Longitudinal outcomes following total hip replacement

Time trends, sequence of events and study of factors influencing implant survival and mortality

Peter Cnudde

UNIVERSITY OF GOTHENBURG

Department of Orthopaedics
Institute of Clinical Sciences
at Sahlgrenska Academy
University of Gothenburg
Sweden

2018

Longitudinal outcomes following total hip replacement

peter.cnudde@icloud.com

Typeset by Team Media Sweden AB
Cover illustration by Pontus Andersson, Pontus Art Production
Printed in Gothenburg, Sweden 2018
BrandFactory AB

ISBN: 978-91-629-0447-0 (PRINT)
ISBN: 978-91-629-0446-3 (PDF)
GUPEA: http://hdl.handle.net/2077/54531

Contents

"The past is the key to the future"

Bruce Doe, 1983

To Marie-Julie & Anna-Helena

List of papers

This thesis is based on the following papers:

Paper I

Linking Swedish health data registers to establish a research database and a shared decision-making tool in hip replacement

Cnudde P, Rolfson O, Nemes S, Kärrholm J, Rehnberg C, Rogmark C, Timperley J, Garellick G.

BMC Musculoskelet Disord. 2016 Oct 4;17(1):414.

Paper II

Trends in hip replacements between 1999 and 2012 in Sweden

Cnudde P, Nemes S, Bülow E, Timperley J, Malchau H, Kärrholm J, Garellick G, Rolfson O.

J Orthop Res. 2017 Aug 28. [Epub ahead of print]

Paper III

Is Preoperative Patient-Reported Health Status Associated with Mortality after Total Hip Replacement?

Cnudde P, Nemes S, Mohaddes M, Timperley J, Garellick G, Burström K, Rolfson O.

Int J Environ Res Public Health. 2017 Aug 10;14(8).

Paper IV

Do Patients Live Longer After Total Hip Replacement Surgery and Is the Relative Survival Diagnosis-specific?

Cnudde P, Rolfson O, Timperley J, Garland A, Kärrholm J, Garellick G, Nemes S.

Accepted for publication in Clin Orthop Relat Res

Paper V

Risk of further surgery on the same or opposite site or mortality after primary total hip arthroplasty. A multi-state analysis of 133,654 patients from the Swedish Hip Arthroplasty Register.

Cnudde P, Nemes S, Bülow E, Timperley J, Whitehouse S, Kärrholm J, Rolfson O.

In Manuscript

Abbreviations

Abbreviation	*Definition*
AJRR	American Joint Replacement Register
AOANJRR	Australian Orthopaedic Association National Joint Register
ASA	American Society of Anaesthesiologists
BMC	Biomedcentral
BMI	Body Mass Index
CCI	Charlson Comorbidity Index
CI	Confidence Interval
DAIR	Debridement, Antibiotics and Implant Retention
ECI	Elixhauser Comorbidity Index
EQ-5D	The 5 dimension self-rated assessment tool (EuroQol)
EU	European Union
FU	Follow-up
GIRFT	Getting It Right the First Time
HCP	Healthcare Professional
HDR	Health Data Register
HR	Hazard Ratio
ICD	International Classification of Diseases
ISAR	International Society of Arthroplasty Registries
LOS	Length Of Stay
MS	Multi-State Analysis
NARA	Nordic Arthroplasty Register Association
NBHW	National Board for Health and Welfare

Abbreviation	*Definition*
NJR	National Joint Register
NORE	Network of Orthopaedic Registries of Europe
NPR	National Patient Register
OA	Osteoarthritis
PIN	Personal Identity Number
PJI	Prosthetic Joint Infection
PROMs	Patient-reported Outcome Measures
PSI	Patient-Specific Instrumentation
RA	Rheumatoid Arthritis
RCT	Randomised Controlled Trial
SALAR	Swedish Association of Local Authorities and Regions
SCB	Statistics Sweden
SD	Standard Deviation
SES	Socio-economic Status
SDM	Shared Decision-making
SPDR	Swedish Prescribed Drug Register
SHAR	Swedish Hip Arthroplasty Register
SODA	Secure Online Data Access
STROBE	Strengthening the Reporting of Observational studies in Epidemiology
THR	Total Hip Replacement
VAS	Visual Analogue Scale
WMA	World Medical Association

Abstract

Osteoarthritis of the hip is a common, debilitating and symptomatic joint disease. The disabling symptoms can be successfully treated with a total hip replacement (THR). It is known that the majority of patients do well following surgery, however some patients will need further surgery on the same or on the other hip or die prematurely in the perioperative period. The causes leading to further surgery for patients and the risks for mortality are multifactorial. The following are important factors in defining the risk for an individual patient: indication for surgery, complexity of operation, patient age, medical comorbidities, physical activity and socio-economic factors, types of implants used and surgical techniques employed, as well as perioperative protocols and post-operative treatment.

The research questions for this project were:

1. Has there been a change in patient-related, surgery-related and socioeconomic factors in patients undergoing elective hip replacements and have the various outcome parameters evolved?
2. Is there an association between self-reported health status and mortality following elective hip replacement?
3. Have patients who underwent THR a better relative survival than the general survival and is this influenced by the diagnosis for which the THR was undertaken?
4. What is the long-term risk of subsequent surgery on the same or the opposite hip and risk of mortality after an elective primary THR? Is there an influence of patient-related, surgery-related and socio-economic factors on subsequent surgery and dying?

Patient level data concerning many of these factors are available in the Swedish Hip Arthroplasty Register and administrative databases of the National Board of Health and Welfare and Statistics Sweden. This information was linked into a single research database. The principles of relative survival analysis and multi-state analysis with multivariable regression for statistical analysis were used. It was decided to study patients undergoing elective THR between 01/01/1999 and 31/12/2012.

Most patients were operated because of primary osteoarthritis and the proportion of patients with this indication increased further during the period of study at the expense of a decreasing number of patients with inflammatory arthritis.. The practice of elective THR has changed during the study-period, and there has been a reduction in 30- and 90-day mortality, an overall improvement of revision rates and patients have reported improved satisfaction and outcomes. Worse health status according to the EQ-5D before THR was associated with higher mortality up to five years after surgery. Patients with a THR had an improved relative survival compared to an age- and sex-matched population. A diagnosis-specific differentiation of relative survival rates post-THR favored patients with hip osteoarthritis. Higher Elixhauser comorbidity index, lower level of education and being widow or single had an adverse effect on survival.

The lifetime risk for bilateral surgery, revision and death was identified using the longitudinally collected data. Despite some changes in practice, the long-term outcome following THR has improved as surgical practices have evolved. A worse self-reported health status is associated with increased mortality in the medium-term. Overall, patients undergoing elective THR will have a better relative survival and a low risk of revision. The risk of receiving further surgery on the same or on the other hip is multifactorial and patients are twice as likely to have their other hip replaced than to die during the study-period. Performing a primary arthroplasty on the contralateral hip is 7 times more likely than a revision procedure on the first implanted hip.

Background and introduction

Total hip replacement

Osteoarthritis (OA) of the hip is a common debilitating and symptomatic joint disease, and affects up to 25% of the population over 85 years of age (1). The causes of OA are multifactorial and the global burden of the disease is increasing (2). If a trial of non-surgical treatment with lifestyle modification (weight control, exercise, walking aids) and analgesia fails to provide the patient with the desired goals of reducing pain, regaining mobility and improving health-related quality of life then a surgical intervention can mitigate the disabling symptoms (3–6). The decision when and whether to proceed to surgery needs to based on a discussion between surgical team and patient and follow the principles of shared decision making (7). The irreversible operation of total hip arthroplasty consists of replacing the affected hip with an artificial ball and socket joint. Sir John Charnley has widely being recognised of popularising successful hip replacement following earlier unsuccessful attempts (8–10). The procedure is considered to be one of the most successful and cost-effective surgical interventions and has been named "the operation of the century" (11, 12). Several publications and national arthroplasty registers have confirmed that survivorship of many types of implants at 10 years is in excess of 95% (13–15). However, it is also well known that in a minority of patients the operation does not provide the expected outcome. Despite this, the future demand for primary as well as revision surgery has been described and most authors anticipate an inexorable increase in incidence (16–22).

The success of a hip replacement cannot solely be defined by the absence of a revision procedure (23). From a patient's point of view the intervention is considered successful if there is an absence of pain related to the joint, a re-establishment of mobility and a long-term uneventful retention of the implanted joint (24). A less successful outcome or failure of the surgical intervention could be characterized by persisting poor function, failure to completely relieve the pain, inability to fulfil patient expectations and the occurrence of adverse events (complications). Complications may occur during or immediately after the surgical procedure or in the longer term. They may necessitate admission to hospital. The complication may lead to further surgery on the hip including revision surgery to replace one or more components and in a small number of cases the patient may die as a result (25).

A great deal is known with regard to the demand and need for redo-operations (revisions) where one or more of the components of the artificial joint need to be exchanged, removed or added. Less is known about the final outcome of the intervention (16, 17, 19, 21). It is recognized that a small proportion of patients will require readmission to hospital within 30-or 90-days of the first hip operation for treatment of adverse events arising as a consequence of the surgical intervention. In addition, some patients might require re-operation(s) on the hip at some later point for treatment of a variety of conditions such as a wound problem, superficial or deep infection, dislocation, implant loosening and other reasons. A proportion of these will require removal and re-implantation of one or both components on one or more occasions. These subsequent contacts with healthcare providers following the original surgery are used as quality indicators for the surgery in some countries.

The number of patients who have recurrent problems resulting in repeated readmissions and reoperations is difficult to track in any healthcare system and is not completely known. Additionally, the clinical outcome for these patients with regard to their perception of pain, their functional performance and overall mobility are also unknown. It is acknowledged that the results of revision surgery are less likely to be as good as the first operation and patients who require multiple procedures are far less likely to have a pain-free, well-functioning hip (26–29). In addition, with every surgical procedure there is a finite risk of death, the highest risk being in elderly, unfit patients. The additional mortality risk to patients who have early problems after surgery is not known. A graphic representation of the convoluted pathway followed by the patients after the surgery is represented in figure 1.

The causes leading to further hospital admissions for patients are likely to be multifactorial (30). The following factors are important in defining the risk of readmission for an individual patient: preoperative functional state, indication for surgery, complexity of operation, patient age, medical comorbidities, physical activity and socio-economic factors, types of implants used, surgical

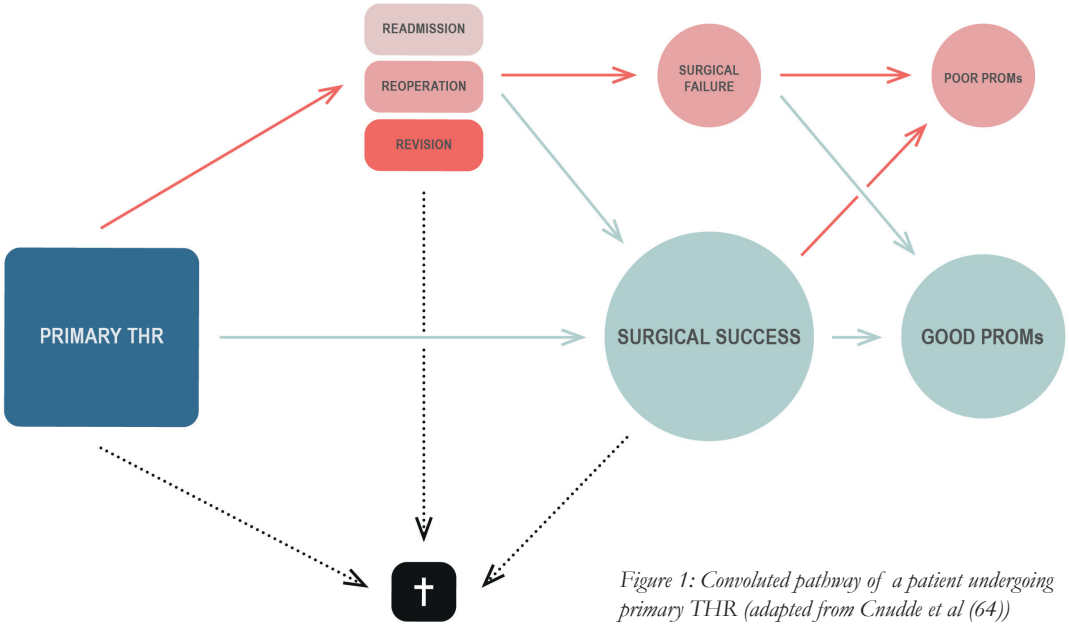


Figure 1: Convoluted pathway of a patient undergoing primary THR (adapted from Cnudde et al (64))

techniques employed, perioperative protocols and post-operative treatment. The influence of a preoperative function score on outcomes has been described in two prospective cohort studies; patients who score worse preoperatively are shown to have a poorer outcome at six months and two years (31, 32).

With the predicted increase in demand and the rise in cost for procedures it is important that the factors important in patient care are optimised and the multifactorial causes leading to suboptimal outcomes are addressed, where feasible, in order to avoid unnecessary additional and avoidable costs. The Getting It Right First Time (GIRFT) initiative can be considered an example of a national approach to optimising outcomes and reduce costs (33, 34).

Information concerning many of these factors is available in the Swedish Hip Arthroplasty Register (SHAR) and databases of the National Board of Health and Welfare and Statistics Sweden. It is possible to study their potential interactions and associations with the longitudinal outcome by combining the information into a single study database.

Registers, the quality registers, the Swedish Hip Arthroplasty Register and arthroplasty registers

The word "register" stems from Latin *registrum*, meaning 'things recorded' and is used in epidemiology for a file of data, related to a population base (35).

Ernest Amory Codman (1869–1940), considered father of the registers, developed his bone sarcoma register in the beginning of the 20th century as part of an assessment of his outcomes and to develop an improved strategic plan for his future patients using the "If not, why not" principle and the "End Result Idea" (36, 37). He could not have realized that long after his death his contributions would be considered of immense value and instrumental in the understanding of the way patients, surgeons, implant manufacturers and decision-makers would use the current registers (36). In an editorial, The Lancet describes the effect of national disease registries on reduction of cost and improving outcomes through comparison, identification and the adoption of, best practice (38). This editorial was based on the work of Larsson et al. where they describe the effect of registries on improved health outcomes, having collected information from 13 leading registries in five countries (39).

Sweden is considered to be one of the pioneering countries in register work and developed the 'Quality Registers' (QR) to 'examine and improve the delivery of the healthcare' (40, 41). In recognition of the importance of the QR's there was an extra-funding agreement in the period 2012–2016 with additional co-funding by the Swedish government (70%) and Swedish Association of Local Authorities and Regions (30%).

The SHAR was set up in 1979 to study all kinds of reoperations including procedures where the implant or its parts are exchanged or removed (revisions). Gradually and over the years there have been changes in the content and the methods of data collection. Since 1992 the orthopaedic departments of the various hospitals within Sweden (University, county, rural and private hospitals) report all primary surgeries and subsequent reoperations to the SHAR based on the Personal Identity Number (PIN) and laterality. The evolution of the SHAR was described by Kärrholm in 2010 (42). There is a continuous and on-going assessment and validation of data quality and completeness. There are up to six steps in the validation process with the first three steps being routine practice for all primary surgeries (Table 1).

It is widely recognised that the pioneering work of the SHAR and its acceptance within the orthopaedic community has led to changes in practice that has resulted in the revision rate following hip replacement surgery in Sweden being amongst the lowest in the world. This has been accomplished by the diligent follow-up of patients with feedback of outcomes to the providers of the healthcare along with post market surveillance of individual implant performance. The SHAR has three main tasks related to hip replacement surgery:

1. Analysing healthcare institutions and their activities
2. Stimulating continuous clinical improvement
3. Performing clinical research

In addition, the SHAR manages post-market surveillance of implants. Since its inception the SHAR has not remained static, but has responded to changing demands and expectations with the introduction of innovative new performance tools. One major development was the introduction of the Patient-reported Outcome Measures (PROMs) program, giving a voice to the patients in healthcare performance evaluation (43–45). As part of the quality control and feedback mechanism the annual report from the SHAR publishes a "Clinical Value Compass" for each and every hospital performing THR (https://registercentrum.blob.core.windows.net/shpr/r/Annual-Report-2016-B1eWEH-mHM.pdf). This graphical representation provides a comparison of the performance on eight quality indicators of every hospital in Sweden with the national average (Fig 2). The eight quality indicators are selected from mortality figures, reoperation data, revision data, PROMs, and data quality. It has now been suggested that a shared decision-making (SDM) instrument should be developed in an attempt to further integrate patients' wishes and expectations with the surgeons' expertise (46–48). The

Table 1. Six steps in the validation process of SHAR data

1	Logical control at the web-based entry
2	Control of completeness using the comparison of SHAR database and the hospital's own patients administrative database
3	Control of completeness between the SHAR database and the national patient register
4	Manual capture of all reoperations with linkage to the primary surgery
5	Routine monitoring of the different hospitals using site visits by the register co-ordinators
6	Targeted validating studies (e.g. infections/periprosthetic fractures)

first step in building such an instrument is to assemble the necessary data from different sources. This involves linking the SHAR database with databases of other governmental agencies.

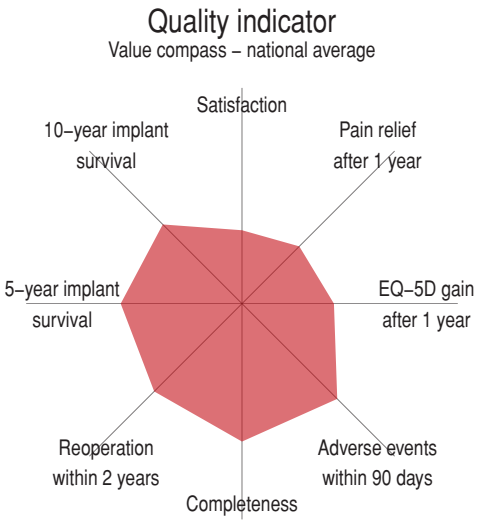


Figure 2: Average Clinical Value Compass for the Swedish Orthopaedic units (adapted from Annual report 2016 (SHAR))

The success of the SHAR has led to the development of regional and national registers in other countries and a collaboration between different established registers around the globe (Nordic Arthroplasty Register Association (NARA), Network of Orthopaedic Registries of Europe (NORE), International Society of Arthroplasty Registries (ISAR)). As a result there are many orthopaedic and other medical interventions and diagnoses that are now monitored by Registries using similar models. In a recent article, Berry describes what can be learnt from the arthroplasty registers by collating observations made from the American, Australian, England & Wales, New Zealand, Swedish national joint registries and the Kaiser Permanente Joint Registry (49). The Scandinavian countries each have established and well-functioning joint registries and the Nordic Countries have been pooling some of their data in a collaboration to analyse specific issues under the NARA banner, set up in 2007 (50). Within the United Kingdom, the National Joint Register (NJR) was established in 2003 as a response to the Capital Hip, 3M® issue (51). The NJR is now the biggest register in the world, and has now over 2.3 million entries covering hip, knees, shoulders, elbows and ankles. The Australian Orthopaedic Association National Joint Register (AOANJRR) was initiated in 1999 and has over 1.1 million entries. The American Joint Replacement Register (AJRR) is one of the more recent national joint registers, expanding quickly and driven by the need to improve outcomes and quality of joint replacement surgery within the USA. The International Society of Arthroplasty Register (ISAR), founded in 2004, has a goal to utilize the strength of cooperation, sharing of information, and further enhance the capacity of individual registries (Table 2).

In line with the initial ideas of Codman, the main aim of the arthroplasty registers is to improve outcomes following joint replacement surgery. Malchau et al. have suggested that further innovation within arthroplasty could well benefit from register-nested trials (52, 53). Gray described the strength of the registries as a knowledge-development tool and concludes that besides the assessment of long-term safety of implants they can also contribute to improvement in patient care and reduction of waste as well as providing a resource for epidemiological studies and research into long-term outcomes (54).

Studies based on a valid interpretation of high quality data can be considered as an extra value from the registers. Opponents as well as supporters of registers have published their critiques (55–59). Register-based research and RCT's fulfill different functions and should be considered as being complementary to each other. Register-based studies are observational in nature and cannot prove or disprove causality. It is likely that the future will focus on register-nested trials as an innovative way to evaluate new implants and techniques. Many reports have been describing the positive effects of arthroplasty registers and the observed improved outcomes for patients as a result of the ongoing feedback mechanism (60–63).

The National Board for Health and Welfare (*NBHW-Socialstyrelsen*)

This government agency is working under the auspices of the Ministry of Health and Social Affairs (http://www.socialstyrelsen.se/english). It is the main administrative authority dealing with healthcare in Sweden. Its tasks are mainly providing guidelines and managing healthcare regulation. The Swedish government has set up health data registers (HDR) and it is mandatory for

Table 2. Example of joint replacement registries

	Country	Start date	Number of THR	PROMs	Revision rate % @10yrs or KM implant surv	Owner
SHAR	Sweden	1979	455,348	V	97% KM surv	Regional/government
NJR	UK	2003	895,292 (31/12/16)	V	5.21%	Government
AOANJRR	Australia	1999	545,831 (31/12/16)	NO	5.1% OA only	Orthopaedic Association
AJRR	USA	2009	169.060 (31/12/15)	V	NA	Freestanding
LROI	Netherlands	2007	227,301 (31/12/16)	V	4.6% @8yrs	Orthopaedic Association
NZJR	New Zealand	1997	110,208 (31/12/15)	V	93.50% KM surv	Orthopaedic Association
DHR	Denmark	1995	161,968 (31/12/16)	NO	92%	Danish Regions
FAR	Finland	1980	188,273 (30/10/17)	NO	12.3%	Government
NRL	Norway	1987	211,234 (31/12/16)	NO	91.50% KM surv	Regional
NARA	Scandinavia	2007	NA	NA	NA	Independent
ISAR	International	2004	NA	NA	NA	Independent

all healthcare providers to report data to these centrally organized HDR. The Cancer Register (1958), The Cause of Death Register (1961), the National Patient Register (NPR, 1964), The Inpatient Care Operations Register (1997) and the Drug Register (2005) do contain a wealth of information and are all part of the governmental HDRs. The data available on these registers has been linked to the SHAR database and will be used for this study looking at pre-existing comorbidity and readmissions mainly from the NPR.

Statistics Sweden (*SCB- Statistiska Centralbyrån*)

Another government agency (www.scb.se) containing data relevant to the analysis of arthroplasty outcome has roots dating back to the 17th century (1686). The parishes of the Church of Sweden were ordered to start keeping records on the Swedish population. The current name (SCB) became official in 1858, after the organization was named *Tabellverket* (Office of Tables) in 1749. According to Swedish law (Official Statistics Act 2001:100) there must be official statistics for general information, investigation and research. The agency is responsible for collecting information on the Swedish population and providing official statistics to inform decision-making, promote debate and allow research. The overall goal of the agency is to produce official statistics of good quality and it strives to be a world-class leader in refining available data into statistical sound and reliable information for researchers, the private sector and the government. They have provided us with individual data on baseline demographics and socioeconomic status.

Linked database (64)

Bozic et al state that "the seamless integration of data, combined with the analytics to see and communicate insightful patterns within it, will be an invaluable tool for improving quality, reducing cost, and advancing research" (65).

The use of linkage of various databases is used increasingly both in the medical world as well as in

other areas. The databank, developed through Swansea University (UK), states that it has developed a research-ready platform using data from primary care, secondary care as well as social services (66, 67). Large amounts of relevant, quality data are a powerful tool, and the amalgamation of these data sets will provide new insights and contribute to the development and analysis of new medical devices, techniques and medication as well as help with the analysis of the existing treatment modalities.

As there is more and more evidence that the outcome following joint replacement surgery can be influenced by socio-economic factors as well as comorbidity it is extremely important to include these variables in the analysis of outcomes (59, 68–71). In the past registries have been criticized for not making adjustments for comorbidity and socioeconomic status as it is believed that they can be associated with poorer outcomes (72). These variables are not normally captured within the databases of the SHAR, but this specific information can be requested from and is available within different government databases. Some previous research projects with roots within the SHAR have been able to combine the necessary information following selective linkage. We therefore felt combining the variables of socioeconomic data and comorbidities in one single validated research database could well be advantageous. In the UK, the strategic plan of the NJR focuses on the ability to link their database with other governmental databases. This should achieve a strengthening and deepening of the study quality by increasing the number of variables and decreasing some of the current unknown variables, not routinely recorded within the NJR. Statisticians from the Bristol group have developed and tested formulas and codes to enable probabilistic matching based on available patient information details, in the absence of a PIN (73).

Study objectives

1. To describe the linkage process to facilitate data expansion into a single research database, the different sources of data, and to study the ethical framework and possible applications of the research database.

2. To define time trends in patient-related and procedure-related factors, that may influence outcomes within the study period.

3. To study the association between pre-operative, self-reported health and midterm mortality.

4. To compare survival patterns of patients undergoing elective THR with the general population using the techniques of relative survival and life tables.

5. To quantify the proportion of patients having surgery on the ipsi- and/or contralateral hip following the initial hip replacement, determine and explore factors leading to an increased risk of further surgery. To study the association between patient-related, socio-economic and procedure-related factors including surgical operation and the type of implant used, and implant and patient survival.

Patients and methods

The Swedish Register system is in a unique position to be able to reliably track the entire patient pathway. It enables detailed modelling of the patients' journey after a hip replacement with regard to confounding variables such as socio-economic status, general health and well-being, comorbidity, patient-related variables, surgery-related variables, hospital-related details and other variables from a variety of reliable sources.

As one of the oldest existing national registers SHAR has the advantage of maturity over the more recently developed registers, especially in the study of long-term or longitudinal outcome. Using the unique PIN, data from the SHAR could be linked with health and socio-economic data and variables using the databases under the auspices of the National Board of Health and Welfare and Statistics Sweden (table 3).

1. **Swedish Hip Arthroplasty Register (SHAR):** contains relevant information regarding laterality, patient age at time of operation, diagnosis, characteristics of the surgery, postoperative complications, outcome measurements (42).
2. **Statistics Sweden (SCB):** contains baseline demographics, socio-economic status, completed level of education, unemployment record, income (both on a household and on an individual basis), residence (municipality), sickness record, rehabilitation record, country of birth.
3. **National Board of Health and Welfare (NBHW) and the Swedish National Patient Register (NPR)**: contain details of medical comorbidities, admissions to hospital care, discharge diagnoses (ICD-9 and ICD-10), dates of admissions and discharges.

Following ethical approval from the Regional Ethical Review Board (Gothenburg dnr 271-14) data from the SHAR was merged with data from the National Board of Health and Welfare and Statistics Sweden using the unique 10-digit PIN maintained by the Swedish Tax Office (*Skatteverket*) (74). Data on every primary hip replacement recorded in the SHAR was forwarded with the PIN and laterality (right or left) to the NBHW where requested variables were added. Subsequently this combined data was returned with a serial number (without PIN) to the SHAR and forwarded to the SCB with serial number and PIN to merge the additional data. This completed dataset is then forwarded to the SHAR without PIN (Fig 3) (64).

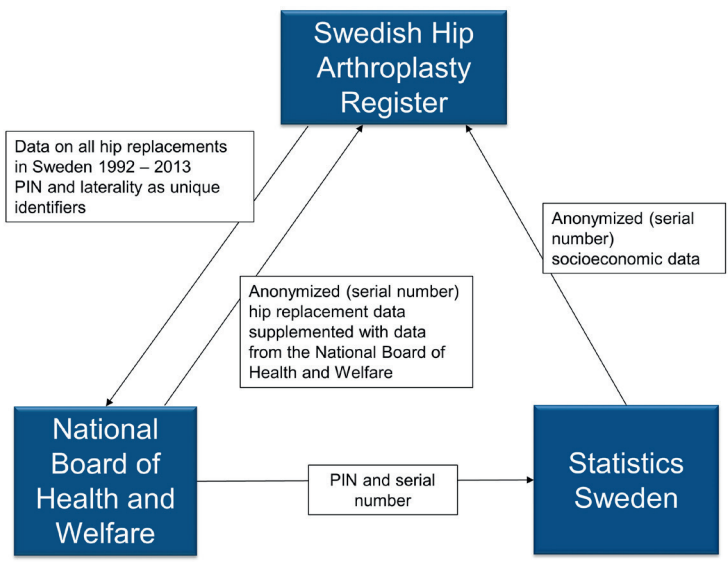


Figure 3: Linkage process between the SHAR, NBHW and the SCB using the PIN number and adding of a serial number providing anonymised data (adapted from Linking Swedish health data registers to establish a research database and a shared decision-making tool in hip replacement by Cnudde et al. (64))

Consequently a master research database comprising 79 files, totalling 96 gigabytes was constructed containing information from patients undergoing hip replacements operated in the time period 1992–2014. There were 279,173 primary procedures recorded in 230,424 patients. Of these, 15,842 patients went on to undergo 16,501 reoperations. Data was stored on encrypted servers (Secure Online Data Access-SODA) that could only be accessed by researchers involved in the project. Data was structured by statisticians and underwent a series of validation processes. Of the total potential number of patients (279,173) only 59 (0.0002%) were lost during the process. Requests and plans have been made and are currently getting finalised to expand the database with additional data on existing patients and additional patients with corresponding data for the subsequent years, keeping the database a more up-to-date research tool.

For the purpose of this study project we only used data of patients who underwent their primary hip replacement surgery between 01/01/1999 and 31/12/2012. We decided to use this data to maximise the number of patients, improve the quality of variables and to maintain an acceptable mid- to long-term follow-up period. During the study period 193,253 THRs were recorded in 164,113 patients. If further data is released from the other organisations in the future, using the same linkage mechanism, the study period can be extended in the future. This would increase both the numbers of patients (and operations) as well as the length of follow-up, thereby increasing the strength of the data (see future projects).

Paper I

Data from patients who received their (total) hip replacement between 01/01/1999 and 31/12/2012 and recorded within SHAR was merged with the data from Statistics Sweden and the National Board of Health and Welfare. In the future it is anticipated that these data will be merged as part of an on-going process. The paper also contains a reference to the data collected on (hemi-) arthroplasties for hip fractures since 2005.

Paper II

The trends paper uses the research database as the basis for the analysis. It contains data on 193,253 THRs in 164,113 patients (75). Patient- and surgery-related data for this analysis have been routinely and prospectively collected and we used the different levels of data as suggested by the international registry collaborations (76). We describe changes in the incidence and prevalence of surgical intervention, changes in clinical diagnosis at intervention with the passage of time, details of comorbidity (ASA and Elixhauser), age at intervention (77–82), BMI, SES (in the form of highest level of achieved education) and surgical technique (fixation, bearing couple, approach). We attempted to describe the trends in the type of hospital attended by patients and the day of the week the surgery took place. The different outcomes described were: length of stay (LOS), reoperation (without change of implant, revision of one or more implant, short- and mid-term mortality. We also attempted to describe an evolution in pre- and postoperative PROMs using EQ-5D, EQ VAS (83), pain VAS and satisfaction VAS as well as Charnley classification (84).

Paper III

We used data from 01/01/2008 to 31/12/2012 to study the association between preoperative patient-reported health status and mortality. The PROMs program in Sweden only reached full nationwide cover in 2008 (43), which was the rationale of using only this 5-year cohort from the linked research database. 42,862 patients with primary OA and complete preoperative PROMs were included. In the event that patients would have received a bilateral procedure during the study period, only the first performed THR was included. The main purpose was to study any association between the patient's self-reported health status and postoperative mortality (Fig 4).

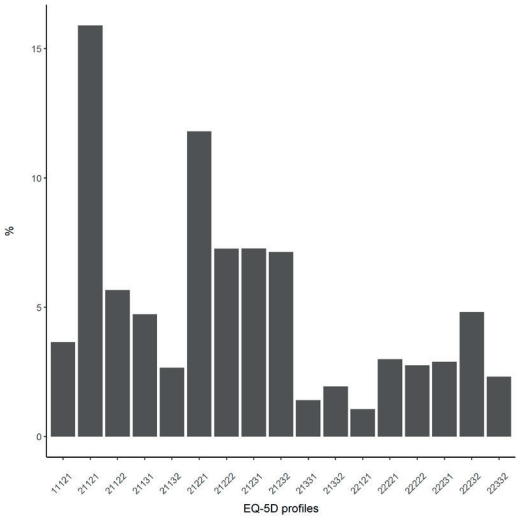


Figure 4: Most frequent EQ-5D combinations within the study population

Paper IV

The data used for the relative survival was from the linked database and the Human Mortality Database (www.mortality.org). Data on 131,808 patients was compared with birth year- and sex-matched data (spanning the same period) form the Human Life-table database and the relative survival was calculated accordingly as being the measured mortality versus the expected mortality. 21,755 patients died during the study period. We only studied patients who received an elective primary THR between 01/01/1999 and 31/12/2012. Median follow-up for survivors was 5.62 years and for study subject who died it was 5.43 years.

Paper V

Patients in the linked database in whom the first hip replacement was performed electively between 01/01/1999 and 31/12/2012 were studied. Data on 133,654 patients with 160,165 primary THRs and 4,719 revisions were available. 22,070 patients deceased during the period. A graphical representation of the sequence of events was constructed (Fig 5).

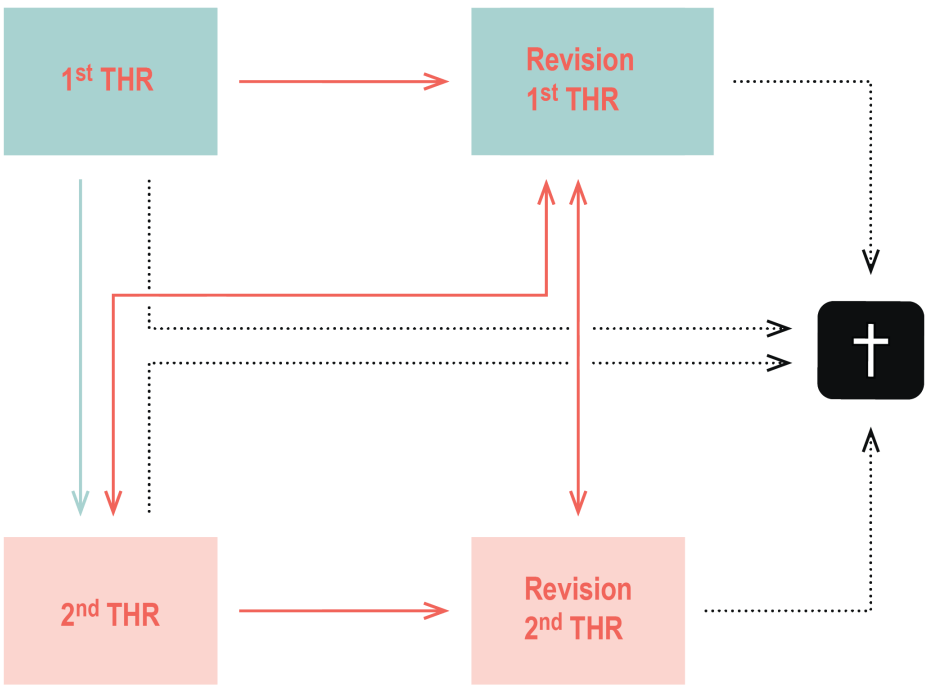


Figure 5: Multi-state analysis possible pathway steps form first hip operation (entry) to death (absorbing state)

Statistical methods

Paper I

This is a pure descriptive paper on how the the databases were merged. We did use some descriptive statistics. Due to the presence of the universal PIN, there was no need to use some mathematical and statistical techniques to check the accuracy of the data aggregation, that are generally described for other data linkage studies in the absence of a universal PIN.

Paper II

Continuous variables were summarized as means and standard deviations, categorical variables as percentages and absolute numbers. We used robust and non-parametric regression for trend analyses. The outcome for the regression analyses was the variable of interest and this was regressed on calendar year.

Paper III

Comparison between the group of survivors and deceased patients was conducted with Student's t-test and χ^2 test for continuous variables categorical variables respectively.

The survival data was subsequently studied, summarised and illustrated with the help of relative survival curves (85–87). This was considered a move away from the traditional Kaplan-Meier survival curves and Cox Proportional Hazards in an attempt to enable us to have better insights in the relation between survival of the studied population compared to the general population and the differences between the levels of the five EQ-5D dimensions. The relative survival ratio is defined as the observed survival in the patient group divided by the expected survival of a comparable group from the general population

$$r(t) \quad \frac{S_O(t)}{S_P(t)}$$

where $S_O(t)$ denotes the observed survival in the studied group and $S_P(t)$ is the population or, expected survival (87). The population or expected survival was estimated from publicly available mortality tables, tabulated for sex and age (in years) (88).

Paper IV

Continuous variables were summarized as means and standard deviations, categorical variables as percentages. Group comparisons were provided with Student's t-test and χ^2-test.

Similar to the previous paper we used relative survival ratios (85–87), comparing the observed survival in the patient group divided by the expected survival of a comparable group (sex and age) from the general population

$$r(t) \quad \frac{S_O(t)}{S_P(t)}$$

where $S_O(t)$ denotes the observed survival in the studied group and $S_P(t)$ is the population or, expected survival as available from life tables (Table 3).The population or expected survival was estimated from publicly available mortality tables, tabulated for sex and age. Life tables have been used extensively in demography and demographic research and describe the extent to which a generation of people (i.e. a birth year for the different sexes) dies off with age and these have been jointly developed and maintained by the Human Life-Table Database http://www.lifetable.de/) under the auspices of the Max Planck Institute for Demographic Research (Germany), the Department of Demography at the University of California at Berkeley (USA) and the *Institut national d'études démographiques* (France).

Multivariable modelling proceeded with Cox Proportional Hazards Model in Transformed Time (89). Model assumptions were checked with Brownian bridges (90). We observed significant deviation from the assumption of proportionality for the Elixhauser comorbidity index (ECI). We mitigated the problem with introducing time dependent coefficients. Graphical examination of the effect of the ECI indicated that there are changes in the effect measures at 5 and 8 years. Thus, we introduced a step function that split the data in 3 epochs, up to 5 years, between 5 and 8 years and above 8 years (Fig 6). The regression model then included an interaction term between the ECI and step function for time. The hazard rates for the ECI for the different epochs are sums of the main and interaction terms.

Paper V

We used the principles of the multi-state (MS) analysis, as described by Putter and Willekens and the R software package (91, 92). MS models are used to describe life histories or the process where subjects move from one state to another state, as there are multiple endpoints within the study period in the case of long-term

Table 3. Lifetable from Sweden for patients born in 1935 and at different ages for the two different sexes (adapted from Human Life-table Database)

birthyear	age	Probability of death	Residual life left	Probability of death	Residual life left
		female		male	
1935	55	0.00945	21.08	0.01238	20.24
1935	56	0.01052	20.28	0.01266	19.49
1935	57	0.01184	19.49	0.01460	18.73
1935	58	0.01270	18.71	0.01457	18.00
1935	59	0.01430	17.95	0.01756	17.26
1935	60	0.01434	17.20	0.01758	16.55
1935	61	0.01687	16.44	0.02019	15.84
1935	62	0.01753	15.71	0.02046	15.15
1935	63	0.02081	14.98	0.02113	14.45
1935	64	0.02323	14.28	0.02617	13.75
1935	65	0.02479	13.61	0.02731	13.10
1935	66	0.02403	12.94	0.02948	12.45
1935	67	0.03025	12.24	0.03584	11.81
1935	68	0.03359	11.60	0.03774	11.22
1935	69	0.03863	10.98	0.04315	10.63
1935	70	0.03796	10.39	0.04489	10.08
1935	71	0.04747	9.78	0.04621	9.52
1935	72	0.05289	9.23	0.05514	8.95
1935	73	0.05419	8.70	0.05996	8.43
1935	74	0.06452	8.16	0.06628	7.92
1935	75	0.07064	7.67	0.07643	7.43
1935	76	0.08083	7.19	0.08370	6.98
1935	77	0.08893	6.76	0.09561	6.54
1935	78	0.09356	6.34	0.09796	6.15
1935	79	0.10967	5.91	0.10421	5.73
1935	80	0.11853	5.54	0.12708	5.31
1935	81	0.12816	5.18	0.14142	4.96
1935	82	0.14413	4.82	0.14124	4.64

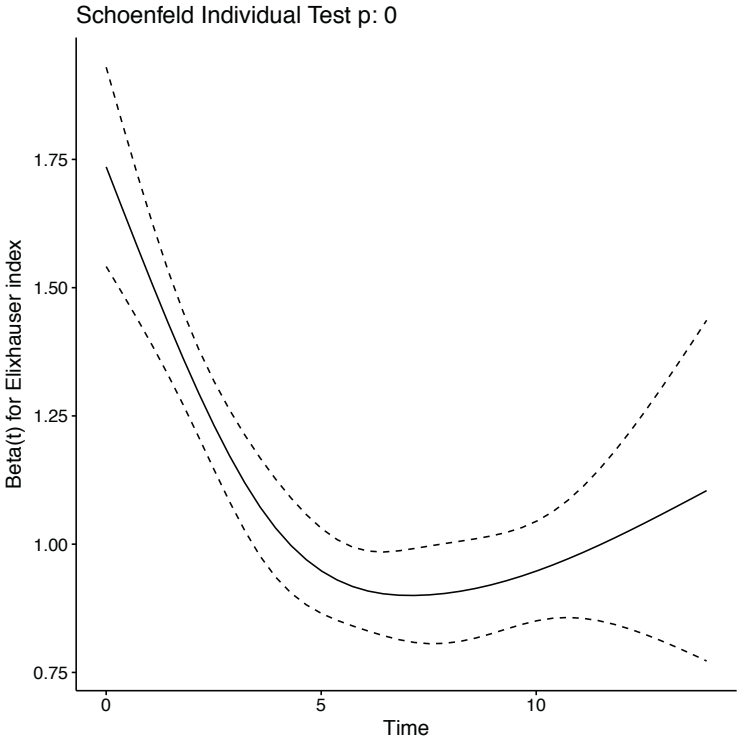


Fig 6: Graphical representation of the evolution of the hazard ratio of the Elixhauser comorbidity index as a function of time.

follow-up. It describes the hip-related timeline between operations, revisions and mortality. We adopted a MS model describing this pathway of patients between a series of discrete states in a continuous time. This disease progression model had five states and described the pathway of a patient from the 1st THR onwards (Fig 4). The patients entered the study at the time of the 1st THR surgery (State 1). The patient can remain in state 1 or subsequently advance into further states. If the patient dies, he or she will move into the end-state 5 (the absorbing state of death)(Fig 7). Probabilities and hazard ratios with a 95% CI were calculated for the different states and the transitions.

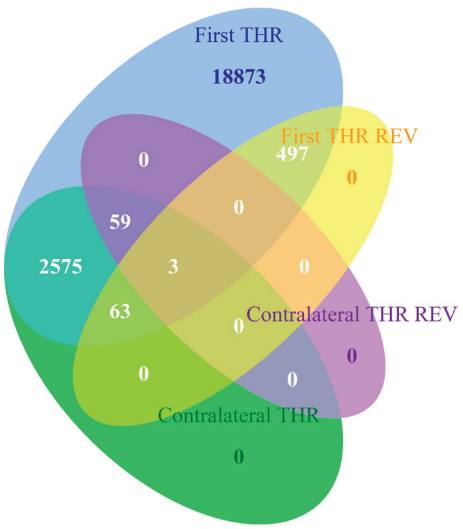


Fig 7: Venn diagram providing information on the state prior to the absorbing state. (First THR=first performed THR; Contralateral THR=subsequent performed THR; First THR REV= Revision of the first performed THR; Contralateral THR REV=revision of subsequent performed THR)

Summary of results

Paper I

Linking Swedish health data registers to establish a research database and a shared decision-making tool in hip replacement

Data were structured by statisticians and underwent a series of validation processes. Of the total potential number of patients (279,173) only 59 (0.0002%) were lost during the process.

This database is the starting point of several research projects identifying factors that influence the outcome of hip arthroplasty. Socio-economic factors, primary diagnosis and comorbidities affect the outcomes and a clinical validated instrument to help the decision-making between the patient and healthcare providers could well be developed as a result of the identification of risk factors, based on a review of a large dataset (Table 4).

Paper II

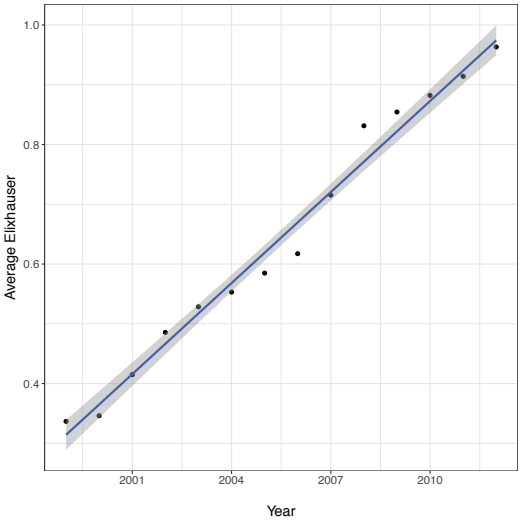
Trends in the Patient Demographics, Socio-Economic Characteristics, Surgical Factors and Outcomes between 1999–2012

In the majority of our study population the main indication for the surgery patients was primary osteoarthritis (OA) and the proportion of patients with this diagnosis increased further during the period at the expense of decreasing number of patients with inflammatory arthritis and hip fracture (Fig 8). Comorbidity and ASA scores increased for each year (Fig 9). The share of all cemented implants has dropped from 92% to 68% with a corresponding increase of all uncemented components from 2% to 16% (Fig 10). The biggest increase is in the age range 61–70 years group (Fig 11). More than 88% of the bearings were metal-on-polyethylene. Length of stay decreased by about 50% to 4.5 days in 2012 (Fig 12). The

Table 4. Example of available demographics, patient-related, surgery-related and socioeconomic data within the study database. Variables available within the different database and accessible within the linked research database (not exclusive).

Variable category	Variables
Swedish Hip Arthroplasy Register	
Demographics	age, gender, weight, height
Diagnosis & comorbidities	ICD-10 code for hip pathology, laterality, ASA classification, self-reported Charnley classification
Date of surgery	date of primary surgery &reoperation
Hospital type	hospital identifier & administrative category
Type of surgery	Primary/reoperatin/revision, THR/hemi-arthroplasty, implant characteristics/surgical approach
PROMS	preoperative EQ-5D, EQ VAS, pain VAS postoperative EQ-5D, EQ VAS, pain VAS, satisfaction VAS postoperative @ 1, 6, 10 years
Preop treatment	physiotherapy & education
National Board of Health and Welfare	
Demographics	cause and date of death
Diagnosis & comorbidities	comorbidities, Elixhauser, Charlson, data from drug and cancer register
Date of surgery	admission & discharge day, administrative category outpatient & inpatient
Hospital type	hospital identifier & administrative category outpatient & inpatient
Statistics Sweden	
Demographics	place of birth, residency, relocation, marital status, income, family circumstances, education, benefits

30-day mortality rate dropped from 0.5% to 0.4% and the 90-day mortality from 1.1% to 0.7% (Fig 13). Re-operation rate at 30 days, 90 days and 2 years decreased from 1.7% to 1.0%, 2.2 to 1.3% and 8.5 to 2.2% respectively (Fig 14). Revisions within the same time frames decreased from 1.7 to 1.0%, 2.2 to 1.3% and 3.3 to 2.0% (2010) respectively (Fig 15). The postoperative PROMs improved despite the preoperative pain scores getting worse (Fig 16–17). We can conclude that in Sweden, the demographics of the patients, the comorbidities and the primary diagnosis for surgery are changing. With regards changes in clinical practices surrounding hip replacement, Sweden has always been considered to be a very conservative country. Some changes have taken place, however, but it is unclear whether the recorded changes in practice have had any influence (positive or negative) to the outcomes such as mortality, re-operations, revisions and PROMs which have each improved during the review period.



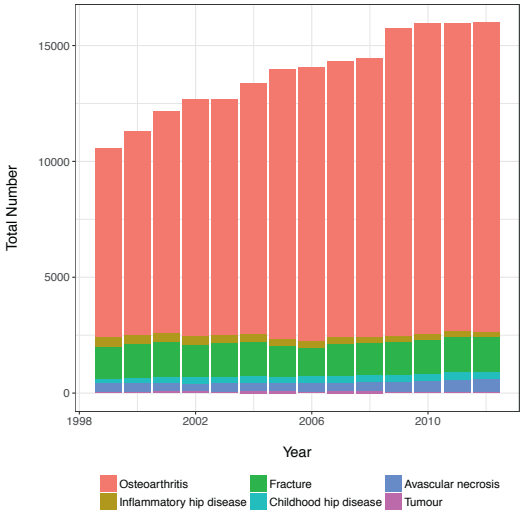


Figure 8: Trends in numbers of primary THR performed and trends in clinical diagnosis at the time of primary THR in Sweden between 1999–2012 (adapted from Cnudde et al (75))

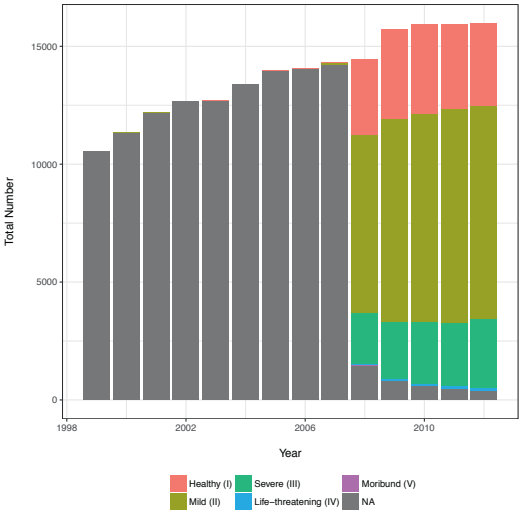


Figure 9: Trends in Elixhauser comorbidity index (A) and ASA score (B) collected preoperatively at the time of the primary THR during study period (adapted from Cnudde et al (75))

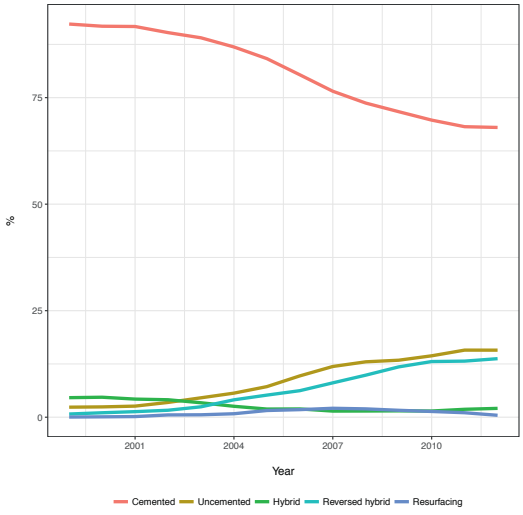


Figure 10: Trends in method of fixation for primary THR during study period (adapted from Cnudde et al (75))

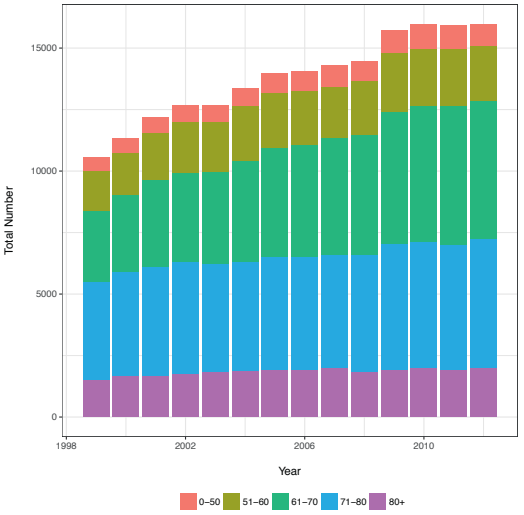


Figure 11: Age range trends of primary THR in Sweden between 1999–2012 (adapted from Cnudde et al (75))

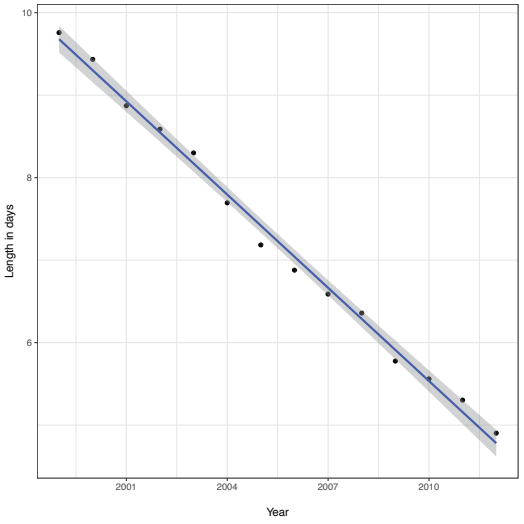


Figure 12: Trends in length of stay for primary THR in Sweden between 1999–2012 (adapted from Cnudde et al (75))

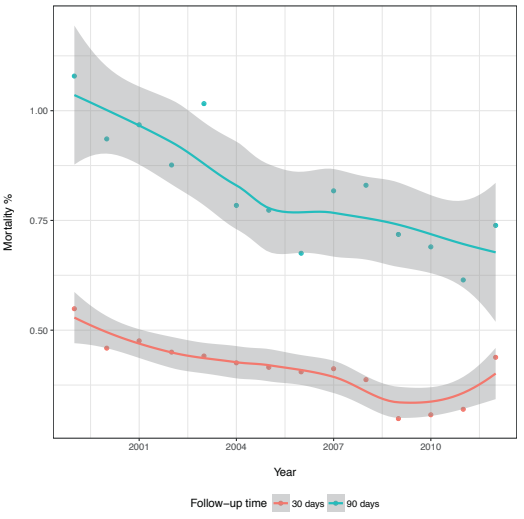


Figure 13: Trends in 30-& 90-day mortality after primary THR (adapted from Cnudde et al (75))

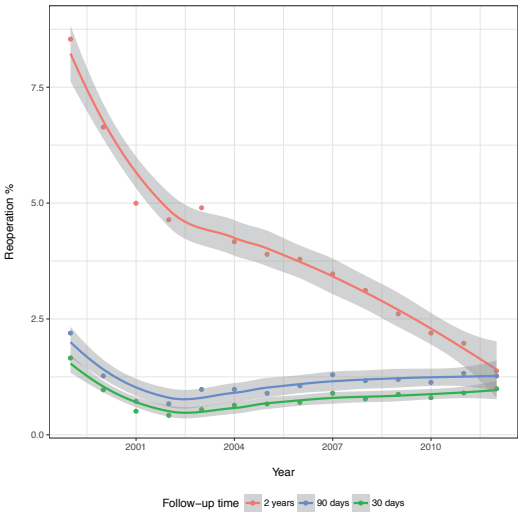


Figure 14: Re-operation trends in the first 30 days, 90 days and 2 years following primary THR (adapted from Cnudde et al (75))

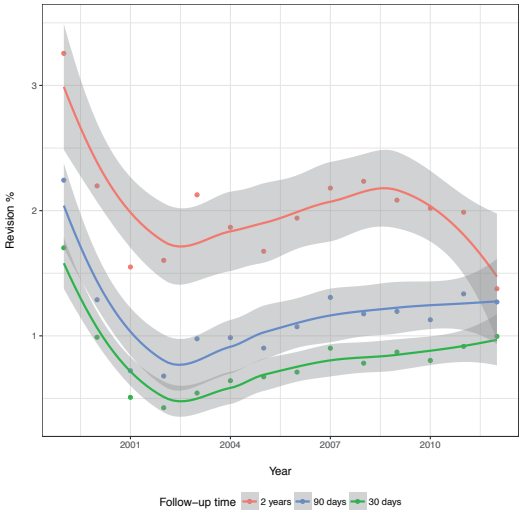


Figure 15: Revision trends in the first 30 days, 90 days and 2 years following primary THR (adapted from Cnudde et al (75))

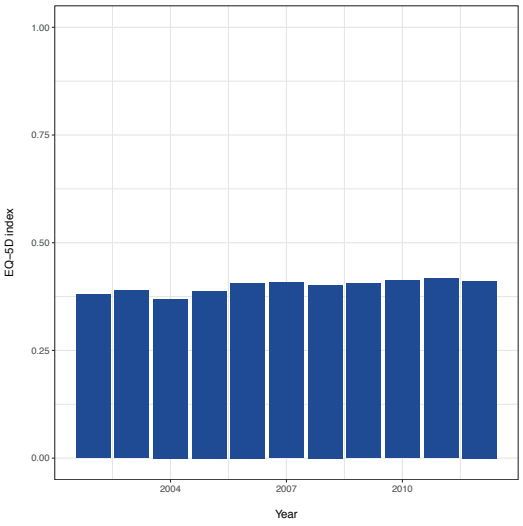


Figure 16: trends in preoperative PROMs prior to primary THR (adapted from Cnudde et al (75))

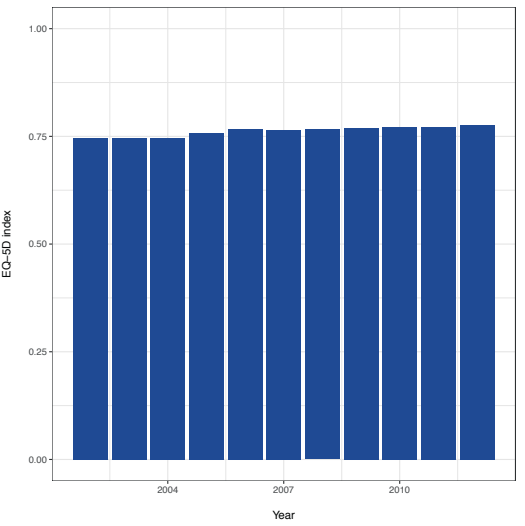


Figure 17: trends in postoperative PROMs following primary THR (adapted from Cnudde et al (75))

Paper III

Pre-operative patient-reported health status influences mortality after total hip replacement

During the study period 1,346 patients out of the 42,862 died (follow-up range 5.0 years, mean 2.4 years, SD 1.4 years). Statistically significant differences between survivors and deceased regarding sex, age at day of operation, hospital type, the five EQ-5D dimensions, the EQ VAS, the pain VAS and educational level were identified and are represented in Table 5.

The investigated cohort of patients, who underwent a THR for primary OA had a better survival than the predicted survival of the general population (Fig 18). Males had worse survival than females and it was obvious from the analysis that the 'protective effect of hip replacement on mortality' was more profound in the more advanced age group (Table 5).

Broken down by the five EQ-5D dimensions, we observed differentiated survival patterns (Fig 19). Patients who reported no problems on any of the EQ-5D dimensions had better survival than the general population and patients who reported moderate or

Table 5. Patient demographics and pre-operative health related quality of life of the cohort. The data is summarized as absolute numbers and percentages for discrete variables and means and standard deviations for continuous variables (adapted from Cnudde et al. (116)).

		Alive	Dead
		n =41 516	n=1 346
Mobility (%)	No problems	3 210 (7.7)	52 (3.9)
	Moderate problems	38 190 (92.0)	1 279 (95.0)
	Severe problems	116 (0.3)	15 (1.1)
Self-care (%)	No problems	32 066 (77.2)	910 (67.6)
	Moderate problems	9 102 (21.9)	403 (29.9)
	Severe problems	348 (0.8)	33 (2.5)
Usual activities (%)	No problems	16 086 (38.7)	460 (34.2)
	Moderate problems	21 125 (50.9)	684 (50.8)
	Severe problems	4 305 (10.4)	202 (15.0)
Pain/discomfort (%)	No problems	631 (1.5)	16 (1.2)
	Moderate problems	23 822 (57.4)	706 (52.5)
	Severe problems	17 063 (41.1)	624 (46.4)
Anxiety/depression (%)	No problems	23 963 (57.7)	711 (52.8)
	Moderate problems	16 079 (38.7)	568 (42.2)
	Severe problems	1 474 (3.6)	67 (5.0)
EQ VAS score (sd)		54.77 (22.17)	50.61 (21.76)
Pain VAS score (sd)		62.39 (15.91)	62.67 (17.34)
Females (%)		23 358 (56.3)	633 (47.0)
Age (sd)		67.70 (10.09)	75.76 (8.83)
Educational level (%)	Low	14 018 (33.8)	658 (48.9)
	Middle	17 038 (41.0)	466 (34.6)
	High	10 460 (25.2)	222 (16.5)
Hospital (%)	University	3018 (7.3)	117 (8.7)
	County	13 026 (31.4)	464 (34.5)
	Rural	17 490 (42.1)	603 (44.8)
	Private	7 982 (19.2)	162 (12.0)

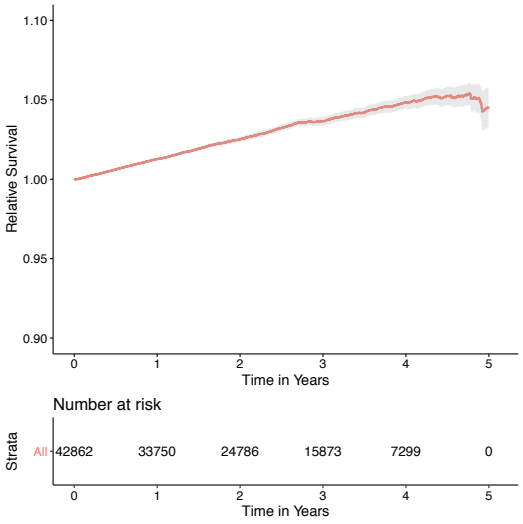


Figure 18: The relative survival of the cohort during the studyperiod (adapted from Cnudde et al (116)).

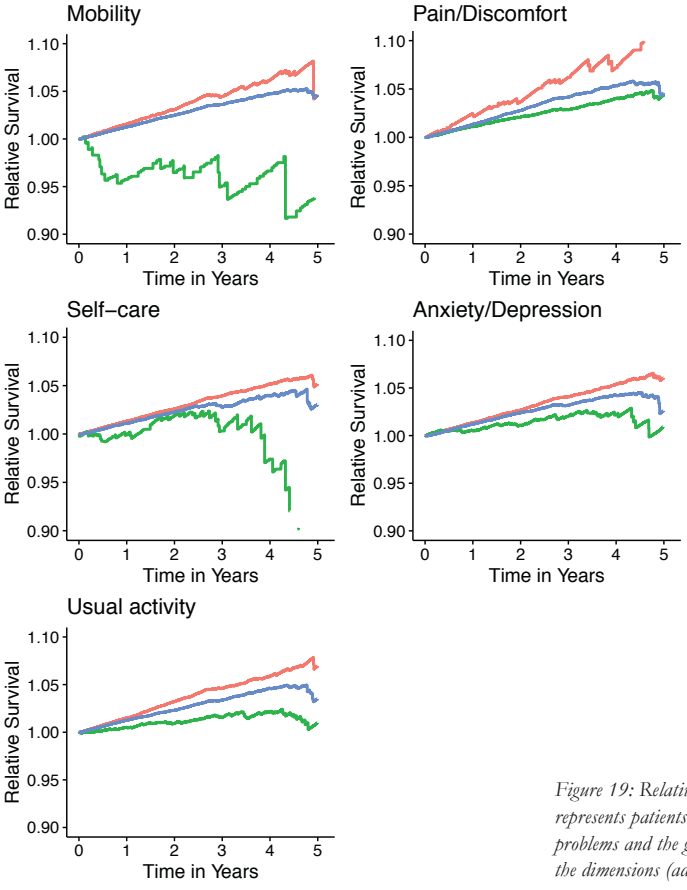


Figure 19: Relative survival by dimension of EQ-5D. The red line represents patients who report no problems, the blue line moderate problems and the green line severe problems preoperatively in each of the dimensions (adapted from Cnudde et al (116)).

severe problems. Patients who reported moderate problems on any of the EQ-5D dimensions had better survival than the general population and patients who reported severe problems. The worse the patient scored on any of the EQ-5D dimensions the higher the hazard rates of increased mortality became. Only a relatively small number of patients (131) reported severe problems on the mobility dimension but they were found to have worse survival than the general population. Patients who reported severe problems on the self-care dimension had a slight drop in survival probability straight after the operation. In the time span between one to four years after the operation these patients had better survival than the general population; after year four the survival chances worsened. Patients who reported severe problems on the dimensions pain/discomfort, usual activities and anxiety/depression had better survival than the general population. This pattern was reinforced by the multivariable regression analysis (Table 6).

Table 6. Results of the relative survival regression analysis on mortality after total hip replacement. The results are presented as Hazard Rates (HR) and associated 95 % confidence intervals (adapted from Cnudde et al. (116)).

		Hazard Rates	95 % CI
Mobility	No problems	*ref*	
	Moderate problems	1.46	1.09–1.96
	Severe problems	2.65	1.43–4.92
Self-care	No problems	*ref*	
	Moderate problems	1.15	1.01–1.31
	Severe problems	1.57	1.08–2.29
Usual activity	No problems	*ref*	
	Moderate problems	1.05	0.93–1.20
	Severe problems	1.28	1.06–1.56
Pain/discomfort	No problems	*ref*	
	Moderate problems	1.07	0.64–1.77
	Severe problems	1.20	0.71–2.00
Anxiety/depression	No problems	*ref*	
	Moderate problems	1.09	0.96–1.22
	Severe problems	1.24	0.95–1.62
EQ VAS (in units of 10)		0.95	0.92–0.98
Pain VAS (in units of 10)		0.96	0.92–1.01
Sex:	Male	*ref*	
	Female	0.86	0.76–0.96
Age:		0.96	0.95–0.97
Operation Year:		0.91	0.86–0.96
Education:	Low	ref	
	Middle	0.93	0.83–1.06
	High	0.85	0.73–1.01
Hospital:	University	*ref*	
	County	0.79	0.65–0.97
	Rural	0.81	0.67–0.99
	Private	0.72	0.56–0.91

Reviewing the EQ VAS data we also discovered an association between decreased survival and a lower patient-reported overall health. The pain VAS was neither clinically nor statistically significantly associated with a difference in survival.

We identified a trend towards better survival after THR with higher obtained educational level, but this observation did not reach statistical significance. In addition to the results in the published paper an analysis per EQ-5D profile was performed for the seven most frequent profiles and is presented in figure 20.

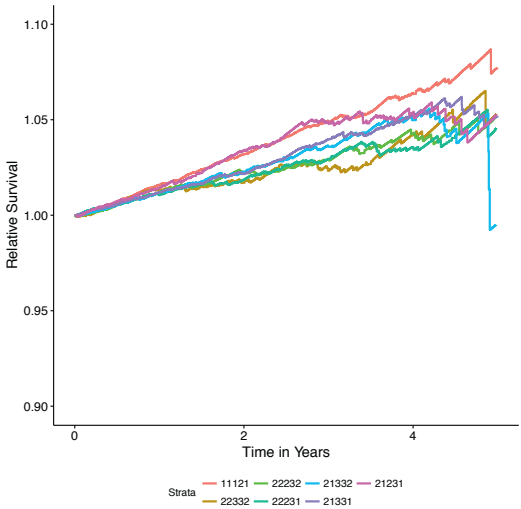


Figure 20: Relative survival for the seven most frequently observed EQ-5D profiles.

Paper IV

Relative survival following elective total hip replacement in Sweden

Between 1999 and 2012 a total of 131,808 patients underwent elective hip replacement. By the end of the follow-up period (31/12/1012) 21,755 had died. There were significant differences for most covariates considered between survivors and deceased patients and these are represented in Table 6. The maximum follow up period was up to 14 years.

In 91% of the study population the indication for hip replacement surgery was primary osteoarthritis (Table 7).

Patients with primary osteoarthritis had better survival than a matched population through the whole follow up period (Fig 21). Patients in whom the main diagnosis for surgery was a sequelae of childhood hip disorder had similar survival rate as a matched population. Patients operated because of avascular necrosis of the femoral head, inflammatory joint disease or secondary osteoarthritis following hip related trauma had a lower survival rate than a matched population. These three diagnoses had a significantly lower survival than patients with primary osteoarthritis, while no statistically significant difference was detected between sequelae childhood hip disorder and primary osteoarthritis (Fig 22).

Females had generally better survival than males. Patients operated at more advanced ages had significantly better survival than their peers of the same age from the general population. Being single or widow and having completed only lower levels of education were associated with lower survival rate. Comorbidities had a negative effect on survival. The year of operation was positively associated with survival rate. Crude and adjusted hazard ratios for the diagnosis, surgical factors, comorbidities, and SES are represented in Table 8.

The mortality after use of all cementless fixation differed from the other types of fixation (i.e., fully cemented, reversed hybrid and hybrid fixation), but the results differed depending on type of analysis employed. Uncemented THR tended to be associated with better survival with a different outcome between the Cox regression analysis, the relative survival rate and the Kaplan-Meier survival analysis (Fig 23).

Table 7. Demographics of the whole cohort, the surviving cohort, and the deceased cohort during study period 1999–2012 (adapted from CORR)

Demographics	Alive	Dead
Number	110,053	21,755
Sex = female (%)	64,228 (58)	11,807 (54)
Age (mean [SD])	66.77 (10)	75.19 (8)
Education (%)		
Low	42,147 (38)	12,591 (58)
Middle	43,330 (39)	6598 (30)
High	24,576 (22)	2566 (12)
Civil status (%)		
Couple	63,884 (58)	10,588 (49)
Single	29,471 (27)	4596 (21)
Widow	16,698 (15)	6571 (30)
Diagnosis (%)		
Primary osteoarthritis	10,1267 (92)	19,410 (89)
Inflammatory joint disease	2500 (2)	733 (3)
Sequelae of a childhood hip disorder	2811 (3)	191 (1)
Femoral head necrosis	3319 (3)	1318 (6)
Secondary osteoarthritis	156 (0)	103 (0)
Fixation (%)		
Cemented	83,644 (76)	20,698 (95)
Uncemented	13,513 (12)	361 (2)
Hybrid	3083 (3)	364 (2)
Reversed hybrid	9813 (9)	332 (2)
Elixhauser index (mean [SD])	0.57 (1)	0.73 (1)
Elixhauser index tabulated (%)		
0	69,777 (63)	12,742 (59)
1	25,094 (23)	4854 (22)
2	10,144 (9)	2469 (11)
3	5038 (5)	1690 (8)
Year of operation (mean [SD])	2006.54 (4)	2002.72 (3)
Follow-up (mean [SD])	5.96 (4)	5.64 (3)

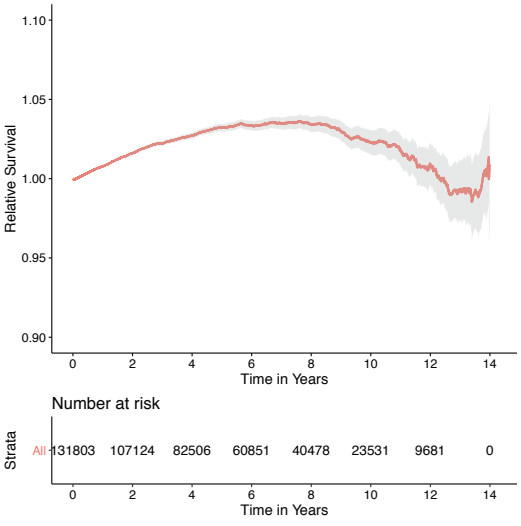


Figure 21: Relative survival curve for the complete study population (adapted from Cnudde et al. in CORR)

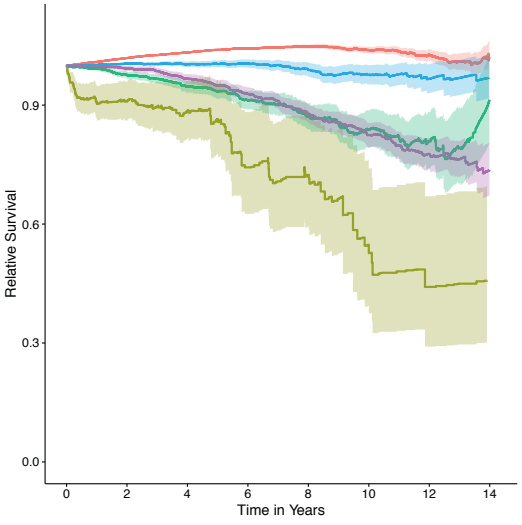
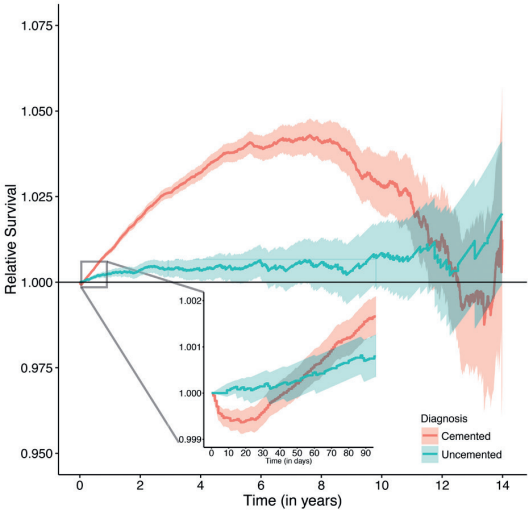


Figure 22: Relative survival curve for the study population per diagnostic indication for surgical intervention with CI (adapted from Cnudde et al. in CORR)



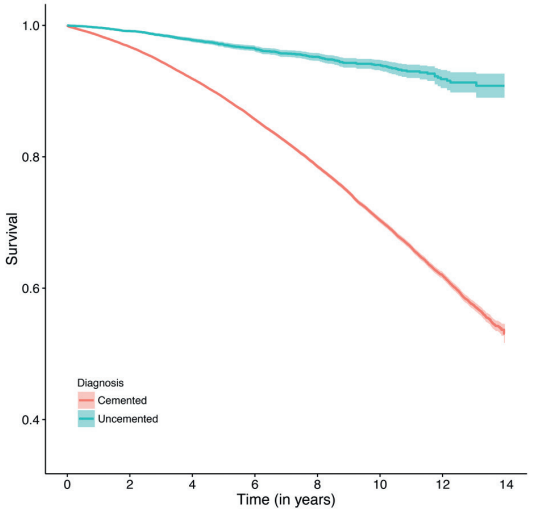


Figure 23 A&B:
A. Relative survival curve of the cemented versus the uncemented group with inset detailed analysis of the first 90 days postoperatively
B. Kaplan-Meier survival analysis of the same cohort

Table 8. Crude and adjusted hazard ratios for different variables; hip-related clinical diagnosis at the time of surgery, patient-related, surgery-related factors and SES (adapted from CORR)

			Adjusted	
Studied variables	**HR**	**95% CI**	**HR**	**95% CI**
Diagnosis				
Primary osteoarthritis			Reference	
Inflammatory joint disease	2.21	2.05–2.38	1.49	1.38–1.61
Sequelae of a childhood hip disorder	1.25	1.09–1.45	1.02	0.88–1.18
Femoral head necrosis	1.68	1.59–1.78	1.69	1.60–1.79
Secondary osteoarthritis	2.35	1.93–2.85	2.46	2.03–2.99
Sex				
Male			Reference	
Female	0.93	0.90–0.95	0.97	0.94–1.00
Age	0.96	0.96–0.97	0.96	0.96–0.96
Civil status				
Couple			Reference	
Single	1.35	1.30–1.40	1.33	1.28–1.38
Widow	0.98	0.95–1.02	1.14	1.10–1.17
Education				
Low			Reference	
Middle	0.94	0.91–0.97	0.90	0.87–0.93
High	0.79	0.76–0.83	0.76	0.73–0.80
Fixation				
Cemented			Reference	
Uncemented	1.00	0.90–1.11	0.78	0.70–0.87
Hybrid	1.27	1.15–1.41	0.93	0.83–1.03
Reversed hybrid	0.96	0.86–1.07	0.93	0.83–1.04
Year of operation	0.95	0.95–0.95	0.95	0.95–0.96
Elixhauser up to 5 years				
0			Reference	
1	1.37	1.31–1.44	1.49	1.42–1.57
2	1.79	1.69–1.90	2.07	1.95–2.20
3+	2.76	2.59–2.94	3.32	3.11–3.55
Elixhauser between 5 and 8 years				
0			Reference	
1	2.20	1.99–2.43	1.52	1.36–1.68
2	2.76	2.42–3.15	1.96	1.72–2.25
3+	3.67	3.13–4.30	2.63	2.23–3.10
Elixhauser over 8 years				
0			Reference	
1	2.62	2.36–2.92	1.33	1.18–1.49
2	3.32	2.86–3.85	1.74	1.48–2.04
3+	4.47	3.67–5.45	2.40	1.95–2.94

Paper V

Risk of further surgery on the same or opposite site or mortality after primary total hip arthroplasty. A multi-state analysis of 133,654 patients from the Swedish Hip Arthroplasty Register

The median follow-up time from the first and from the second THR until death or censoring (emigration) was respectively 5.56 years (95 % CI: 5.52–5.59) and 4.17 years (95 % CI: 4.12–4.21). Patient demographics are described in table 9.

We identified that transition probabilities and the probability of staying in a state were highly time dependent (Fig 24). Patients were twice as likely (transition ratio = 2.13, 95 % CI 2.07–2.19) to have their other hip replaced than to die during the study period. However, towards the end point of the study, probabilities were converging. A contralateral primary hip replacement was 7.5 times (95 % CI 7.31–7.89) more likely than revision of the first hip. A hip-related time line is represented in figure 25.

We calculated hazard ratios for the most frequent transitions. We identified influence of sex, indication for arthroplasty of the first hip, comorbidity, surgical approach, implant fixation, and highest level of obtained education as variables influencing transition. The influences on transitions are represented as graphs, tables and Forrest plots.

Table 9. Patient demographics of complete study group

n	133654
Age (mean (sd))	67.99 (10.87)
Sex (%)	
Male	57058 (42.7)
Female	76596 (57.3)
Diagnosis	
Primary osteoarthritis	122568 (91.7)
Inflammatory joint disease	3199 (2.4)
Sequel childhood hip disorder	3148 (2.4)
Femoral head necrosis	4735 (3.5)
Elixhauser Index (mean (sd))	0.61 (0.96)
Surgical approach	
Lateral	59355 (44.4)
Posterior	74299 (55.6)
Fixation (%)	
Cemented	104560 (78.2)
Uncemented	13500 (10.1)
Hybrid	3336 (2.5)
Reversed Hybrid	9981 (7.5)
Resurfacing	1666 (1.2)
Clinic type (%)	
University	14080 (10.5)
County	44897 (33.6)
Rural	55126 (41.2)
Private	19551 (14.6)

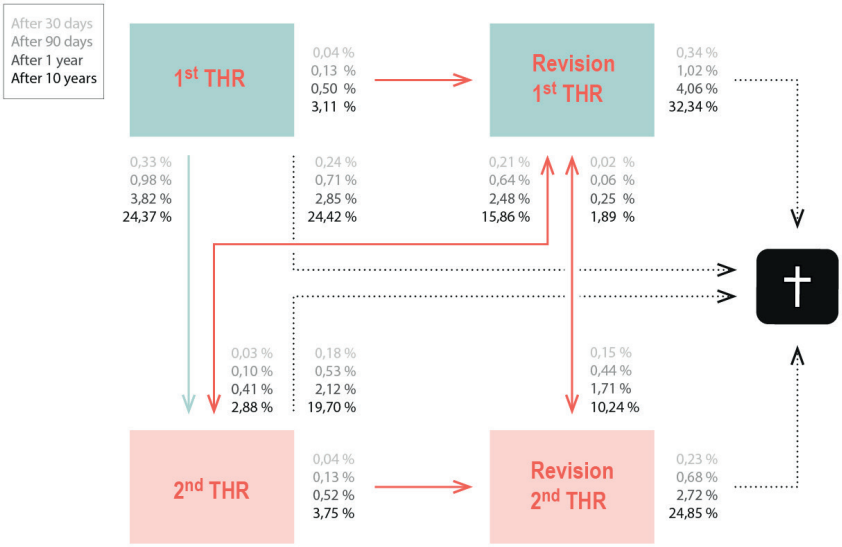


Figure 24: Multi-state analysis with transition probabilities at different times point following the first hip replacement

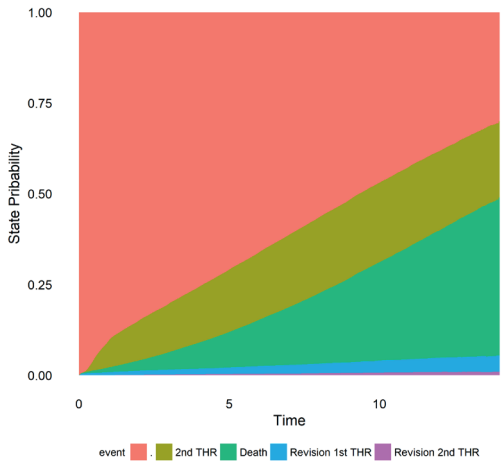


Figure 25: State occupation probabilities at different points in time during study period

Strengths, limitations and bias

Strengths

The studies are based on existing data of the research database of the SHAR and the administrative databases of the SCB and Socialstyrelsen. This has minimized time and the costs for this project. The sample size is sufficient large, containing almost all elective hip replacements performed during the study period as part of the nationwide collection of information on THR within the SHAR. The quality of observational studies depends on quality and validity, reliability, coverage and completeness of the data. The SHAR is a well-established, nationwide, prospective observational hip arthroplasty register. We are aware that the coverage (100%), completeness (98.6%) and validity of the SHAR data is extremely high and has been so during its existence (42). The population registers should cover migration and it is a requirement by law that people who move abroad for more than a year (intentional or effective) should be de-registered (93). The SHAR data has been prospectively and independently collected by the local surgeons and hospital teams and this data has then subsequently gone through a rigorous process of quality control with up to 6 different steps (table 1). The history and longevity of the SHAR makes it possible to study long-term trends and allows us to pick-up infrequent complications like early mortality. Using the amalgamation of the data sources into a single research database allows us to adjust for some confounders such as SES, comorbidity and potentially study readmissions and subsequent episodes of hospital care resulting from adverse events. For some purposes registry-based studies are more useful than traditional RCT's and the influence of the registers on the evolution of practices that improve the quality of clinical care and their contribution to value-based medicine is now considered as being reflective of real-life practice.

For ethical reasons, the research question of the third paper can only be answered using observational data. In order to answer the research question there need to be a sufficient number of "observations" to provide statistically robust evidence for whether, or not, associations exist. Besides using the STROBE (strengthening the reporting of observational studies in epidemiology) statement, we used the guidelines for reporting 'big data' as suggested by Costa et al. and were able to describe the nature of datasets, the variables and the significance of the results (Table 10) (94, 95).

Table 10. BJJ big data interim reporting guidelines and current research

Bone and Joint Journal Big Data Interim Reporting Guidelines							
	Methods						Results
	datasets				variables		significance
	purpose	data quality	denominators	linkage	code list	validation	
Paper I	National audit programme	99% see annual reports	Countrywide Swedish Population undergoing THR	V	in methods	V	not applicable
Paper II	National audit programme	99% see annual reports	Countrywide Swedish Population undergoing THR	V	in methods	V	p<0.05 clinical significance=v
Paper III	National audit programme	99% s ee annual reports	Countrywide Swedish Population undergoing THR	V	in methods	V	p<0.05 clinical significance=v
Paper IV	National audit programme	99% see annual reports	Countrywide Swedish Population undergoing THR	V	in methods	V	p<0.05 c linical significance=v
Paper V	National audit programme	99% see annual reports	Countrywide Swedish Population undergoing THR	V	in methods	V	p<0.05 clinical significance=v

Limitations

Whereas the independence of data collectors can be seen as an advantage and a form of objectivity, the diligence applied to produce accurate coding will vary between the different systems. The quality of the data can however be subjected to a 6-step verification process.

It will be unavoidable that there will be some missing data: some citizens fail to deregister and it is estimated that there is an over-coverage of 0.1% for Nordic citizens, but this might well be higher for other groups (93). Further analysis of the official data shows that emigration of Scandinavian residents out of Sweden is extremely low and previous work from the register has revealed that the uptake of arthroplasty in the migrant population is extremely low. In common with other Western European countries with accessible health services there is the possibility of health tourism and this cannot be accounted for. We are aware that a number of revisions will not be recorded and this has been described in previous work. Reoperations for infections as well as open reduction and internal fixation of periprosthetic fractures are not routinely recorded in most registers and studies of the SHAR have confirmed poor reporting of these procedures (96, 97). Lindgren et al. validated reoperations for infections using a combination of patient records, the Swedish Drug Prescription Register (SDPR) and found a completeness of 67% of the reoperations for infection (96). It is likely that with the updated guidelines and principles of debridement, antibiotics and implant retention (DAIR) with exchange of femoral heads and liners, the recording of implant infection has become more accurate. Chatziagorou et al. performed a linkage study between the SHAR data and the NPR and were able to demonstrate that 32% of the periprosthetic fractures have not been recorded in the SHAR (98). In the case of revisions or failures for infection, patients might not have had operations; they may remain under observation on long-term suppression therapy. In addition episodes of surgery might not be recorded or patients may undergo a surgical procedure without exchange of implants with no record of the intervention.

Our studies have purposely excluded patients with simultaneous bilateral procedures, Although bilateral operation are infrequently undertaken within Sweden, the results may be influenced by eliminating these cases from the study population. There is an evolution in minimum data set requirements within registers with the passage of time (42). Some of the data, now routinely collected, such as BMI and ASA grade was not available in earlier sets of registry data. Using cross-tabulation we have encounters a few cases of revisions where the data recorded pathways that were not possible. A few of the PIN's might have been re-assigned and have led to some erratic results. Cases were removed from the analysis where nonsensical results were identified (for example dying prior to revision).

In the case of register studies there is a theoretical risk of data mining. This analysis has been performed using well-defined and rigorous study questions/hypotheses and data mining (or dredging) was avoided. When analyses delivered findings of statistical significance but doubtful clinical relevance these findings are clearly discussed. Throughout the study results were interpreted by practicing clinicians.

The length of follow-up is clearly important when interpreting the data. Interventions are taking place at a younger age and with increasing life expectancy the time-in-situ of the implant is increasing exposing the implant to an increased potential from complications. The life-time risk for revision might well have to be adapted and the strength of evidence might only be valid on the implants and techniques studied (99). Outcomes are associated with the implants and technologies that were used at the time point of the intervention and many changes have taken place with the passage of time such as the introduction of highly cross-linked poly-ethylene, the routine use of bigger femoral heads, small changes in implant geometry and extension of the range of implants assuming equivalence of outcome with the newer prostheses.

For socio-economic status we are aware that multiple variables can be identified as determining the SES. Examples are household and individual income as well as education level and occupation. The database records many of these variables but based on previous work the decision was made to use highest level of recorded educational achievement, categorized in 3 levels, as a marker for SES. It is possible that the influence of SES on outcome might not be comprehensively described as a result of this decision (100–102).

Bias and register-based research

Bias has been described as deviation from the truth/any factor that tends to deviate the results or the conclusions of study systematically away from the truth. Bozic et al state in their "Orthopaedic Healthcare worldwide"

column that any form of bias that leads to erroneous conclusions must always be taken into account whatever the size of the data (65). I used some background reading on bias and register studies to identify and explain some potential sources of bias related to register studies (Table 11) that may apply to the studies in these papers are discussed (103–106)(http://methods.cochrane.org/bias/assessing-risk-bias-included-studies).

Selection bias

Bias may be caused by analysing a study population that is different and not representative of the overall population. The chance of selection bias within cohort studies is small but exists. Whilst selection bias is reported to be less of a problem in register type studies based on a national surveillance program, it is well known that some patients will not be offered arthroplasty surgery because of medical comorbidities. Such a selection process is unavoidable and even in a well-designed RCT this group of patients will be excluded and subject to allocation bias.

The patient's idea of success does not always correlate with what the surgeon believes is a good outcome. Not all implants that fail on clinical or radiological criteria go on to a revision procedure. Some patients will not be willing to go through a further intervention. On occasion the surgeon may advise that the risk/benefit ratio is not in favour of revision surgery on the grounds of complexity or patient-related factors. Outcomes in the private sector are likely to be influenced by cherry-picking.

It needs to be understood that the selection process in offering revision surgery is usually based on a multidisciplinary discussion between different health-care professionals. With an extremely high rate of case follow-up and data completeness selection bias should not be considered an issue.

Performance bias

Performance bias results from differences that may occur in the quality of care provided to the participants in the study. The design of register-based research largely avoids performance bias as there is unlikely to be a systematic allocation of better surgical skilled surgeons for one group, compared to another. We are unable to assess the differences in quality of care provided by the different providers. However, we are confident that the quality of the care in the different hospitals is comparable, as can be seen in the clinical value compasses of the different hospitals. The implant selection will, however, be based on personal preference. Blinding is impossible in register-based studies, all patients have received the studied intervention. There will be a difference in quality of care provided between surgeons, hospitals and regions. As the data is collected prospectively and nationwide, the data should be a true reflection of the real world.

Detection bias

There is the potential for artifact in studies, which can result from the use of poorly validated outcome measures, not collecting the data correctly or under diagnosing adverse outcomes. The outcomes applied in these studies are well-validated and objective measurements of the results of treatments. There are potential issues with coding and that is inherent in the system. With regards to comorbidity, individuals who have no contacts with healthcare would score 0 on the

Table 11. Types of bias in register-based research

Bias	Risk in register-based studies	How to avoid
Selection bias	minimal	nationwide collection
Performance bias	minimal	all surgeons/all hospitals
Detection bias	existing	combination SHAR/NPR Validated outcome measures
Attrition bias	minimal	Limit loss to follow-up minimize missing data Analysis of excluded patients/flowcharts
Reporting bias	existing	research plan no data mining
Other Bias Misclassification	existing	unavoidable to a certain extent

comorbidity indices, but are they really healthy? A review of the patients was undertaken, studying the difference in survival between patients with and without hospital visits prior to THR and we found that people without recorded hospital visits during the year preceding the intervention had a better survival than the patients who had a contact with the secondary care but scored 0. As already mentioned earlier some mortality and revisions for infection/periprosthetic fractures might not be recorded in case of emigration.

Attrition bias

If there is a loss of participants, attrition bias occurs as the results in subjects that did not run to completion are discounted. Given the nationwide set up of the SHAR and the strong linkage that can be made with other governmental organizations, we are sure we are able to track the Swedish population thereby accurately describe the longitudinal outcome. There are no systematic differences in the patients included or excluded from the studies. We have on several occasions studied the outcomes of patients that were omitted as part of missing data. Flowcharts were used to clearly identify patient groups that were not studied. Patients who are not returning PROMs questionnaires might be poorly performing and this subgroup has been studied before.

Reporting bias

Bias may be caused by intentionally and selectively revealing or suppressing information. We have attempted to avoid this as all the studied material and the research questions have been answered whether or not the findings reveal statistical or clinical significance.

Other bias

Misclassification bias is something that could well be possible as the difference between primary and sequelae of childhood diseases is not always clear cut (107).

Ethical Considerations

The general public and patients expect the medical profession to uphold standards in healthcare, originally described in the 'Oath of Hippocrates' and subsequently adapted in different legislations and guidance from national medical councils. As practitioners of the 'art of medicine', it is adamant that the "*primum non nocere*" principle is central in all our activities, whether it is clinical practice, research or our day-to-day life. The declaration of Helsinki, developed and updated regularly by the World Medical Association (WMA) has reiterated this necessity of the "first do no harm" principle (108).

There is near universal acceptance in Scandinavia of the need for research and development in healthcare. Good epidemiological research in Sweden and the Nordic countries is facilitated by the way healthcare is organised and delivered for its population and by the structure of the nationwide registries. This is further enhanced by the trust of the population in research and development, the universal acceptance and overarching social equality. Of fundamental importance in identifying and tracking the population is the adaptation of an unique and universal personal identifier (109). Using the Personal Identity Number (PIN) the databases were merged providing a combination of both surgical-specific data, general medical data consisting of previous medical history and postoperative surgical events, contacts with healthcare providers, medication usage and socio-economic data (74). The data is safely stored on encrypted servers and the PIN has been removed and replaced by a unique identifier without any connection to the PIN (Fig 3)(109). Data is thereby "pseudonymised" and the unwarranted re-identification of data prevented. This research project, based and reliant on the merger of the databases of the SHAR, Statistics Sweden and the National Board for Health and Welfare, has been and will be subjected to the legislation and ethical principles of Sweden, the European Union and the WMA (64). The potential harm to the individual patient is, as a result, minimized as researchers are unable to identify individual patients because the unique personal identifiers (PIN) have been replaced by different identifiers (a number between 1 and infinity) and the PIN's are not in the possession of the research team. This makes the research compliant with the ethical principles for medical research involving human subjects (WMA) and the Swedish Personal Data Act (1998) and Swedish Patient Data Law (2009). Besides all the above efforts there are further clear warnings to make sure that patients' privacy as well as their health information should be protected and respected (65).

Register-based research does not need written consent from participants. For reasons of public interest both the EU (EU directive on Data Protection 95/46) as well as the Swedish Legislation allow the use of personal data for research purposes to be used with consent from the participating individual, if it has been obtained or without consent if the data is processed anonymously or in a key–coded form. Getting consent for data-collection and its subsequent use in scientific research would be practically infeasible and uneconomical. This deviation from the informed consent regulation is based on the judgment that doing good, justice and solidarity outweigh the risks of harm and autonomy (35). Also in accordance to the Swedish Patient Act (2008:355) patients receive information about being registered and have a full right to opt out. During the 35 years history of SHAR, few patients have applied to see their data and only two have decided to opt-out. The linking process and the current project was granted ethical approval from the medical division of the regional ethical committee in Gothenburg under the Dnr 271-14.

In 2014 Benson et al described the ethical standards we, as orthopaedic surgeons, should adhere to and stated that treatment should be offered on the best available evidence (110). Whereas there have been great advances in the past, the introduction of some newer implants and some modifications to clinical practice and have not resulted in an improved outcome, but have actually caused patients harm and have blemished the orthopaedic profession (111). Deeper analysis could well expose a lack of ethical principles and scientific evidence in the development of the newer technologies (112, 113). In absence of well-enough designed and powered RCT's in orthopaedics, register studies have been considered an extremely valid alternative (52, 55, 60, 112, 114). The proven benefits for the patients are an improved healthcare and a reduction in potential harm. As a consequence, many Western countries have subsequently endorsed joint replacement registers (72, 115). The relative low revision rate of THRs in Sweden (compared to USA/UK/Australia) has been attributed partially to a well-functioning and validated SHAR, with

engagement of the population, clinicians, the decision-makers and the Swedish Orthopaedic Association.

The effect of preoperative self-reported health on mortality could in theory lead to an ethical dilemma. The association between decreased preoperative mobility and self-care and higher postoperative mortality may make healthcare professionals reconsider the value of the procedure in this patient population (116). In this case, the evidence is based on an observational study using registry data. However, the set-up of an appropriately powered RCT to confirm the findings of this analysis would in my view be unethical. The intervention, whilst it has a risk to life, should be offered to a patient in a joint decision-making process allowing the possibility to deliver a reduction of pain, improved mobility and thereby an improvement in the quality of life. The increased mortality risk is certainly something the surgical teams will have to discuss prior to the surgery, so the patient can make a well-informed and balanced decision. The paper on the association between preoperative patient-reported health status and mortality after THR should in no way be used to deter surgeons providing patients with a life-changing operation, but has to be used to assess and discuss risks at an individual patient level as part of an informed, joint decision-making process (116).

The operation of total hip replacement, described as "the operation of the 21st century", has delivered benefit to millions of patients and has been deemed to be extremely cost-effective (11, 12). It is anticipated that further improvements of PROMs is unlikely to be delivered by further improvisation with implants but will probably result from making sure the right operation is performed for the right patient at the right time (112). If healthcare professionals and patients are able to make these decisions using the information available and analysed in a structured and a safe way then this can be seen as of huge benefit for the not only the individual patient but also the society. The cost of dealing with postoperative adverse events or complications can outstrip the cost of the primary intervention. If we can avoid sentiments such as "all surgery was necessary with exception of the initial intervention", reducing harm as a result of a shared decision-making tool based on the results of the research based on well validated studies then both the individual as well as the society can be considered winners and can be considered a victory for ethical driven research and innovation.

Discussion

Total hip replacement

One in four people are predicted to suffer from symptomatic hip OA in at least one joint by the time they reach 85. In addition, today's expectations and demands to remain living a painfree and mobile life is making it clear that there will be an ongoing reliance on hip replacement surgery for the foreseeable future (1). Different outcomes following hip replacements are possible and unfortunately surgical teams are not always able to match patients' expectations and deliver the surgical ideal and outcome aimed for (24, 117). A well-functioning, everlasting and painless artificial joint, without risk to life and health would be an ideal outcome but it is obvious that this ideal, with a "forgotten hip" (118), cannot always be achieved. Potential unsatisfactory outcomes are perioperative or premature death, adverse events, re-admissions, revisions and other types of re-operations. These unplanned events occur in a minority of patients. Poor patient-reported outcome scores are more likely to occur and patient's expectations are not matched. Despite advances in technology and the utilization of newer implants, improved technology, the use of navigation, patient-specific instrumentation (PSI) and robotics the outcomes of joint replacements might not have improved as much as expected and its clinical benefits still need to be evaluated (111, 119–123).

Revisions and re-operations come at a huge expense for the patient both from a financial point of view as well as suffering. Revisions carry a further risk of subsequent revisions and reoperations. The implant survival is considerably lower in multiply revised joints than primary or first revisions procedures and in many cases the operations are performed for the same reasons as the original revision (124). PROMs are significantly worse following subsequent operations and there is higher inherent 30-and 90- day mortality after a revision procedure. It additionally places a tremendous burden on the provision of healthcare and comes at a huge cost for the society. The mean cost of a revision has been estimated in the USA as $ 77,851 (125). With an increase in demand, an ageing population with increased comorbidities, increased life expectancy, and higher expectations at the time of both primaries and revision procedures, mechanisms to mitigate future revision procedures must be explored.

Registers and linkage

In the initial phases this project has been concentrating on the development and the fine-tuning of the tools to investigate the longitudinal outcome, i.e. the theme of this research. The work describing the merger of the SHAR databases with the different administrative databases of the different government organisations into a single research database was published in BMC musculoskeletal medicine (64). It was obvious from previous work that there was a need to include socio-economic factors, patient-related factors as well as surgical-related factors when analyzing potential outcomes following THR and the advantages of a linked research database was the obvious solution.

Berry describes in his annotation titled "Joint Registries, what can we learn in 2016" that registries can provide the orthopaedic community with a real-time observation of changes in practice (49). In our trends work we have identified some changes in practice during the study period. Whilst Sweden has always been conservative in implant choice and has embraced "the stepwise introduction" of new technologies and techniques, there has been a change in implant choice towards a 32 mm headsize, an increased use of highly cross-linked poly-ethylene, and a move towards uncemented implants, especially in the younger population group. An important change in indication for surgery has been identified with a trend towards operating on younger, more obese and less healthy patients. Despite these challenges and the changes the long-term outcome seems to be further improving with a reduction in early postoperative mortality, a significant decrease in 2-year reoperation and revision rate. There seems to be however an increase in short term (30 and 90-day) re-operation and revision rate and that should be the subject of a further in-depth investigation to ascertain the cause(s). The increase in early revisions within Sweden is in agreement with the study of Pedersen and Thiens using the NARA database (126, 127). This increase in early reoperation and revision rate and its potential important impact on lifetime health risk will need to be further studied. The importance of cross-referencing data between registries for validation has been suggested (49). Whether or not the increase in early reoperation and revision rate is solely associated with the increased use of uncemented implants and the increased risk of early (intraoperative)

periprosthetic fractures and the tendency of dealing with early prosthetic joint infections surgically will have to be confirmed, but currently this is considered to be the most likely explanation.

We have identified an increasing satisfaction as measured with postoperative PROMs. This a very positive development and likely caused by improvements in surgical techniques, changes in perioperative care with increased attention to preoperative patient education and ability to manage patient expectations.

Mortality and relative survival

Whilst death is extremely rare (<0.4%) within the first 30 days after surgery and the overall mortality rates are improving, it is still important to consider this outcome in both primary as well as revision surgery. We are aware of the effects of comorbidity, as measured by presence or absence of comorbidity, ASA scores, or comorbidity indices, on peri- and postoperative mortality. With an increased attention to self-rated health, these measures could well be useful in predicting mortality. The feasibility and usability of PROMs in the preoperative setting seem to be gaining momentum and are now part of the routine preoperative assessment in Sweden (128, 129). The association between the risk of dying in the postoperative period (up to 5 years postoperative) and the prospectively collected PROMs (EQ-5D, EQ VAS and pain VAS) at the time of surgical work-up, can be used in the preoperative discussion with patients and has got implications in the decision-making process. It was evident from the analysis that patients who report poor mobility and/or who are struggling with self-care are at an increased risk of dying following the surgery. Whilst we suggest there is an association between preoperatively recorded PROMs and mortality it would probably need a randomized controlled trial (RCT) to prove causation. This however could be considered to be an impossible undertaking and could even be considered unethical. The main reasons to offer patients a new hip are to provide them with an improved mobility and improved quality of life as well as the reduction of pain. Denying patients potentially life-changing surgery on the basis of reduced mobility would be counterintuitive. I do believe it is however important to discuss the increased risk of death with the patient in the preoperative setting and it might be important for the health care decision makers to recognize that besides the fact there is an increased cost to the patient and the society of waiting for surgery, a further deterioration of the mobility might impact on the changes of survival following surgery.

We also confirmed the diagnosis-specific differentiation of relative survival rates following total hip replacement. Patients with primary osteoarthritis as the main indication for their THR have a higher survival rate compared to other diagnoses and the survival rate is also significantly higher than the general population during our studied time period. Patients who underwent total hip replacement due to sequelae of a childhood hip disorder have similar survival rate to the general population while patients with femoral head necrosis, inflammatory joint disease and trauma induced secondary osteoarthritis had significantly lower relative survival rates. With exception of a non-significant difference in survival rate in patients undergoing a THR for sequelae of childhood diseases, our findings are in line with the findings of Lie et al. (130). A recent analysis using Danish healthcare registers have identified an increased risk of dying of patients with RA undergoing THR, compared to patients with OA (131). Of the studied fixation techniques cemented, hybrid and reverse hybrid had similar survival rate. Patients with uncemented prosthesis had a better survival. This finding requires some caution as the average age for patients with cemented prosthesis was 70 years while patients where an uncemented implant was used were on average 55 at the time of their primary operation. Whilst we have attempted to adjust for age this can be considered difficult as such differences cannot be easily and correctly adjusted, because of the excessive difference in mean age at the time of surgery. The difference between the regression analysis, the Kaplan-Meier survival graph and the relative survival rate have confirmed our suspicions that the age at the time of surgery could well have a bigger influence. If one would only study the relative survival graph it would be tempting to think that cement has a protective effect after the initial period of excess mortality, but this is likely due to increased effect of patient selection in the older age group. The increased mortality in the early postoperative period in the patients receiving a cemented implant has once again been demonstrated but is reversed between 50 and 60 days. This finding has been studied in more detail by Garland et al using a different cohort of patients with an excess mortality in the early postoperative period when cemented stems were used (132). A more detailed study on the effects of fixation on reoperation, revision and mortality might well be necessary to provide the necessary answers to this question. However it is unclear whether or not the final answer will ever be clear. Osteoporosis has been considered a powerful predictor of life expectancy (133, 134). There is the profound effect of selection bias related to bone condition and physiological age which cannot be controlled for.

Multi-state analysis

Using the MS analysis and after adjustment we have to contradict some studies on the effect of approach on mortality and revision risk (135, 136). We found there was no influence of the approach on the risk of dying or revision surgery at 1 or 10 years. For this study we did not take the PROMs into consideration and we are well aware of some studies highlighting improved PROMs with a posterior approach at short and long term.

We found that having lower completed levels of education and being widow or single had an adverse effect on survival. The effect of socioeconomic factors have been long recognised (137). A recent study concluded that mortality, attributable to lower levels of completed education, is comparable in magnitude to mortality attributable to individuals being current rather than former smokers and the association between education and mortality could be causal (138). Likewise it is well known that widowers have higher mortality rates than married people (139) and that married people have a longer life expectancy, compared with unmarried persons (140, 141).

As expected the higher a patient scored on the ECI the stronger the association with mortality becomes. The ECI ranks highest among different comorbidity indices that have the ability to predict long term mortality (142). In a different study from looking at the predictive value of comorbidity indices however we found that the predictive value of the indices was poor and less good than age and sex (143).

Interpretation and ramifications

The results of the present study, based on a nationwide prospective collection of data can largely uphold the findings in the literature and the perception of clinicians. Namely, that total hip replacement patients have a better survival that the general population. A common reasoning behind this is the patient selection and perioperative work-up. Generally in order to have a hip replacement surgery patient need to be in good health or will have some measures to improve their health status as part of their perioperative work-up for surgery.

I have been able to establish that the principal diagnosis for performing the surgery influences the relative survival. However there is no information about mortality in these patient groups, should they not undergo a total hip replacement.

So far I believe we will be able to use this high quality and validated data to provide some answers to questions of longevity and complications. Further and ongoing analysis will in my view be able to provide answers towards "the million dollar question" of providing the right implant and surgical intervention for the right patient in the right setting at the right time and the development of a SDM tool.

In view of the anticipated increase in demand of hip replacement surgery due to the increased global burden of hip OA it will become more than ever necessary to be able to use the surgical and financial resources wisely to the benefit of the patients with painful hips, a decreased mobility and a poor quality of life caused by an intrinsic hip problem.

Despite all the information available in this dissertation and the literature the decision to proceed or not to proceed with joint replacement surgery should not be taken lightly and only on the basis of the patient preferences and following an assessment of the balance between benefits and potential risks or complications (144, 145). The results of my research illustrate the possible pathways and risks associated with hip replacement surgery. These pathways and the factors influencing the outcome have, in my opinion, been presented in a comprehensive and pedagogic way. The information and the way this information is graphically represented, could be helpful for clinicians, patients and their interactions. It is recognized that a joint replacement usually is a life-changing procedure. If performed on the right patient with the right expectations, for the right reasons, in the right setting with the right implant and technique it is extremely likely to be successful in the long-term.

Conclusions

I Combining administrative databases with the SHAR database is possible and provides variables not routinely collected in the arthroplasty registers.

II Despite the changes in patient-related characteristics and changes in surgical techniques, the outcomes of THR (mortality, revision rate, PROMs) are improving.

III Worse preoperative patient-reported health status is associated with an increased mortality up to 5 years post surgery.

IV Hip replacement patients, who underwent their surgery electively and because of primary OA, have an overall improved relative survival rate compared to a birth year- and sex-matched population and a low risk for revision.

V Multi-state analysis allows us to depict the hip-related timeline for patients undergoing elective surgery. The contralateral operation is the most likely next state and is seven times more likely than a revision procedure.

Future and ongoing projects

I anticipate some further research into the identification of patients undergoing multiple revisions as well as extending the length of follow-up far beyond the current maximum of up to14 years. With an ageing population and a trends towards surgery at younger age, it is imperative to extend the follow-up period and analyse the outcomes of hip replacement surgery well into the second and third decade.

The four most common reasons for reoperations/revisions following surgery are mainly aseptic loosening, dislocation/instability, infection, and periprosthetic fracture. It is necessary to explore whether there is an increased risk of unsatisfactory outcomes and further contacts with the healthcare providers as a result of the reoperation/revision for similar or different reasons than the reason of failure of the implant at the time of first revision. Despite the anticipation that the information about (re-)revisions following aseptic loosening is likely to be complete and relatively accurate, there is an awareness of incomplete data for subsequent operations for dislocation/instability as closed reductions will not necessarily be recorded in the SHAR. This is also the case for surgical treatment for infections and periprosthetic fractures as some of these interventions are not recorded in the SHAR databases especially if no exchange of components has taken place. Despite all the efforts from the team at SHAR, we realize that no complete information is available for patients undergoing further surgery within SHAR for the above reasons but the information might well be obtained using the linked database and patient from the NPR. Identifying the right codes for readmissions and adverse events and when and if necessary analyzing the patients notes retrospectively might well be providing the right answer and providing a more detailed and accurate picture of the problems of adverse events and readmissions not necessitating exchange of implanted components.

The effect of comorbidity like diabetes, inflammatory arthritis, and specific neurological diseases, such as epilepsy and Parkinson's disease on outcomes following THR deserves a further investigation if we want to provide the patient with the right information prior to surgery. Identification of these patients within the database has been proven to be possible and is underway. Currently we are analyzing and discussing the different methods to perform an in-depth analysis such as exact matching, propensity score matching or we could revert as in paper V to a MS analysis, using only the selected cohort of patients.

In this thesis we have concentrated on THR for elective reasons, however the SHAR there is a wealth of information on hip replacement surgery for hip fractures. Multi-state analysis techniques could be used to study the effect of (early) revision or reoperation on mortality in this patient group. In a next phase I would like to study the impact of neurologic diseases on outcomes of hip replacement surgery following hip fracture as it is anticipated there could well be an increase patients suffering from neurological conditions (for example Parkinson's disease, dementia) fracturing their hip and needing acute surgery. I believe that avoiding complications and reoperations might even be more important in these frail patients, presenting with an acute hip fracture.

The effect of fixation of the femoral implants on the early mortality has been investigated in great detail. It is known that cementing the femoral component might be protective of revision surgery on the short term. However further long term studies are necessary to understand to complete impact of early revisions in the case of periprosthetic fractures and the risk of late periprosthetic fractures in the ageing population at risk of developing osteoporotic fractures.

Summary in English

Longitudinal outcomes following total hip replacement

Time trends, sequence of events and study of factors influencing implant survival and mortality

Osteoarthritis of the hip is a common debilitating and symptomatic joint disease. The disabling symptoms can be successfully treated with a total hip replacement (THR). It is known that the majority of patients are doing well following surgery, however some patients will need further surgery on the same or on the other hip or die prematurely in the perioperative period. The causes leading to further surgery for patients and mortality are multifactorial. The following are important factors in defining the risk for an individual patient: indication for surgery, complexity of operation, patient age, medical comorbidities, physical activity and socio-economic factors, types of implants used, surgical techniques employed, as well as perioperative protocols and post-operative treatment.

The research questions for this project were:

1. Has there been a change in patient-related, surgery-related and socioeconomic factors in patients undergoing elective hip replacements and have the various outcome parameters evolved?
2. Is there an association between self-reported health status and mortality following elective hip replacement?
3. Have patients who underwent THR a better relative survival than the general survival and is this influenced by the diagnosis for which the THR was undertaken?
4. What is the long-term risk of subsequent surgery on the same or the opposite hip and risk of mortality after an elective primary THR? Is there an influence of patient-related, surgery-related and socio-economic factors on subsequent surgery and dying?

Patient level data concerning many of these factors are available in the Swedish Hip Arthroplasty Register and administrative databases of the National Board of Health and Welfare and Statistics Sweden. This information was linked into a single research database. The principles of relative survival analysis and multi-state analysis with multivariable regression for statistical analysis were used. We decided to study patients undergoing elective THR between 01/01/1999 and 31/12/2012.

Most patients were operated on because of primary osteoarthritis and this share increased further during the period at the expense of decreasing number of patients with inflammatory OA and hip fracture. The practice of elective THR has changed during the study-period, however despite these changes there has been a reduction in 30- and 90-day mortality, an overall improvement of revision rates and patients have reported improved satisfaction and outcomes. Worse health status according to the EQ-5D before THR was associated with higher mortality up to five years after surgery. Patients with a THR had an improved relative survival compared to an age- and sex-matched population. There was a diagnosis-specific differentiation of relative survival rates in favor of patients with hip osteoarthritis. Higher Elixhauser comorbidity index, level of education and being a widow(er) or single, had an adverse effect on survival. The lifetime risk for bilateral surgery, revision and death was identified using the longitudinally collected data.

Despite some changes in practice, the long-term outcome following THR has improved. A worse self-reported health status is associated with increased mortality in the medium-term. Overall patients, undergoing an elective THR will have a better relative survival and a low risk of revision. The risk of receiving further surgery on the same or on the other hip is multifactorial, and patients are twice as likely to have their other hip replaced than to die during the study-period. Replacing the contralateral hip is seven times more likely than a revision procedure on the first implanted hip.

Summary in Swedish

Långsiktiga resultat efter total höftprotesoperation

Tidstrender, händelsernas sekvens och studie av faktorer som påverkar implantatöverlevnad och mortalitet

Höftartros är en vanligt förekommande ledsjukdom som förorsakar smärta och nedsatt funktion. Symptomen kan framgångsrikt behandlas med total höftprotesoperation. För majoriteten har operationen avsedd effekt men vissa patienter behöver opereras om i samma höft eller på andra sidan eller dö i förtid under i samband med operationen. Det finns flera orsaker till varför man kan behöva en ytterligare operation. Viktiga riskfaktorer är: bakomliggande ledsjukdom, operationens svårighetsgrad, aktivitetsgrad, socioekonomiska faktorer, vilka implantat som använts, kirurgisk teknik samt vårdprocesser och rehabilitering i samband med operationen.

Forskningsfrågeställningarna i den här avhandlingen var:

1. Har det skett någon förändring i patientrelaterade, socioekonomiska eller kirurgiska faktorer bland patienter som genomgått planerad total höftprotesoperation och hur har utfallsparametrarna förändrats?
2. Finns det något samband mellan patientrapporterade utfallsmått och dödlighet efter planerad total höftprotesoperation bättre överlevnad än patienter?
3. Har patienter som genomgått planerad total höftprotesoperation bättre överlevnad än normalbefolkningen?
4. Vilken är långtidsrisken för om operation på samma sida eller operation på andra sidan efter planerad total höftprotesoperation? Hur påverkar patientrelaterade, kirurgiska och socioekonomiska faktorer risken för ytterligare operationer eller att dö.

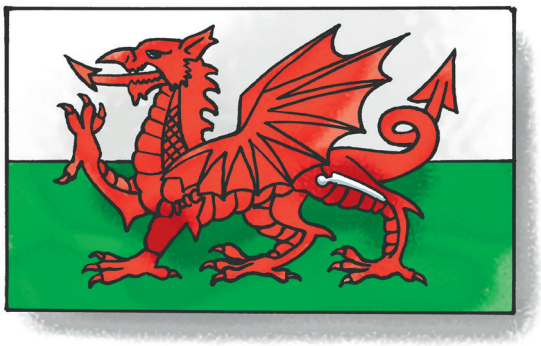
Data på individnivå avseende dessa faktorer finns tillgängliga i Svenska Höftprotesregistret, Socialstyrelsens hälsodataregister och i Statistiska Centralbyråns register. Information från dessa register sambearbetades till en forskningsdatabas. Principerna för relativ överlevnadsanalys och ”multi-state” analys med multivariabel regression användes vid statistiska beräkningar. Vi undersökte patienter som genomgått planerad total höftprotesoperation mellan 1999-01-01 och 2012-12-31.

De flesta patienterna opererades på grund av primär artros och den andelen ökade på bekostnad av minskad andel patienter med inflammatorisk ledsjukdom. Höftproteskirurgin har förändrats under studieperioden och resultaten visar att dödlighet inom 30 och 90 dagar har minskat, revisionsfrekvensen (om operation med byte av protesdelar) har minskat och patientrapporterade utfallsmått har förbättrats.

Sämre hälsotillstånd mätt med EQ-5D före total höftprotesoperation var förenat med högre dödlighet upp till fem år efter operationen. Patienter med total höftprotesoperation hade bättre relativ överlevnad jämfört med en ålders- och könsmatchad normalbefolkning. Det fanns en diagnos-specifik differentiering av relativ överlevnad till förmån för patienter med primär höftartros. Högre samsjuklighet mätt med Elixhausers komorbiditesindex, låg utbildningsgrad och att vara änka/änkling eller ensamstående hade negativ inverkan på överlevnad. Livstidsrisken för att behöva opereras på andra sidan, genomgå revision eller att dö identifierades med hjälp av longitudinellt insamlad data.

Det har skett förändringar inom höftproteskirurgin och långtidsresultaten har förbättrats. Sämre hälsotillstånd var förenat med ökad dödlighet på medellång sikt. Sett till hela populationen som genomgick planerad höftprotesoperation, var den relativa dödligheten lägre och risken för att behöva revision var låg. Många faktorer avgör risken att behöva opereras i andra höften eller att genomgå revision och under studieperioden var sannolikheten att opereras i andra höften dubbelt så hög som risken att dö. Sannolikheten att byta ut andra höften var sju gånger större än att behöva genomgå en revision i den första opererade höften.

Summary in Welsh



Deilliannau hydredol yn dilyn ailosodiad clun

Tueddiadau dros amser, dilyniant o ddigwyddiadau ac astudio y ffactorau sy'n dylanwadu ar goroesiad mewnblaniad a marwolaethau

Mae osteoarthritis yn y glun yn glefyd cyffredin, sy'n wanhaol ac yn symptomatig. Mae'r symptomau yn anablu, a gellir eu trin yn llwyddiannus trwy osod clun newydd (THR). Gwyddom fod y mwyafrif o'r cleifion yn gwneud yn dda yn dilyn y llawdriniaeth; fodd bynnag bydd ar rai cleifion angen llawdriniaeth bellach ar yr un glun neu ar y glun arall.

Mae'r ffactorau achosol sy'n arwain at lawdriniaeth bellach ar gyfer cleifion, yn ogystal ag at farwolaeth, yn niferus. Mae'r canlynol yn ffactorau pwysig o ran diffinio'r risg ar gyfer claf unigol: arwydd bod angen llawdriniaeth, pa mor gymhleth yw'r llawdriniaeth, oedran y claf, cydafiachusrwydd meddygol, gweithgarwch corfforol a ffactorau economaidd-gymdeithasol, y mathau o fewnblaniadau a ddefnyddir, y technegau llawfeddygol a ddefnyddir, yn ogystal â'r protocolau amdriniaethol a'r driniaeth ar ôl y llawdriniaeth.

Roedd y cwestiynau ymchwil ar gyfer y prosiect hwn fel a ganlyn:

1. A fu unrhyw newid o ran y ffactorau sy'n ymwneud â'r claf, y ffactorau sy'n ymwneud â'r llawdriniaeth, a'r ffactorau economaidd-gymdeithasol ar gyfer y cleifion sy'n dewis cael clun newydd, ac a yw paramedrau amrywiol y canlyniadau wedi esblygu?
2. A oes yna gysylltiad rhwng statws iechyd hunangofnodedig a marwolaeth yn dilyn triniaeth ddewisol i gael clun newydd?
3. A yw cyfraddau goroesi cymharol cleifion a gafodd THR yn well na'r gyfradd oroesi gyffredinol, ac a yw'r diagnosis a arweiniodd at y THR yn effeithio ar hyn?
4. Beth yw'r risg hirdymor o ran llawdriniaeth ddilynol ar yr un glun, neu ar y glun arall, yn ogystal â'r risg o farwolaeth, yn dilyn THR cynradd dewisol? A yw'r ffactorau sy'n ymwneud â'r claf, y ffactorau sy'n ymwneud â'r llawdriniaeth, a'r ffactorau economaidd-gymdeithasol yn effeithio ar lawdriniaeth ddilynol neu farwolaeth?

Mae data lefel y claf, sy'n berthnasol i nifer o'r ffactorau hyn, ar gael ar Gofrestr Cymalffurfiad y Glun Sweden, ac yng nghronfeydd data Bwrdd Cenedlaethol Ystadegau Iechyd a Lles Sweden. Cafodd yr wybodaeth hon ei chysylltu i greu un gronfa ddata ymchwil. Defnyddiwyd egwyddorion dadansoddiad o oroesiad cymharol a dadansoddiad amlgyflwr gydag atchweliad amlnewidynnol ar gyfer dadansoddiad ystadegol. Penderfynwyd astudio cleifion a gafodd THR dewisol rhwng 01/01/1999 a 31/12/2012.

Cafodd y mwyafrif o'r cleifion lawdriniaeth o ganlyniad i osteoarthritis sylfaenol, a chynyddodd y dangosydd hwn ymhellach yn ystod y cyfnod, a hynny ar draul nifer gostyngol o gleifion a oedd yn dioddef o osteoarthritis ymfflamychol a thoriadau clun. Mae'r arfer o gynnal THR dewisol wedi newid yn ystod y cyfnod astudio; fodd bynnag, er gwaethaf y newidiadau hyn, mae gostyngiad wedi bod o ran marwolaethau mewn 30 a 90 o ddiwrnodau, yn ogystal â gwelliant cyffredinol o ran y cyfraddau adolygu, ac mae'r cleifion wedi cofnodi gwell boddhad a chanlyniadau. Roedd statws iechyd gwaeth cyn THR, yn ôl yr EQ-5D, yn gysylltiedig â nifer uwch o farwolaethau, a hynny hyd at bum mlynedd ar ôl y llawdriniaeth. Roedd goroesiad cleifion a oedd wedi cael THR yn well o gymharu â phoblogaeth o'r un oed a rhyw. Roedd gwahaniaethiad diagnosis-benodol o'r cyfraddau goroesi cymharol yn dilyn THR yn ffafrio cleifion ag osteoarthritis yn y glun. Roedd mynegrif cydafiachusrwydd Elixhauser uwch, lefel addysgol, a bod yn weddw neu'n sengl, wedi cael effaith andwyol ar y siawns o oroesi. Nodwyd y risg oes ar gyfer llawdriniaeth ddwyochrog, adolygiad a marwolaeth gan ddefnyddio'r data a gasglwyd mewn modd hydredol.

Er gwaethaf rhai newidiadau o ran arfer, mae'r canlyniad hirdymor yn dilyn THR wedi gwella. Mae statws iechyd hunangofnodedig gwaeth yn gysylltiedig â marwolaeth yn y tymor canolig. Yn gyffredinol, bydd cleifion sy'n cael THR dewisol yn goroesi'n well, yn gymharol, a bydd yna risg isel y bydd yn rhaid cynnal adolygiad. Mae yna nifer o ffactorau sy'n ymwneud â'r risg o lawdriniaeth bellach ar yr un glun neu ar y glun arall, ac mae cleifion ddwywaith yn fwy tebygol o gael ail glun newydd nag y maent o farw yn ystod y cyfnod astudio. Mae cael llawdriniaeth ar y glun gydgyferbyniol seithwaith yn fwy tebygol na chael triniaeth adolygol ar y glun gyntaf a fewnblannwyd.

Summary in Dutch

Longitudinale evolutie na totale heupprothese.

Tendens, opeenvolging van gebeurtenissen en analyse van factoren die het behoud van de prothese en de sterfte bepalen.

Artrose van de heup is een frequent voorkomende, slepende en symptomatische gewrichtsaandoening. Het is algemeen bekend dat de symptomen van het gewrichtslijden succesvol kunnen behandeld worden door het plaatsen van een artificieel heupgewricht. Het merendeel van de patiënten doet het uitstekend na de ingreep. Er zijn echter patiënten die verdere ingrepen moeten ondergaan aan de heup, aan dezelfde of aan de tegenovergestelde zijde ,of vroegtijdig sterven in de perioperatieve periode.

De factoren die leiden tot verdere ingrepen of tot een vroegtijdige dood zijn multifactorieel bepaald. De volgende factoren zijn belangrijk bij het bepalen van het risico voor een individuele patiënt: indicatie voor chirurgie, complexiteit van de ingreep, leeftijd van de patiënt, medische comorbiditeiten, lichamelijke activiteit, socio-economische omstandigheden, type implantaat, chirurgische technieken, alsook het perioperatieve protocol en de postoperatieve behandeling.

De onderzoeksvragen voor dit project waren:

1. Is er een evolutie in de patiëntgerelateerde, chirurgiegerelateerde en sociaal-economische factoren bij patiënten die een geplande heupchirurgie ondergaan en in welke mate zijn de verschillende uitkomstparameters mee geëvolueerd?
2. Is er een associatie tussen zelf-gerapporteerde gezondheidstoestand en overlijden na electieve heupprothesechirurgie?
3. Hebben patiënten die een geplande heupprothesechirurgie hebben ondergaan een betere relatieve overlevingskans dan de doorsneebevolking en is dit verschil in overleving beïnvloed door de indicatie waarvoor de ingreep werd ondernomen?
4. Wat is het langetermijnrisico voor verdere chirurgie op dezelfde of de tegenovergestelde heup en wat is het risico voor overlijden na een electieve ingreep? Is er een invloed van de patiëntgerelateerde, chirurgiegerelateerde en socio-economische factoren op de daaropvolgende operaties en overlijden?

Patiëntengegevens omtrent deze factoren zijn beschikbaar in het Zweeds Heup Implantaat Register (SHAR) en in de administratieve databases van de Nationale Raad voor Volksgezondheid en Welzijn (Socialstyrelsen) en Statistiek Zweden (SCB). De informatie werd samengebracht in een gecombineerde onderzoeksdatabank. De principes van relatieve overlevings- en multistaatanalyse met multivariabele regressie werden gebruikt als statistische methodologie. Patiënten, die electief tussen 01/01/1999 en 31/12/2012 werden geopereerd, waren het onderwerp van dit studieproject.

Het merendeel van de patiënten onderging de ingreep omwille van primaire artrose en er was een toename in die indicatie tijdens de studieperiode ten nadele van een vermindering in patiënten geopereerd omwille van een inflammatoire pathologie. Gedurende de studieperiode was er een evolutie in de chirurgische praktijk, maar ondanks de wijzigingen is er een daling in de mortaliteit na 30 en 90 dagen, een daling van het aantal reoperaties en in het algemeen is er een verbeterde tevredenheid en uitkomstparameters. Een mindere gezondheidstoestand volgens de EQ-5D in de preoperative periode is geassocieerd met een hogere kans op overlijden tot vijf jaar na de operatie. Patiënten hebben een betere relatieve overleving na het ondergaan van een electieve heupoperatie waarbij het gewricht wordt vervangen. Er is een diagnosespecifiek verschil in relatieve overleving afhankelijk van de reden voor de ingreep waarbij patiënten met een degeneratieve reden voor de heupartrose het beter doen.. Hogere Elixhauser comorbiditeitsindex, een lager behaald

niveau van onderwijs en niet –samenlevend zijn, hebben een negatieve invloed op de overlevingskansen. Het levenslange risico voor bilaterale chirurgie, revisie en dood werden bepaald op basis van de longitudinale verzamelde gegevens.

Ondanks enkele veranderingen in de praktijk zijn de resultaten op lange termijn nog steeds aan het verbeteren. Een mindere preoperatieve gezondheidstoestand is geassocieerd met een verhoogde kans op overlijden op de middellange termijn. In het algemeen, hebben patiënten na een geplande ingreep een betere relatieve overleving en een geringe kans op een reoperatie. Het risico op een verdere operatie aan dezelfde of de andere heup is multifactorieel bepaald en patiënten hebben dubbel de kans op een operatie waarbij de andere heup wordt vervangen dan te overlijden tijdens de studieperiode. Het vervangen van de contralaterale heup is 7 keer meer voorkomend dan een heringreep van de eerste geïmplanteerde heup.

Project Collaborators

Supervisors

Ola Rolfson, MD, PhD – Associate Professor, Orthopaedic Surgeon with the Department of Orthopaedics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg and Director of the Swedish Hip Arthroplasty Register.

Henrik Malchau, MD, PhD – Professor, Harvard Medical School and Co-director Emeritus of the Harris Orthopaedic Laboratory at Massachusetts General Hospital, Boston, MA, USA, affiliated with the Swedish Hip Arthroplasty Register and Orthopaedic Surgeon with the Department of Orthopaedics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg.

Johan Kärrholm, MD, PhD – Professor, Orthopaedic Surgeon with the Department of Orthopaedics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg and Director of the Swedish Hip Arthroplasty Register.

Göran Garellick, MD, PhD – Professor Emeritus at the Department of Orthopaedics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Sweden, Former Director of the Swedish Hip Arthroplasty Register.

Collaborators/co-authors

Kristina Burström, PhD – Associate Professor Department of learning, Informatics, Management and Ethics (LIME), Health Outcomes and Economic Evaluation Research Group and Department of Public Health, Equity and Health Policy Research Group, Karolinska Institute, Stockholm, Sweden.

Erik Bülow – PhD student, Biostatistician with the Swedish Hip Arthroplasty Register, Gothenburg, Sweden.

Ann Garland, MD, PhD – Orthopaedic Surgeon with the Department of Orthopaedics, Visby Hospital, Visby, Sweden.

Maziar Mohaddes, MD, PhD – Orthopaedic Surgeon with the Department of Orthopaedics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg and affiliated with the Swedish Hip Arthroplasty Register.

Szilárd Nemes, PhD – Associate Professor, Biostatistician with the Swedish Hip Arthroplasty Register, Gothenburg, Sweden.

Clas Rehnberg, PhD – Professor, Department of learning, Informatics, Management and Ethics (LIME), Health Outcomes and Economic Evaluation Research Group, Karolinska Institute, Stockholm, Sweden.

A. John Timperley, FRCS, DPhil(Oxon) – Professor Exeter University, Consultant Orthopaedic Surgeon at the Princess Elizabeth Orthopaedic Centre, Exeter, UK.

Sarah Whitehouse, PhD – Biostatistician in Orthopaedics, Queensland University of Technology, Brisbane, Australia.

Acknowledgements

This incredible journey of mine has been made easier by some great support and encouragement from some remarkable people. My sincere gratitude goes to everybody who has contributed to make this journey possible and smooth sailing.

Whilst my thanks go out to everybody involved, I would like to offer a special word of thanks to:

Ola Rolfson for volunteering to be my main supervisor and stepping into the unknown, the late evenings discussing the past, present and the future. His never-ending support has been invaluable.

Johan Kärrholm for the superb advice, the continuous feedback and making me feel part of the register and academic family.

Henrik Malchau for providing me the opportunity to start the Swedish adventure and providing me with the extensive networking opportunities.

Göran Garellick for allowing me to become part of the register gang.

Szilard Nemes for his patience to make statistics look easy, explaining the essence of statistics and redoing the graphs again (and again) to make them look much improved.

John Timperley for giving me some great opportunities early in my career, the great support and the belief in me.

Graham Gie for providing me with the science of what a sound hip replacement looks like.

Maziar Mohaddes for helping me adapt to the academic world and 'this is Sweden'.

Peter Grant for his hospitality, the professional advice and the persistence of surgical solutions.

Colleagues and staff at Mölndal Sjukhus for making me feel welcome, adapting to the language barriers and introducing me to the Swedish social life.

The team at SHAR: Kajsa Erikson, Johanna Vinblad, Karin Lindborg, Karin Pettersson, Karin Davidsson for the sustained help, the patience and the introduction to 'Swedish fika'.

My colleagues at HDUHB, Wales, UK for understanding the reason I set off on the journey and providing the support to allow the continuity of the arthroplasty service.

Subroto Chatterji for the evenings in the Ginger, the professional support and guidance, and of course, the literary suggestions.

Michelle Gerard-Wilson for allowing me to disappear and her understanding of why this journey was important to me. Being one of the cornerstones of the multidisciplinary arthroplasty service, her database and continuous feedback was exceptional.

Liz Peel for the excellent physiotherapy service, the great support, the understanding, and being the other cornerstone of the multidisciplinary arthroplasty service, and all the life advice that was required.

Charlotte Vitse and *Daniel Odin* for the design and help with the graphics.

Amanda Davies thank you for your understanding over the last 3 years.

My both parents for giving me all these opportunities and their never-ending support to become what I am today.

Marie-Julie and *Anna-Helena* my two beautiful daughters, for allowing me to leave to pursue my dream and fulfill this once-in-a-lifetime opportunity.

References

1. Murphy LB, Helmick CG, Schwartz TA, Renner JB, Tudor G, Koch GG, et al. One in four people may develop symptomatic hip osteoarthritis in his or her lifetime. Osteoarthritis Cartilage. 2010;18(11):1372–9.

2. Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, et al. The global burden of hip and knee osteoarthritis: estimates from the Global Burden of Disease 2010 study. Annals of the Rheumatic Diseases. 2014;73(7):1323–30.

3. Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res (Hoboken). 2012;64(4):465–74.

4. Nelson AE, Allen KD, Golightly YM, Goode AP, Jordan JM. A systematic review of recommendations and guidelines for the management of osteoarthritis: The chronic osteoarthritis management initiative of the U.S. bone and joint initiative. Semin Arthritis Rheum. 2014;43(6):701–12.

5. Thorstensson CA, Garellick G, Rystedt H, Dahlberg LE. Better Management of Patients with Osteoarthritis: Development and Nationwide Implementation of an Evidence-Based Supported Osteoarthritis Self-Management Programme. Musculoskeletal Care. 2015;13(2):67–75.

6. Aresti N, Kassam J, Nicholas N, Achan P. Hip osteoarthritis. BMJ. 2016;354:i3405.

7. Stiggelbout AM, Van der Weijden T, De Wit MP, Frosch D, Legare F, Montori VM, et al. Shared decision making: really putting patients at the centre of healthcare. BMJ. 2012;344:e256.

8. Charnley J. Total hip replacement by low-friction arthroplasty. Clin Orthop Relat Res. 1970;72:7–21.

9. Gomez PF, Morcuende JA. Early attempts at hip arthroplasty--1700s to 1950s. Iowa Orthop J. 2005;25:25–9.

10. Hernigou P. Earliest times before hip arthroplasty: from John Rhea Barton to Themistocles Gluck. Int Orthop. 2013;37(11):2313–8.

11. Learmonth ID, Young C, Rorabeck C. The operation of the century: total hip replacement. The Lancet.370(9597):1508–19.

12. Lansingh VC, Carter MJ, Martens M. Global cost-effectiveness of cataract surgery. Ophthalmology. 2007;114(9):1670–8.

13. Garellick G, Karrholm J, Lindahl H, Malchau H, Rogmark C, Rolfson O. Swedish Hip Arthroplasty Register Annual Report 2014. 2015.

14. Kandala NB, Connock M, Pulikottil-Jacob R, Sutcliffe P, Crowther MJ, Grove A, et al. Setting benchmark revision rates for total hip replacement: analysis of registry evidence. Bmj. 2015;350:h756.

15. Junnila M, Laaksonen I, Eskelinen A, Pulkkinen P, Ivar Havelin L, Furnes O, et al. Implant survival of the most common cemented total hip devices from the Nordic Arthroplasty Register Association database. Acta Orthop. 2016;87(6):546–53.

16. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. The Journal of bone and joint surgery American volume. 2007;89(4):780–5.

17. Bozic KJ, Kurtz SM, Lau E, Ong K, Vail TP, Berry DJ. The epidemiology of revision total hip arthroplasty in the United States. The Journal of bone and joint surgery American volume. 2009;91(1):128–33.

18. Nemes S, Gordon M, Rogmark C, Rolfson O. Projections of total hip replacement in Sweden from 2013 to 2030. Acta Orthopaedica. 2014;85(3):238–43.

19. Mont MA, Issa K. Updated projections of total joint arthroplasty demands in America: Commentary on an article by Steven M. Kurtz, PhD, et al.: "Impact of the economic downturn on total joint replacement demand in the United States. Updated projections to 2021". Journal of Bone and Joint Surgery – American Volume. 2014;96(8):e68.1-e.2.

20. Nemes S, Rolfson O, A WD, Garellick G, Sundberg M, Karrholm J, et al. Historical view and future demand for knee arthroplasty in Sweden. Acta Orthop. 2015;86(4):426–31.

21. Patel A, Pavlou G, Mujica-Mota RE, Toms AD. The epidemiology of revision total knee and hip arthroplasty in England and Wales: a comparative analysis with projections for the United States. A study using the National Joint Registry dataset. Bone Joint J. 2015;97-B(8):1076–81.

22. Inacio MCS, Graves SE, Pratt NL, Roughead EE, Nemes S. Increase in Total Joint Arthroplasty Projected from 2014 to 2046 in Australia: A Conservative Local Model With International Implications. Clin Orthop Relat Res. 2017;475(8):2130–7.

23. Wylde V, Blom AW. The failure of survivorship. J Bone Joint Surg Br. 2011;93(5):569–70.

24. Bozic KJ, Rubash HE. The painful total hip replacement. Clin Orthop Relat Res. 2004(420):18–25.

25. Crawford RW, Murray DW. Total hip replacement: indications for surgery and risk factors for failure. Ann Rheum Dis. 1997;56(8):455–7.

26. Lubbeke A, Katz JN, Perneger TV, Hoffmeyer P. Primary and revision hip arthroplasty: 5-year outcomes and influence of age and comorbidity. J Rheumatol. 2007;34(2):394–400.

27. Patil S, Garbuz DS, Greidanus NV, Masri BA, Duncan CP. Quality of life outcomes in revision vs primary total hip arthroplasty: a prospective cohort study. J Arthroplasty. 2008;23(4):550–3.

28. Adelani MA, Crook K, Barrack RL, Maloney WJ, Clohisy JC. What is the prognosis of revision total hip arthroplasty in patients 55 years and younger? Clin Orthop Relat Res. 2014;472(5):1518–25.

29. Postler AE, Beyer F, Wegner T, Lutzner J, Hartmann A, Ojodu I, et al. Patient-reported outcomes after revision surgery compared to primary total hip arthroplasty. Hip Int. 2017;27(2):180–6.

30. Yu S, Garvin KL, Healy WL, Pellegrini VD, Jr., Iorio R. Preventing Hospital Readmissions and Limiting the Complications Associated With Total Joint Arthroplasty. J Am Acad Orthop Surg. 2015;23(11):e60–71.

31. Fortin PR, Clarke AE, Joseph L, Liang MH, Tanzer M, Ferland D, et al. Outcomes of total hip and knee replacement: preoperative functional status predicts outcomes at six months after surgery. Arthritis Rheum. 1999;42(8):1722–8.

32. Fortin PR, Penrod JR, Clarke AE, St-Pierre Y, Joseph L, Belisle P, et al. Timing of total joint replacement affects clinical outcomes among patients with osteoarthritis of the hip or knee. Arthritis Rheum. 2002;46(12):3327–30.

33. Ng Man Sun S, Gillott E, Bhamra J, Briggs T. Implant use for primary hip and knee arthroplasty: are we getting it right first time? J Arthroplasty. 2013;28(6):908–12.

34. Barratt H, Turner S, Hutchings A, Pizzo E, Hudson E, Briggs T, et al. Mixed methods evaluation of the Getting it Right First Time programme – improvements to NHS orthopaedic care in England: study protocol. BMC health services research. 2017;17(1):71.

35. Ahrens W, Pigeot I, SpringerLink (Online service). Handbook of Epidemiology. Available from: http://dx.doi.org/10.1007/978-0-387-09834-0 http://sfxeu11.hosted.exlibrisgroup.com/sfxgub?url_ver=Z39.88-2004&ctx_ver=Z39.88-2004&ctx_enc=info:ofi/enc:UTF-8&rfr_id=info:sid/sfxit.com:opac_856&url_ctx_fmt=info:ofi/fmt:kev:mtx:ctx&sfx.ignore_date_threshold=1&rft.object_id=3710000000078687&svc_val_fmt=info:ofi/fmt:kev:mtx:sch_svc&.

36. Brand RA. Ernest Amory Codman, MD, 1869–1940. Clin Orthop Relat Res. 2009;467(11):2763–5.

37. Hicks CW, Makary MA. A prophet to modern medicine: Ernest Amory Codman. BMJ. 2013;347:f7368.

38. National disease registries for advancing health care. Lancet (London, England). 2011;378(9809):2050.

39. Larsson S, Lawyer P, Garellick G, Lindahl B, Lundstrom M. Use of 13 disease registries in 5 countries demonstrates the potential to use outcome data to improve health care's value. Health Aff (Millwood). 2012;31(1):220–7.

40. Emilsson L, Lindahl B, Köster M, Lambe M, Ludvigsson JF. Review of 103 Swedish Healthcare Quality Registries. Journal of Internal Medicine. 2015;277(1):94–136.

41. Adami HO, Hernán MA. Learning how to improve healthcare delivery: the Swedish Quality Registers. Journal of Internal Medicine. 2015;277(1):87–9.

42. Kärrholm J. The Swedish Hip Arthroplasty Register (http://www.shpr.se). Acta Orthopaedica. 2010;81(1):3–4.

43. Rolfson O, Karrholm J, Dahlberg LE, Garellick G. Patient-reported outcomes in the Swedish Hip Arthroplasty Register: results of a nationwide prospective observational study. Journal of Bone and Joint Surgery-British Volume. 2011;93B(7):867–75.

44. Rolfson O, Bohm E, Franklin P, Lyman S, Denissen G, Dawson J, et al. Patient-reported outcome measures in arthroplasty registries Report of the Patient-Reported Outcome Measures Working Group of the International Society of Arthroplasty Registries Part II. Recommendations for selection, administration, and analysis. Acta Orthop. 2016;87 Suppl 1:9–23.

45. Rolfson O, Eresian Chenok K, Bohm E, Lubbeke A, Denissen G, Dunn J, et al. Patient-reported outcome measures in arthroplasty registries. Acta Orthop. 2016;87 Suppl 1:3–8.

46. Makoul G, Clayman ML. An integrative model of shared decision making in medical encounters. Patient Education and Counseling. 2006;60(3):301–12.

47. Weinstein JN, Clay K, Morgan TS. Perspective – Informed patient choice: Patient-centered valuing of surgical risks and benefits. Health Aff. 2007;26(3):726–30.

48. Bozic K. Orthopaedic Healthcare Worldwide: Shared Medical Decision Making in Orthopaedics. Clin Orthop Relat Res. 2013;471(5):1412–4.

49. Berry DJ. Joint registries: what can we learn in 2016? Bone Joint J. 2017;99-B(1 Supple A):3–7.

50. Havelin LI, Fenstad AM, Salomonsson R, Mehnert F, Furnes O, Overgaard S, et al. The Nordic Arthroplasty Register Association: a unique collaboration between 3 national hip arthroplasty registries with 280,201 THRs. Acta Orthop. 2009;80(4):393–401.

51. Riordan P, Bickler G, Lyons C. Lessons of a hip failure. Registers of joint replacement operations should be set up. BMJ. 1998;316(7149):1985.

52. Malchau H, Graves SE, Porter M, Harris WH, Troelsen A. The next critical role of orthopedic registries. Acta Orthop. 2015;86(1):3–4.

53. Malchau H, Porter ML. Editorial Comment: 2014 Meeting of The International Society of Arthroplasty Registers. Clin Orthop Relat Res. 2015;473(11):3368–9.

54. Gray BH. Registries as a Knowledge-Development Tool The Experience of Sweden and England. Urban Institute, Health Policy Centre; 2013.

55. Graves SE. The value of arthroplasty registry data. Acta Orthop. 2010;81(1):8–9.

56. Konan S, Haddad FS. Joint Registries: a Ptolemaic model of data interpretation? Bone Joint J. 2013;95-B(12):1585–6.

57. Inacio MC, Paxton EW, Dillon MT. Understanding Orthopaedic Registry Studies: A Comparison with Clinical Studies. The Journal of bone and joint surgery American volume. 2016;98(1):e3.

58. Jacofsky DJ. The myths of 'big data' in health care. Bone Joint J. 2017;99-B(12):1571–6.

59. Stammers JG, Kuo A, Hart AJ, Smeeth L, Skinner JA. Registry Data-Valuable Lessons But Beware the Confounders. J Arthroplasty. 2017;32(9S):S63-S7.

60. Herberts P, Malchau H. How outcome studies have changed total hip arthroplasty practices in Sweden. Clin Orthop Relat Res. 1997(344):44–60.

61. Paxton EW, Inacio MC, Khatod M, Yue EJ, Namba RS. Kaiser Permanente National Total Joint Replacement Registry: aligning operations with information technology. Clin Orthop Relat Res. 2010;468(10):2646–63.

62. Paxton EW, Inacio MC, Singh JA, Love R, Bini SA, Namba RS. Are There Modifiable Risk Factors for Hospital Readmission After Total Hip Arthroplasty in a US Healthcare System? Clin Orthop Relat Res. 2015;473(11):3446–55.

63. Paxton EW, Inacio MC, Khatod M, Yue E, Funahashi T, Barber T. Risk calculators predict failures of knee and hip arthroplasties: findings from a large health maintenance organization. Clin Orthop Relat Res. 2015;473(12):3965–73.

64. Cnudde P, Rolfson O, Nemes S, Karrholm J, Rehnberg C, Rogmark C, et al. Linking Swedish health data registers to establish a research database and a shared decision-making tool in hip replacement. BMC musculoskeletal disorders. 2016;17(1):414.

65. Schilling PL, Bozic KJ. The big to do about "big data". Clin Orthop Relat Res. 2014;472(11):3270–2.

66. Ford DV, Jones KH, Verplancke JP, Lyons RA, John G, Brown G, et al. The SAIL Databank: building a national architecture for e-health research and evaluation. BMC health services research. 2009;9:157.

67. Lyons RA, Jones KH, John G, Brooks CJ, Verplancke JP, Ford DV, et al. The SAIL databank: linking multiple health and social care datasets. BMC Med Inform Decis Mak. 2009;9:3.

68. Allen Butler R, Rosenzweig S, Myers L, Barrack RL. The Frank Stinchfield Award: the impact of socioeconomic factors on outcome after THA: a prospective, randomized study. Clin Orthop Relat Res. 2011;469(2):339–47.

69. Gordon M, Stark A, Skoldenberg OG, Karrholm J, Garellick G. The influence of comorbidity scores on re-operations following primary total hip replacement COMPARISON AND VALIDATION OF THREE COMORBIDITY MEASURES. Bone & Joint Journal. 2013;95B(9):1184–91.

70. Gordon M, Paulsen A, Overgaard S, Garellick G, Pedersen A, Rolfson O. Factors influencing health-related quality of life after total hip replacement – a comparison of data from the Swedish and Danish hip arthroplasty registers. BMC musculoskeletal disorders. 2013;14(1):1–6.

71. Barrack RL, Ruh EL, Chen J, Lombardi AV, Jr., Berend KR, Parvizi J, et al. Impact of socioeconomic factors on outcome of total knee arthroplasty. Clin Orthop Relat Res. 2014;472(1):86–97.

72. Pugely AJ, Martin CT, Harwood J, Ong KL, Bozic KJ, Callaghan JJ. Database and Registry Research in Orthopaedic Surgery: Part 2: Clinical Registry Data. The Journal of bone and joint surgery American volume. 2015;97(21):1799–808.

73. Sayers A, Ben-Shlomo Y, Blom AW, Steele F. Probabilistic record linkage. Int J Epidemiol. 2016;45(3):954–64.

74. Ludvigsson J, Otterblad-Olausson P, Pettersson B, Ekbom A. The Swedish personal identity number: possibilities and pitfalls in healthcare and medical research. Eur J Epidemiol. 2009;24(11):659–67.

75. Cnudde P, Nemes S, Bulow E, Timperley J, Malchau H, Karrholm J, et al. Trends in hip replacements between 1999 and 2012 in Sweden. J Orthop Res. 2017.

76. Rolfson O, Rothwell A, Sedrakyan A, Chenok KE, Bohm E, Bozic KJ, et al. Use of Patient-Reported Outcomes in the Context of Different Levels of Data*. The Journal of Bone & Joint Surgery. 2011;93(Supplement_3):66–71.

77. Saklad MDM. GRADING OF PATIENTS FOR SURGICAL PROCEDURES. Anesthesiology. 1941;2(3):281–4.

78. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. Medical care. 1998;36(1):8–27.

79. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Medical care. 2005;43(11):1130–9.

80. Fitz-Henry J. The ASA classification and peri-operative risk. Ann R Coll Surg Engl. 2011;93(3):185–7.

81. Sharabiani MT, Aylin P, Bottle A. Systematic review of comorbidity indices for administrative data. Medical care. 2012;50(12):1109–18.

82. Menendez ME, Neuhaus V, van Dijk CN, Ring D. The Elixhauser comorbidity method outperforms the Charlson index in predicting inpatient death after orthopaedic surgery. Clin Orthop Relat Res. 2014;472(9):2878–86.

83. EuroQol G. EuroQol--a new facility for the measurement of health-related quality of life. Health Policy. 1990;16(3):199–208.

84. Charnley J. The long-term results of low-friction arthroplasty of the hip performed as a primary intervention. J Bone Joint Surg Br. 1972;54(1):61–76.

85. Pohar M, Stare J. Relative survival analysis in R. Computer Methods and Programs in Biomedicine. 2006;81(3):272–8.

86. Pohar M, Stare J. Making relative survival analysis relatively easy. Computers in Biology and Medicine. 2007;37(12):1741–9.

87. Perme MP, Stare J, Estève J. On estimation in relative survival. Biometrics. 2012;68(1):113–20.

88. Statistics, Sweden. The future population of Sweden 2012–2060. In: Institute F, editor. 2012. p. Table 3 page 220.

89. Stare J, Henderson R, Pohar M. An individual measure of relative survival. Journal of the Royal Statistical Society: Series C (Applied Statistics). 2005;54(1):115–26.

90. Stare J, Pohar M, Henderson R. Goodness of fit of relative survival models. Statistics in Medicine. 2005;24(24):3911–25.

91. Putter H, Fiocco M, Geskus RB. Tutorial in biostatistics: competing risks and multi-state models. Stat Med. 2007;26(11):2389–430.

92. Willekens F, Putter H. Software for multistate analysis. Demographic Research. 2014;31(14):381–420.

93. Ludvigsson JF, Almqvist C, Bonamy AK, Ljung R, Michaelsson K, Neovius M, et al. Registers of the Swedish total population and their use in medical research. Eur J Epidemiol. 2016;31(2):125–36.

94. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ. 2007;335(7624):806–8.

95. Perry DC, Parsons N, Costa ML. 'Big data' reporting guidelines: how to answer big questions, yet avoid big problems. Bone Joint J. 2014;96-B(12):1575–7.

96. Lindgren JV, Gordon M, Wretenberg P, Karrholm J, Garellick G. Validation of reoperations due to infection in the Swedish Hip Arthroplasty Register. BMC musculoskeletal disorders. 2014;15:384.

97. Lindgren V, Gordon M, Wretenberg P, Karrholm J, Garellick G. Deep infection after total hip replacement: a method for national incidence surveillance. Infect Control Hosp Epidemiol. 2014;35(12):1491–6.

98. Georgios Chatziagorou HL, Göran Garellick, Johan Kärrholm. Demographics Of Periprosthetic Femoral Fractures In Sweden. What Is New? 18 th EFORT Congress; Vienna, Austria2017.

99. Abdel MP, Roth PV, Harmsen WS, Berry DJ. What is the lifetime risk of revision for patients undergoing total hip arthroplasty? a 40-year observational study of patients treated with the Charnley cemented total hip arthroplasty. Bone Joint J. 2016;98-B(11):1436–40.

100. Clement ND, Muzammil A, Macdonald D, Howie CR, Biant LC. Socioeconomic status affects the early outcome of total hip replacement. J Bone Joint Surg Br. 2011;93(4):464–9.

101. Cleveland RJ, Schwartz TA, Prizer LP, Randolph R, Schoster B, Renner JB, et al. Associations of educational attainment, occupation, and community poverty with hip osteoarthritis. Arthritis Care Res (Hoboken). 2013;65(6):954–61.

102. Greene M, Rolfson O, Nemes S, Gordon M, Malchau H, Garellick G. Education Attainment is Associated With Patient-reported Outcomes: Findings From the Swedish Hip Arthroplasty Register. Clin Orthop Relat Res. 2014;472(6):1868–76.

103. Jepsen P, Johnsen SP, Gillman MW, Sorensen HT. Interpretation of observational studies. Heart. 2004;90(8):956–60.

104. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928.

105. Viswanathan M, Berkman ND, Dryden DM, Hartling L. Assessing Risk of Bias and Confounding in Observational Studies of Interventions or Exposures: Further Development of the RTI Item Bank. AHRQ Methods for Effective Health Care. Rockville (MD)2013.

106. Thygesen LC, Ersboll AK. When the entire population is the sample: strengths and limitations in register-based epidemiology. Eur J Epidemiol. 2014;29(8):551–8.

107. Ganz R, Leunig M, Leunig-Ganz K, Harris WH. The etiology of osteoarthritis of the hip: an integrated mechanical concept. Clin Orthop Relat Res. 2008;466(2):264–72.

108. World Medical A. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191–4.

109. Ludvigsson JF, Håberg SE, Knudsen GP, Lafolie P, Zoega H, Sarkkola C, et al. Ethical aspects of registry-based research in the Nordic countries. Clinical Epidemiology. 2015;7:491–508.

110. Benson M, Boehler N, Szendroi M, Zagra L, Puget J. Ethical standards for orthopaedic surgeons. Bone Joint J. 2014;96-B(8):1130–2.

111. Zagra L. Advances in hip arthroplasty surgery: what is justified? EFORT Open Rev. 2017;2(5):171–8.

112. Malchau H, Bragdon CR, Muratoglu OK. The stepwise introduction of innovation into orthopedic surgery: the next level of dilemmas. J Arthroplasty. 2011;26(6):825–31.

113. Reito A, Lehtovirta L, Lainiala O, Makela K, Eskelinen A. Lack of evidence-the anti-stepwise introduction of metal-on-metal hip replacements. Acta Orthop. 2017;88(5):478–83.

114. Malchau H, Garellick G, Eisler T, Karrholm J, Herberts P. Presidential guest address: the Swedish Hip Registry: increasing the sensitivity by patient outcome data. Clin Orthop Relat Res. 2005;441:19–29.

115. Khan T. Epidemiological Studies in Orthopaedics. A Brief Overview. 2017;6(4):38–9.

116. Cnudde P, Nemes S, Mohaddes M, Timperley J, Garellick G, Burstrom K, et al. Is Preoperative Patient-Reported Health Status Associated with Mortality after Total Hip Replacement? Int J Environ Res Public Health. 2017;14(8).

117. Judge A, Cooper C, Williams S, Dreinhoefer K, Dieppe P. Patient-reported outcomes one year after primary hip replacement in a European Collaborative Cohort. Arthritis Care Res (Hoboken). 2010;62(4):480–8.

118. Behrend H, Giesinger K, Giesinger JM, Kuster MS. The "forgotten joint" as the ultimate goal in joint arthroplasty: validation of a new patient-reported outcome measure. J Arthroplasty. 2012;27(3):430–6 e1.

119. Anand R, Graves SE, de Steiger RN, Davidson DC, Ryan P, Miller LN, et al. What is the benefit of introducing new hip and knee prostheses? The Journal of bone and joint surgery American volume. 2011;93 Suppl 3:51–4.

120. Nieuwenhuijse MJ, Nelissen RG, Schoones JW, Sedrakyan A. Appraisal of evidence base for introduction of new implants in hip and knee replacement: a systematic review of five widely used device technologies. BMJ. 2014;349:g5133.

121. Renner L, Janz V, Perka C, Wassilew GI. What do we get from navigation in primary THA? EFORT Open Rev. 2016;1(5):205–10.

122. Banerjee S, Cherian JJ, Elmallah RK, Pierce TP, Jauregui JJ, Mont MA. Robot-assisted total hip arthroplasty. Expert Rev Med Devices. 2016;13(1):47–56.

123. Lopez-Lopez JA, Humphriss RL, Beswick AD, Thom HHZ, Hunt LP, Burston A, et al. Choice of implant combinations in total hip replacement: systematic review and network meta-analysis. BMJ. 2017;359:j4651.

124. J. Kärrholm HL, H. Malchau, M Mohaddes, C. Rogmark, O.Rolfson. The Swedish Hip Arthroplasty Register. Annual Report 2015. 2016:98–9.

125. Gwam CU, Mistry JB, Mohamed NS, Thomas M, Bigart KC, Mont MA, et al. Current Epidemiology of Revision Total Hip Arthroplasty in the United States: National Inpatient Sample 2009 to 2013. J Arthroplasty. 2017;32(7):2088–92.

126. Thien TM, Chatziagorou G, Garellick G, Furnes O, Havelin LI, Makela K, et al. Periprosthetic femoral fracture within two years after total hip replacement: analysis of 437,629 operations in the nordic arthroplasty register association database. The Journal of bone and joint surgery American volume. 2014;96(19):e167.

127. Pedersen AB, Mehnert F, Havelin LI, Furnes O, Herberts P, Karrholm J, et al. Association between fixation technique and revision risk in total hip arthroplasty patients younger than 55 years of age. Results from the Nordic Arthroplasty Register Association. Osteoarthritis Cartilage. 2014;22(5):659–67.

128. Golightly YM, Allen KD, Nyrop KA, Nelson AE, Callahan LF, Jordan JM. Patient-Reported Outcomes to initiate a provider-patient dialog for the management of hip and knee osteoarthritis. Seminars in Arthritis and Rheumatism. (0).

129. Jansson KA, Granath F. Health-related quality of life (EQ-5D) before and after orthopedic surgery. Acta Orthop. 2011;82(1):82–9.

130. Lie SA, Engesaeter LB, Havelin LI, Gjessing HK, Vollset SE. Mortality after total hip replacement: 0–10-year follow-up of 39,543 patients in the Norwegian Arthroplasty Register. Acta Orthop Scand. 2000;71(1):19–27.

131. Cordtz RL, Zobbe K, Hojgaard P, Kristensen LE, Overgaard S, Odgaard A, et al. Predictors of revision, prosthetic joint infection and mortality following total hip or total knee arthroplasty in patients with rheumatoid arthritis: a nationwide cohort study using Danish healthcare registers. Ann Rheum Dis. 2017.

132. Garland A, Gordon M, Garellick G, Karrholm J, Skoldenberg O, Hailer NP. Risk of early mortality after cemented compared with cementless total hip arthroplasty: a nationwide matched cohort study. Bone Joint J. 2017;99-B(1):37–43.

133. Abrahamsen B, Osmond C, Cooper C. Life Expectancy in Patients Treated for Osteoporosis: Observational Cohort Study Using National Danish Prescription Data. J Bone Miner Res. 2015;30(9):1553–9.

134. Qu X, Huang X, Jin F, Wang H, Hao Y, Tang T, et al. Bone mineral density and all-cause, cardiovascular and stroke mortality: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;166(2):385–93.

135. Lindgren V, Garellick G, Karrholm J, Wretenberg P. The type of surgical approach influences the risk of revision in total hip arthroplasty: a study from the Swedish Hip Arthroplasty Register of 90,662 total hipreplacements with 3 different cemented prostheses. Acta Orthop. 2012;83(6):559–65.

136. Hunt LP, Ben-Shlomo Y, Clark EM, Dieppe P, Judge A, MacGregor AJ, et al. 90-day mortality after 409,096 total hip replacements for osteoarthritis, from the National Joint Registry for England and Wales: a retrospective analysis. Lancet (London, England). 2013;382(9898):1097–104.

137. Lantz PM, House JS, Lepkowski JM, Williams DR, Mero RP, Chen J. Socioeconomic factors, health behaviors, and mortality: results from a nationally representative prospective study of US adults. Jama. 1998;279(21):1703–8.

138. Krueger PM, Tran MK, Hummer RA, Chang VW. Mortality Attributable to Low Levels of Education in the United States. Plos One. 2015;10(7):13.

139. Shor E, Roelfs DJ, Curreli M, Clemow L, Burg MM, Schwartz JE. Widowhood and Mortality: A Meta-Analysis and Meta-Regression. Demography. 2012;49(2):575–606.

140. Hu Y, Goldman N. Mortality Differentials by Marital Status: An International Comparison. Demography. 1990;27(2):233–50.

141. Philipov D, Scherbov S. Differences by union status in health and mortality at older ages: Results for 16 European countries. Demographic Research. 2016;35(19):535–56.

142. Sharabiani MTA, Aylin P, Bottle A. Systematic Review of Comorbidity Indices for Administrative Data. Medical Care. 2012;50(12):1109–18.

143. Bulow E, Rolfson O, Cnudde P, Rogmark C, Garellick G, Nemes S. Comorbidity does not predict long-term mortality after total hip arthroplasty. Acta Orthop. 2017:1–6.

144. Dieppe P, Lim K, Lohmander S. Who should have knee joint replacement surgery for osteoarthritis? International Journal of Rheumatic Diseases. 2011;14(2):175–80.

145. Jevsevar D, Bozic K. Orthopaedic Healthcare Worldwide: Using Clinical Practice Guidelines in Clinical Decision Making. Clin Orthop Relat Res. 2015:1–3.