyses on the role of the overall number of surgeons per county per 100,000 inhabitants for each year, as not all orthopedic surgeons perform hip arthroplasty, *i.e.,* some perform surgery on other joints or are involved in clinical research. This may have lessened our chances of finding an association between the number of orthopedic surgeons and the IR of THA procedures.
We could not exclude the possibility of collinearity between some of the covariates examined in the linear regression analyses (Aim III). However, it should be noted that the regression coefficients did not appear unstable, as they were not associated with large variances and only minor changes were found when comparing the unadjusted and adjusted regression coefficients. The coefficients of variation for the specific covariates showed huge variation (between 4% to 275%). This finding refutes the presence of major collinearity in the dataset.

The primary concerns in relation to confounding in aim II and III were differences in the age- and sex distribution of the populations we compared. We were, however, able to control for this possible confounding effect by performing age and sex standardization of all IRs according to both a Danish and European standard population. Further, we did stratified analyses according to the diagnoses for primary THA, which is an alternative way of dealing with possible confounding.

Finally, we had no information on a number of other factors which may additionally had an impact on the variation in IRs in the aim III, *e.g.,* general practitioners' and patients' preferences for the surgery, waiting time, local guidelines about clinical decision-making, or the number of nurses, anesthesiologists and other health staff that actively participate in performing surgery, and subsequently were not able to control for those factors.

5.3. Aim IV: Predictors of short and long term implant failure after primary THA

Detailed data, including laterality (right or left) of both the primary THAs and revisions are available in the DHR.

Information bias can be introduced to aim IV if information about primary THA, failure, and confounders is misclassified. We found 8 cases registered in the DHR as third primary THAs, and these cases should have been registered as first revisions. We found a further 39 cases registered as first revision, although these cases were actually re-revisions. These cases were all excluded from the analyses in order to reduce the risk of information bias.
Misclassification of possible predictors for THA failure, including sex and age is most unlikely because this information is based on the unique civil registry number. Patients without a valid civil registry number were excluded from age or sex analyses. Misclassification of diagnoses for primary THA is probably also of minor importance in this study because of the relatively high positive predictive value of the diagnoses used in this study, as described in aim I.

We were able to construct the complete hospitalization history for each patient since 1977 and until the date of THA. We relied on routinely coded hospital discharge diagnoses to compute the Charlson comorbidity index. These data may have however been influenced by misdiagnoses, miscoding of diagnoses, variation of coding, incompleteness of coding the primary and secondary diagnoses, or limitations in the specificity of available codes (90). We cannot entirely exclude the possibility that the misclassification of particular diagnoses has occurred, which would have affected the classification of comorbidity index score, and thus the risk estimates.

Lastly, a registration completeness of revisions in DHR of 81% (before exclusion of hemiarthroplasty patients), may have had impact on revision rates and could give rise to information bias regarding failure, if the chance of being registered with a revision was dependent or at least associated with any of the studied predictors. We did actually find some differences in the registration completeness of revisions according to sex and age (Aim I).

Estimates of adjusted relative risk were mutually adjusted for the possible predictors, *i.e.* age, sex, diagnosis for primary THA, and comorbidity, and non-patient related covariates previously reported to be associated with implant failure, *i.e.,* fixation technique and hospital type. Our results suggest that these factors are not “true” confounders, *i.e.,* independently associated with both primary THA procedures received and risk of implant failure, as adjustment for these factors had only a minor effect on the relative risk estimates.

Further, a number of factors, *e.g.,* genetic factors, medication during follow-up, timing of surgery, surgeon volume, smoking, alcohol intake, patient’s social status, physical activity of the patients, or rehabilitation programs, may possibly also be associated with the failure rate. The size of unmeasured and residual confounding is therefore unknown.

6. OVERALL DISCUSSION

6.1. Aim I: The data validity in the DHR

The high overall registration completeness for THA procedures in the DHR appears to be in agreement with reports from other studies (16;91-93). However, it is difficult to ascertain from these reports whether the analyses were made on an individual or a group level. It is important to note that comparisons on a group level may result in misleading estimates of completeness, since it is unknown whether the specific patients are registered in both data sources.

The lower registration completeness of revisions, compared with primary THAs in our study was at least partly related to use of different definitions for revision.
The absolute differences in registration completeness of primary THA and/or revisions according to sex and age were small and probably not clinically important.

A lower degree of completeness for university hospitals when compared with other hospitals appeared to be explained by low reporting rates from three university hospitals.
In general, registration completeness increased with increasing number of THA procedures, and the reasons for that were not clear.

It is not possible to directly compare our estimates of a moderate–to-high positive predictive value of the registered primary diagnosis with the estimates from other studies since; as such data have not previously been reported.

The low positive predictive value of the diagnosis of a fresh fracture of the proximal femur found in our study may be explained by the use of various definitions of this diagnosis in clinical practice. Thus, from the review of the original medical records and preoperative radiographs, it was evident that there was confusion about the distinction between the diagnosis of a fresh fracture of the proximal femur and late sequelae from a fracture of the proximal femur. This has later been clarified with the surgeons.
The relatively low positive predictive value of postoperative complications found in our study was not due to the voluntary nature of follow-up registration, since we only reviewed the medical

records of patients who were registered in the DHR with follow-up examinations. Thus, the current follow-up registration of the postoperative complications should be revised.

6.2. Aim II: IRs of primary THAs and revision and future demands

It is somehow problematic to make comparisons of our results with other countries, due to differences in the age distribution of the populations, methods of collecting and reporting the data, and study periods. Most of the published studies on the incidence of THA have only reported crude data, making direct comparisons with data from other studies difficult. Although some of the existing studies have performed age standardization, it is often difficult to interpret how the standardization was done (13;14;17;24).

Nevertheless, the steady increase in IRs of primary THAs and revisions found in our study appears consistent with the reports from a number of other countries (8;12;14-17;28;94).
The increase in IRs of THA procedures may be related to a number of factors, more that it can be explained by demographic changes. These include changes in age limits for performing THA, increased willingness to perform surgery on patients with severe comorbidity, increased patient demands, implementation of financial incentives for increasing the surgical activity and changes in the organization of the health care system by establishing fewer but more specialised and efficient units, with a high operating volume.

The higher IRs of THAs procedures in females found in our study, and the fact that the IRs peaked for persons aged 70-79 years, were also in accordance with previous reports from other populations (8;13;14;17;25;32;93).

The decrease in IRs of primary THAs due to rheumatoid arthritis found in our study has also been seen in Sweden (8),and could be explained by the progressive decline in the incidence of rheumatoid arthritis seen in a number of populations over the last few decades (95-97) or by the introduction of modern drug treatment, which improved outcome of rheumatoid arthritis.

Very few studies have reported on the expected need for THAs (15;31;32). The existing predictions are solely based on demographic projections. At the moment, it is difficult to imagine that the annual age-independent increase in IRs of primary THA in Denmark will continue to be 5.2% in the coming decades. Such a development would represent a serious economic challenge for the health care system, and allocation of sufficient economic resources and staff would be problematic.

6.3. Aim III: Regional variation in the IRs of primary THAs and revisions

The recent changes in the Danish healthcare system with reorganization of the surgical activities imply that THA procedures to some extent have been centralized at units outside the university hospitals. This explains our findings of a lower and decreasing activity at university hospitals. Two recent reports from Canada and Sweden (8;25) describe similar findings. However, other factors may also be responsible for the lower activity at the university hospitals. A higher proportion of patients treated due to secondary arthrosis or with higher comorbidity, or treatment with specific types of hip surgery on young patients rather than THA (*e.g.,* Ganz osteotomy), could drain the resources for performing THA, *e.g.,* surgeon time and beds (98).

Our findings of a substantial regional variation in crude IRs of primary THAs and revisions were in general agreement with the results from other studies (14;25;27;28;99).

It might be expected that regional variation in crude IRs is due to differences in the age and sex distribution of the population in various counties, as the IRs of THA procedures are closely related to increasing age and female sex. However, despite the age- and sex-standardization, the regional variations persisted in our study.

We examined a number of factors that may possibly explain the regional variation, including the availability of orthopedic surgeons which should reflect the surgical capacity (25), the proportion of patients with primary osteoarthritis, which is considered to be easier to perform THA on compared with patients with secondary arthrosis, and the preoperative hip function of the patients, as this may reflect differences in thresholds for offering surgery in the different counties. We also hypothesized that higher GDP may be associated with higher IRs of primary THA, as well as higher population density (25). The absence of an explanation for the regional variation reflects the need for a common and evidence-based consensus among patients, surgeons and politicians on the criteria for providing primary THA and revision.

6.4. Aim IV: Predictors of short and long term implant failure after primary THA

Predictors for short term implant failure after primary THA

The male sex as a predictor for short term THA failure can be due to the fact that males in our study sustained more dislocation compared with the females, which is in contrast with findings from Woolson et al. (100). However, the same study found an increased risk for failure among elderly patients as we did. This could be related to an increased risk of falls (101-103) due to balance disturbance, malnutrition, postoperative confusion, medication use, reduced vision, muscle weakening, and a generally limited range of movement because of stiffness of other joints. Two previous studies have further reported a high prevalence of dislocation in patients over the age of 80 years during the first year of follow-up (100;104). Moreover, the risk of hip fracture increases with age (105) as the bone mineral density declines at a rate of 1-2% per year after 35-40 years of age (106).

Concerning diagnoses for primary THA, a higher dislocation rate has previously been reported when THA is performed after trauma or in patients with congenital dislocation of the hip (107-109) which is in accordance with our findings. Avascular necrosis, which we also found to have a high risk for THA failure in the short time window in our analyses, is associated with various etiologic factors (107) perhaps causing a higher risk of falls and subsequent adverse effects on the bones including reduced mineral density, and impaired growth and remodelling (105).

Our findings of a high comorbidity index score as a predictor for THA failure agreed with Mahomed et al. (14), who investigated the association between comorbidity in patients older than 65 year and postoperative complications and mortality within 90 days after hip replacement.

Predictors for long term implant failure after primary THA

A few other studies (8;49;52) have also reported that males have a higher risk for overall THA failure. However, women have been reported to have a worse functional status than men before primary THA (110), suggesting that women are operated on at a more advanced stage of their disease. Our findings could indicate that the same pattern may apply after primary THA.

However, the most concerning cause of the increased risk for failure for males would be if general practitioners and orthopedic surgeons were consciously or unconsciously using different thresholds for men and women, when deciding which patients should undergo a revision. Similar patterns have previously been reported in other fields of medicine (111;112). The risk of possible sex discrimination is possibly greater when the decision- making on the THA or revision is not based on a clear clinical consensus.

Our findings of a decline in IRRs for failure with increasing age are also in accordance with the results of existing studies (8;16;49). The decline may be explained by the decrease in body weight and physical activity after the age of 70 years in both men and women (113;114), causing a reduced load on the femoral component and on the acetabulum.

Regarding diagnoses for primary THA, the reported risk estimates for THA failure are not consistent in the existing literature (49;50;115-117). These inconsistencies may be ascribed to the heterogeneity of the clinical characteristics of the study populations and the possible improper use of statistics to analyze the failure risk. The time-dependency aspect of the diagnoses for primary THA has not previously been discussed.

Our finding of a high comorbidity index score as a strong predictor for long term THA failure indicates that the diseases which have previously been found to be associated with increased bone resorption and hip fracture, included in the Charlson comorbidity index (118-122), have an important role in the chain of causes that may lead to implant failure because of aseptic loosening. The reduced risk of failure in patients with a medium comorbidity index may on the other hand reflect that the Charlson comorbidity index is initially developed to predict mortality among patients admitted to a department of internal medicine. The index may therefore not be totally applicable to THA patients; in particular when using time to failure as the outcome instead of overall mortality.

7. MAIN CONCUSSIONS

The main conclusions of this thesis are:

I. The Danish Hip Arthroplasty Registry is a potentially valuable tool for quality improvement and research due to its high degree of registration completeness of THAs procedures, and its moderate-to-high positive predictive value of registration for the diagnoses for primary THA. However, information on several diagnoses for primary THA and on postoperative complications should be used with caution.

II. The overall annual IRs of primary THAs and revisions in Denmark increased during the period from 1996 to 2002 by 30% and 10%, respectively. The needs for THA procedures in the coming decades may exceed the current capacity due to the ageing population and a continued age- and sex-independent increase in the surgical activity.

III. We found substantial variation in IRs of primary THAs and revisions among different types of hospitals and different counties in Denmark during the period 1996-2002. The variations could not be explained by different regional age- and sex-distribution of the populations, or by a range of investigated county specific patient and healthcare system- related factors.

IV. Male sex and high comorbidity index were time-independent predictors of THA failure and were associated with an increased implant failure on both a short and long term. In contrast, age and diagnoses for primary THA were time-dependent predictors of THA failure with a varying impact during different time windows after primary THA.

8. PERSPECTIVES

The studies presented in this thesis demonstrate that the DHR constitutes a potentially valuable tool for investigation of a number of issues which may arise from both clinical and research settings. The value of the DHR data may prove to be even greater than similar data registered elsewhere because of the unique possibility in Denmark for linking the data to other population-based data sources. In Denmark, these data sources include clinical databases such as the Danish National Registry of Patients, the Cancer Registry, the Central Personal Registry, the Danish Transfusion Database, the National Prescription Database, and a number of clinical biochemical and microbiological databases. Moreover, DHR can be linked to a number of orthopedic clinical databases, including the Danish Knee Arthroplasty Registry, the Danish Shoulder Arthroplasty Registry, the Ganz Registry, and the Danish Artificial Cruciate Ligaments Registry. These individual orthopedic databases will be merged into the Danish Common Orthopedic Registry on a common IT-platform on January 1, 2006. In addition, DHR data can be merged with primary data from cohort or survey studies, for instance the study “Diet, Cancer and Health”.

These databases linkages may be an effective and appropriate method to extend the usability of the DHR data and should be further explored in the very near future. This data linkage will make it possible a) to facilitate the development of the comorbidity index specific for THA patients in order to achieve better adjustment analyses, b) to compare survival of THA patients with survival of the general population using proper statistical methods, c) to investigate the predictors of THA failure or poor patient’s prognosis after THA in relation to different medical conditions in general or different primary diagnoses for THA, d) to identify pre-, per-, and postoperative factors which may be associated with increased bleeding tendency after THA surgery particularly in relation to various drug use, or e) to closer monitor IRs of THA procedures in order to predict changes in IRs and healthcare system in future, in particular in situations when clinical trials are not possible for ethical or economical reasons.

In Denmark, attempts have been made within many fields of medicine and surgery to develop and implement indicators for the quality of the performance of the healthcare system. This thesis emphasizes the need for formal indicators to measure the quality of THA surgery in order to improve patient outcome. The only indicator which has been used so far in the DHR is the revision rate. In order to provide a detailed and informative picture about the quality of THA surgery in Denmark, it is essential to develop additional indicators, *e.g.,* radiograph derived measures of early aseptic loosening, postoperative complication rates, functional status, or the quality of life.

Although this thesis supports that the clinical database already has a number of strong features, the DHR should be continuously developed and updated in order to secure its long term quality.

9. ENGLISH SUMMARY

The aims of this thesis were: *1)* to examine the data quality of the Danish Hip Arthroplasty Register (DHR) and its usability for study of the THA epidemiology (Aim I), *2)* to estimate the IRs of primary THAs and revisions in Denmark in the period 1996-2002, and the expected needs for primary THA in Denmark in the coming decades (Aim II), *3)* to estimate the existence of regional variation in the IRs of THA procedures in Denmark in the period 1996-2002, and further to examine the role of patient- and healthcare system-related factors in relation to any regional variation (Aim III), and *4)* to assess whether the effect of the possible predictors for THA failure, including sex, age, diagnoses for primary THA, and comorbidity vary during the short and long follow-up after primary THA surgery (Aim IV).
For studying aims I-IV, we used data from the DHR, which was established in 1995, in combination with data from a number of different national population-based registries and other data sources.

The registration completeness (Aim I) of the DHR between 1995 and 2000 was assessed using the Danish National Registry of Patients as a reference, which is a nationwide and population-based registry of all somatic hospital admissions since 1977. The study included 27,076 patients with THA procedures. The positive predictive value of registered data was assessed by a review of medical records and preoperative radiographs using a standardized form. The overall registration completeness for primary THAs and/or revisions was 94%. Overall, the diagnoses for primary THA could be confirmed in 84% of the reviewed patients. However, postoperative complications were only confirmed in two thirds of the reviewed patients.

The IRs of primary THA and revisions in Denmark between 1996 and 2002, the demands for primary THA in Denmark until 2020, and association between a number of patient- and healthcare system factors and regional variation (Aims II and III) was estimated by linking the data from the DHR with the StatBank Denmark. All IRs were standardized according to age and sex. The study included 37,144 primary THA patients and 6,446 revisions. The IRs of primary THAs and revisions increased by 30% and 10% during the study period. The relative increase in IRs of primary THAs was found to be similar in both females and males. The increase in IRs was seen for all age groups, but was highest among patients aged 50-59 years. A decrease in IRs was seen in patients with rheumatoid arthritis, who underwent primary THA. Over the study period, IRs of primary THAs for

university and other hospitals increased as well as IRs of revisions for other hospitals, whereas a decrease in IR of revisions was seen for university hospitals. We found substantial regional differences in the IRs of THA procedures which could not be explained by differences in age and gender distribution of the county populations, or by a range of patient and healthcare system related factors. IRs of primary THAs were estimated to increase by 22% in 2020 compared with 2002, based only on the expected changes in the age distribution of the population. However, assuming that the annual age and sex- independent increase in the IRs seen in the period 1996-2002 continues, the IR of primary THA was estimated to increase by 210% in 2020.

The association between patient related factors, including sex, age, diagnoses for primary THA, and comorbidity and the risk of short and long term implant failure after primary THA (Aim IV) was investigated on DHR data linked to data from the Central Personal Registry and the Danish National Registry of Patients. The study included 36,984 primary THA patients registered in the DHR between 1 January 1995 and 30 June 2003. Separate analyses were done for three follow-up windows, including 0 to 30 days, 31 day to 6 months, and 6 months to 8.6 years after primary THA. We found that males or high comorbidity index were time-independent predictors of THA failure, and remained strong predictive factors for failure irrespective of the follow-up period. In contrast, age and diagnoses were time dependent predictors of THA failure with a varying impact during different time windows after primary THA.

We conclude that the DHR is a potentially valuable tool for quality improvement and research.

10. DANISH SUMMARY

Formålet med afhandlingen var: *1)* at undersøge datakvaliteten i Dansk Hoftealloplastik Register (DHR) og anvendeligheden af DHR for undersøgelse af THA epidemiologi (Formål I), *2)* at beregne IR af primær THA og revisioner i Danmark i perioden 1996 til 2002, samt at estimere forventede IR af primær THA og revisioner i Danmark i de næste 15 år (Formål II), *3)* at undersøge tilstedeværelsen af regional variation i IR af primær THA og revisioner i Danmark i perioden 1996 til 2002. Endvidere undersøgte vi betydningen af flere patient- og sundhedsvæsen-relaterede faktorer i forhold til enhver regional variation (Formål III), *4)* at vurdere hvorvidt effekten af mulige prædiktorer for THA udskiftning eller fjernelse, så som køn, alder, diagnose hos primær THA patienter og konkurrerende sygdomme, varierer i forhold til kort- og langtids follow-up efter primær THA operation (Formål IV).
Alle fire formål blev undersøgt ved hjælp af data fra DHR, som er etableret i 1995 i kombination med flere landsdækkende populations-baserede registre og andre datakilder.

Kompletheden af dataregistrering (Formål I) i DHR mellem 1995 og 2000 blev undersøgt i forhold til data registreret i Landspatientregisteret. I studiet indgik 27.076 THA patienter. Primære diagnoser og postoperative komplikationer blev herefter valideret på baggrund af data indsamlet ved standardiseret gennemgang af sygehusjournaler og røntgenbilleder af bækken og hofte. Kompletheden af registreringen af THA operationer var 94%. Overordnet kunne primære diagnoser for gennemgåede THA patienter bekræftes i 84% af tilfældene. Postoperative komplikationer blev bekræftet hos to tredje del af patienterne.

IR af primær THA og revisioner i Danmark i perioden 1996 til 2002, forventet IR af primær THA i og med år 2020, samt betydningen af flere patient- og sundhedssystem-relaterede faktorer i forhold til regional variation i IR af THA procedurer (Formål II og III) blev beregnet ved datakobling fra DHR og Danmarks Statistik. Alle IR var standardiserede i forhold til den danske population fra 1996 og Europæisk standardpopulation. Vi identificerede henholdsvis 37.144 og 6.446 patienter med primær THA og revision. Vi fandt en stigning i IR af primær THA og revisioner på henholdsvis 30% og 10% i perioden 1996 til 2002, samt stigning i IR separat for mænd og kvinder og alle aldersgrupper. Der var et fald i IR hos patienter som fik primær THA på grund af rheumatoid artrit. En stigning i IR af THA operationer blev observeret på både universitetshospitaler og andre sygehuse, bortset fra fald i revisioner på universitetshospitaler. Der var betydelig variation i amtsspecifikke IR af THA operationer som ikke kunne forklares med en række patient- og sundhedssystem-relaterede faktorer. IR af primær THA forventes at blive 22% højere i 2020 i forhold til 2002, hvis beregningerne kun baseres på forventede ændringer i aldersfordeling i den danske befolkning. Såfremt det antages at den årlige alders- og kønsuafhængige stigning i IR som er set mellem 1996-2002 vil fortsætte, så vil IR af primær THA stige 210% i 2020 i forhold til 2002.

Sammenhæng mellem patientrelaterede faktorer, så som køn, alder, primær diagnose, og konkurrerende sygdomme og risikoen for THA udskiftning eller fjernelse på kort og lang sigt (Formål IV) blev undersøgt ved at koble DHR med Central Patient Registeret og Landspatientregisteret. Studiet var baseret på 36.984 patienter som fik indsat primær THA mellem 1. januar 1995 og 30. juni 2003. Der blev gennemført separate analyser for tre tidsperioder; mellem 0 og 30 dage, 31 dage og 6 måneder, og mellem 6 måneder og 8,6 år efter primær THA operation. Vi fandt at mandligt køn, samt højt index af konkurrerende sygdomme var tids-uafhængige prædiktorer for THA udskiftning eller fjernelse uanset hvilken tidsperiode, der blev undersøgt. Omvendt var alder og diagnose tidsafhængige prædiktorer for THA udskiftning eller fjernelse med varierende effekt i forhold til forskellige tidsperioder efter primær THA.

DHR alene og i kombination med andre datakilder anvendt i denne ph.d.-afhandling udgør en potentiel vigtig datakilde til forskning såvel som til kvalitetsudvikling af THA operationer.

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APPENDIX 12.1: Review of the medical records

Patient nummer__________________

1. CPR-nummer__________________
2. Grundlidelse registreret i DHR: ☐ 1. Primær artrose
   ☐ 2. Frisk proksimal femurfraktur
   ☐ 3. Senfølger efter proksimal femurfraktur
   ☐ 4. Acetabulumfraktur
   ☐ 5. Traumatisk hofteluksation
   ☐ 6. Atraumatisk caputnekrose
   ☐ 7. Reumatoid artrit
   ☐ 8. Mb. Bechterew
   ☐ 9. Andet artrit
   ☐ 10. Kongenit hofteluksation
   ☐ 11. Mb. Calve-Legg-Perthes
   ☐ 12. Epifysiolyse
   ☐ 13. Acetabulumdysplasi
   ☐ 14. Andet
3. Aktuelle side: ☐ 1. højre ☐ 2. venstre ☐ 3. begge hofter samtidig
4. Operationsdato:______________
5. Sygehuskode________________
6. Første ambulant kontrol: ☐ 1. ja, dato______ ☐ 2. nej ☐ 3. uoplyst
7. Reumatoid artrit (anamnese): ☐ 1. ja ☐ 2. nej
8. Morbus Bechterew (anamnese): ☐ 1. ja ☐ 2. nej
9. Kongenit hofteluksation (anamnese): ☐ 1. ja ☐ 2. nej
10. Morbus Calve-Legg-Perthes (anamnese): ☐ 1. ja ☐ 2. nej
11. Epifysiolyse (anamnese): ☐ 1. ja ☐ 2. nej
12. Acetabulum dysplasi: ☐ 1. ja ☐ 2. nej
13. Traumatisk hofteluksation (anamnese): ☐ 1. ja ☐ 2. nej
14. Acetabulum fraktur,opereret (anamnese): ☐ 1. ja ☐ 2. nej
15. Acetabulum fraktur (bagkant), ikke opereret: ☐ 1. ja (er der traum. hoftelux ?)
   ☐ 2. nej
16. Alkoholisme: ☐ 1. ja (atraumatisk sekundær caputnekrose?)
   ☐ 2. nej
   ☐ 3. uoplyst
17. Haemofili:
   ☐ 1. ja (atraumatisk sekundær caputnekrose?)
   ☐ 2. nej

18. Steroidbehandling, ved kronisk sygdom:
   ☐ 1. ja (atraumatisk sekundær caputnekrose?)
   ☐ 2. nej
19. Cytostatika:
   ☐ 1. ja (atraumatisk sekundær caputnekrose?)
   ☐ 2. nej
20. CT scanning: ☐ 1. ja, diagnose______________
   ☐ 2. nej

21. MR scanning: ☐ 1. ja, diagnose_____________
☐ 2. nej

22. Frisk proksimal femurfraktur (primær indsat THA inden 3 måneder og ikke opereret før), anamnese:
☐ 1. ja
☐ 2. nej

23. Senfølge efter proksimal femurfraktur, anamnese:
☐ 1. pt. er ikke opereret selv om der er verificeret fraktur, men har senere udviklet caput nekrose eller pseudoartrose (efter 3 måneder)
☐ 2. først hemialloplastik og senere THA
☐ 3. først osteosyntese og senere THA
☐ 4. nej

24. Konklusionsdiagnose (journal gennemgang):
☐ 1. Primær artrose
☐ 2. Frisk proksimal femurfraktur
☐ 3. Senfølger efter proksimal femurfraktur
☐ 4. Acetabulumfraktur
☐ 5. Traumatisk hofteluksation
☐ 6. Atraumatisk caputnekrose
☐ 7. Reumatoid artrit
☐ 8. Mb. Bechterew
☐ 9. Andet artrit
☐ 10. Kongenit hofteluksation
☐ 11. Mb. Calve-Legg-Perthes
☐ 12. Epifysiolyse
☐ 13. Acetabulumdysplasi
☐ 14. Andet
☐ 15. kan ikke klassificeres
☐ 16. coxae vara med artrose
☐ 17. coxae valga med artrose

25. Første ambulant kontrol efter operation: ___________________

APPENDIX 12.2: Review of the radiographs

Patient nummer__________________

1. CPR nummer__________________
2. Grundlidelse registreret i DHR:
   - ☐ 1. Primær artrose
   - ☐ 2. Frisk proksimal femurfraktur
   - ☐ 3. Senfølger efter proksimal femurfraktur
   - ☐ 4. Acetabulumfraktur
   - ☐ 5. Traumatisk hofteluksation
   - ☐ 6. Atraumatisk caputnekrose
   - ☐ 7. Reumatoid artrit
   - ☐ 8. Mb. Bechterew
   - ☐ 9. Andet artrit
   - ☐ 10. Kongenit hofteluksation
   - ☐ 11. Mb. Calve-Legg-Perthes
   - ☐ 12. Epifysiolyse
   - ☐ 13. Acetabulumdysplasi
   - ☐ 14. Andet
3. Aktuelle side: ☐ 1. højre ☐ 2. venstre ☐ 3. begge hofter samtidig
4. Sygehuskode:____________
5. Røntgendato:____________
6. RTG optagelse: ☐ 1.bækken ☐ 2. AP
7. Tönnes klassifikation: ☐ 0.
   - ☐ 1. sklerosering af caput femoris eller acetabulum medlet afsmaltet ledspalte og minimal dannelse af osteofyter
   - ☐ 2. cystedannelse i caput femoris eller acetabulum med moderat tab af ledspalte
   - ☐ 3. store cyster i caput femoris eller acetabulum med moderat til fuldstændig tab af ledspalte, med eller uden destruktion af caput femoris
   - ☐ 4. kan ikke klassificeres
8. Center-edge (CE) vinkel: ☐ 1. måles ☐ 2. ej
9. Center-edge vinkel, hvor mange grader_________________
10. Acetabulum stejlhed (AA vinkel): ☐ 1. måles ☐ 2. ej
11. AA vinkel, hvor mange grader________________
12. Atraumatisk caput nekrose:
    - ☐ 1. sklerosering af caput femoris
    - ☐ 2. affladning af caput femoris
    - ☐ 3. sammenfald af caput femoris
    - ☐ 4. flere punkter samtidig
    - ☐ 5. nej
13. Corpus- collum (CC) vinklen: ☐ 1. måles ☐ 2. nej
14. Corpus- collum vinkel, hvor mange grader_______________
15. Acetabulum fraktur, opereret: ☐ 1. ja ☐ 2. nej

16. Acetabulum fraktur (bagkant), ikke opereret: ☐ 1. ja (traumatisk hoftelux?)
☐ 2. nej

17. Morbus Calve-Legg-Perthes: ☐ 1. ændret form af caput femoris (breddeøget)
☐ 2. højtstående trochanter major
☐ 3. afkortet collum femoris
☐ 4 flere punkter samtidig
☐ 5. nej

18. Atraumatisk subluksation eller luksation caput femoris:
☐ 1. ja
☐ 2. nej

19. Frisk femur fraktur: ☐ 1 ja
☐ 2. nej

20. Artrit forandringer: ☐ 1. caput erosion
☐ 2. caput deformeret
☐ 3. cystedannelse i caput
☐ 4. ledspalten symetrisk forsnævret
☐ 5. medial protrusion
☐ 6. flere punkter samtidig
☐ 7. nej

21. CT scanning ___________________

22. MR scanning _________________

23. Knogle scintigrafi______________

24. Der er følger efter tidligere osteosyntese på røntgen: ☐ 1. ja
☐ 2. nej

25. Der er følger efter tidligere THA på røntgen: ☐ 1. ja
☐ 2. nej

26. Konklusionsdiagnose røntgen:
☐ 1. Primær artrose
☐ 2. Frisk proksimal femurfraktur
☐ 3. Senfølger efter proksimal femurfraktur
☐ 4. Acetabulumfraktur
☐ 5. Traumatisk hofteluksation
☐ 6. Atraumatisk caputnekrose
☐ 7. Reumatoid artrit
☐ 8. Mb. Bechterew
☐ 9. Andet artrit
☐ 10. Kongenit hofteluksation
☐ 11. Mb. Calve-Legg-Perthes
☐ 12. Epifysiolyse
☐ 13. Acetabulumdysplasi
☐ 14. Andet
☐ 15. kan ikke klassificeres
☐ 16. coxae vara med artrose
☐ 17. coxae valga med artrose

FÆLLES KONKLUSIONSDIAGNOSE (JOURNAL OG RØNTGEN) (1-17)____________

Entry, documentation, and export of data, collected through the review of medical records and radiographs was done using the EpiData Version 2.1b, EpiData Association, Denmark.

APPENDIX 12.3: Charlson Comorbidity Index

ICD-8 and ICD-10, and scoring for 19 disease categories used to calculate the Charlson Comorbidity Index

Disease category	ICD-8	ICD-10	Score
Myocardial infarction	410	I21-I23	1
Congestive heart failure	427.09; 427.10; 427.11; 427.19; 428.99; 782.49	I50; I11.0; I13.0; I13.2	1
Peripheral vascular disease	440; 441; 442; 443; 444; 445	I70- I74; I77	1
Cerebrovascular disease	430-438	I60-I69; G45; G46	1
Dementia	290.09-290.19; 293.09	F00-F03; F05.1; G30	1
Chronic pulmonary disease	490-493; 515-518	J40-J47; J60-J67; J68.4; J70.1; J70.3; J84.1; J92.0; J96.1; J98.2-J98.3	1
Connective tissue disease	712; 716; 734; 446; 135.99	M05; M06; M08; M09; M30-M36; D86	1
Ulcer disease	530.91; 530.98; 531-534	K22.1; K25-K28	1
Mild liver disease	571; 573.01; 573.04	B18; K70.0-K70.3; K70.9; K71; K73; K74; K76.0	1
Diabetes	249.00; 249.06; 249.07; 249.09; 250.00; 250.06; 250.07; 250.09	E10.0; E10.1; E10.9; E11.0; E11.1; E11.9	1
Hemiplegia	344	G81; G82	2
Moderate to severe renal disease	403; 404; 580-584; 590.09; 593.19; 753.10-753.19; 792	I12; I13; N00-N05; N07; N11; N14; N17-N19; Q61	2
Diabetes with end organ damage	249.01-249.05; 249.08; 250.01-250.05; 250.08	E10.2-E10.8; E11.2-E11.8	2
Any tumor	140-194	C00-C75	2
Leukemia	204-207	C91-C95	2
Lymphoma	200-203; 275.59	C81-C85; C88; C90; C96	2
Moderate to severe liver disease	070.00; 070.02; 070:04; 070.06; 070.08; 573.00; 456.00-456.09	B15.0; B16.0; B16.2; B19.0; K70.4; K72; K76.6; I85	3
Metastatic solid tumor	195-199	C76-C80	6
AIDS	079.83	B21-B24	6

APPENDIX 12.4: Papers I-IV