The clinical utility of patient-reported outcome measures in total hip replacement and lumbar spine surgery

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List of papers

This thesis is based on the following papers:

I. Low back surgery prior to total hip replacement is associated with worse patient-reported outcomes
Eneqvist T, Nemes S, Brisby H, Garellick G, Fritzell P, Rolfson O.
Bone Joint J. 2017 Jun;99-B(6):759–765.

II. Patients with a previous total hip replacement experience less reduction of back pain following lumbar back surgery
Eneqvist T, Bülow E, Nemes S, Brisby H, Garellick G, Fritzell P, Rolfson O.
J Orthop Res. 2018 Apr 12. [Epub ahead of print]

III. Does the order of total hip replacement and lumbar spine surgery influence patient-reported outcomes?
Eneqvist T, Nemes S, Brisby H, Garellick G, Fritzell P, Rolfson O.
In Manuscript

IV. Can patient-reported outcomes predict reoperations after total hip replacement?
Eneqvist T, Nemes S, Bülow E, Mohaddes M, Rolfson O.
Int Orthop. 2018 Feb;42(2):273–279.

V. How do EQ-5D-3L and EQ-5D-5L valuations compare in a Swedish total hip replacement population?
Eneqvist T, Nemes S, Kärrholm J, Burström K, Rolfson O.
In Manuscript

Abbreviations

Abbreviation	*Definition*
C	Concordance index
CT	Computed tomotography
EQ	EuroQol
HRQoL	Health-related quality of life
LBP	Low back pain
LSS	Lumbar spine surgery
LSSS	Lumbar spinal stenosis surgery
MCID	Minimal clinical important difference
MDC	Minimal detectable change
MID	Minimal important difference
MRI	Magnetic resonance imaging
OA	Osteoarthritis
ODI	Oswestry Disability Index
OLS	Ordinary least squares
PIN	Personal identity number
PRO	Patient reported outcome
PREM	Patient-reported experience measurements
PROM	Patient-reported outcome measurement
RCT	Randomized clinical trial
SD	Standard deviation
SHAR	Swedish Hip Arthroplasty Register
THR	Total hip replacement
TTO	Time trade off
VAS	Visual analog scale

Abstract

Background

Beginning in the late 1990s, the Swedish Hip Arthroplasty Register (SHAR) and the Swespine have successfully implemented programs to collect patient-reported outcomes measures (PROMs). The use of PROMs has enabled assessment of patients' health-related quality of life (HRQoL), physical function and pain following total hip replacement (THR) and lumbar spine surgery (LSS). The nationwide collection of PROMs has made it possible to evaluate changes of care, compare providers, investigate factors influencing outcomes that matter for patients, and it has contributed to improvement in clinical practice.

Objective

The overall objective of this thesis is to investigate different ways to utilize PROMs following total hip replacement and lumbar spine surgery. Specifically, this thesis aims to:

- Investigate PROMs in patients who have undergone LSS prior to THR and in patients who have undergone THR prior to LSS compared to matched patients with isolated THR or LSS.
- Investigate if the order of THR and LSS affects PROMs one year following the last procedure in patients with both procedures performed within a period of two years.
- Investigate if PROMs can predict the risk for reoperation following THR.
- Assess the measurement properties of EQ-5D-5L compared to EQ-5D-3L in a Swedish THR population and to estimate how different severity levels of the two versions of the questionnaire conforms.

Patients and methods

For Paper I-III, data including PROMs on patients with THR and LSS performed in 2002–2012 were obtained from SHAR and Swespine and linked to identify those who occurred in both registers. In Paper IV, data from SHAR on patients with THR in 2002–2014 were used to establish the relationship between PROMs and reoperation. For Paper V, patients eligible for THR in western Sweden during 2015 were invited to answer EQ-5D-3L and EQ-5D-5L with a two-week separation before and after surgery. Logistic and linear regression analyses were used to investigate research questions.

Results

Patients with both THR and LSS performed had worse one-year PROMs following the last procedure compared to patients with surgery in only one location. Patients eligible for both THR and LSS within a short period of time had better outcomes following the last procedure if surgery started with LSS. PROMs collected one year following THR predicted the risk of subsequent reoperation. Patients frequently utilized the additional response options of EQ-5D-5L and ceiling effects at the one-year follow-up were reduced compared to EQ-5D-3L. EQ VAS estimates for different severity levels conformed well between questionnaires.

Conclusion

This thesis contributes to the understanding of patient-reported outcomes for patients who undergo both THR and LSS. Given their ability to predict reoperations following THR, PROMs can be utilized to identify patients at increased risk, which may may be used to improve follow-up routines and care. Since EQ-5D-5L better describes health-related quality of life in THR patients, the introduction of the extended questionnaire as a standard tool in SHAR will enable a more accurate assessment of the procedure.

Introduction

For many years to come the number of primary total hip replacements and lumbar spine surgeries will continue to increase, not only in Sweden but also in a global perspective (1, 2). Several factors are able to explain this increase. Improved implant technology and surgical techniques make surgical procedures available for both older and younger patients. Due to improvements in general medical practice and educational level, the general health is improving resulting in increased life span, an increasing population and increased demand for these surgical procedures.

Both hip osteoarthritis and spinal stenosis are common degenerative diseases in the general population. Subsequently, the concurrence of these musculoskeletal disorders is commonly encountered in clinical practice. Hip osteoarthritis and spinal stenosis often present with similar symptoms, which may make it difficult to determine the origin of pain. The "hip-spine syndrome" was first described by Ofierski et al in the late 1970s. ref (72–75) Due to the increasing life span of the population, more and more people are likely to need total hip replacement (THR) and lumbar spine surgery (LSS) in one or both locations over time. In the presence of concurrent symptomatic conditions in the hip and lumbar spine, the location with which to begin has long been the subject of debate. Knowledge about the outcome in patients in whom both procedures are performed is limited.

For patients with hip osteoarthritis where non-surgical treatment is ineffective, total hip replacement is a well-established and cost-effective treatment. The survival of some prosthetics has been reported to be above 95% at 10-years follow-ups. Since complications are uncommon after THR, few patients require reoperation following a standard THR procedure. Most providers of joint replacement surgery have abandoned regular follow-ups after routine THRs. Unfortunately, an important minority operated with THRs will experience complications, and some will need reoperation due to early or late complications. An event of this kind might be devastating for the individual patient, often resulting in impaired function and disability (3–5). In addition, these events are very costly to society and the health care system. The opportunity to detect patients running a higher risk of reoperation could possibly reduce the suffering and costs associated with patients with complications following THR.

Patient-reported outcome measures (PROMs) are essential tools in the assessment of outcomes following THR procedures (6). One of the most commonly used health-related quality of life (HRQoL) instruments is the original three level form of the EQ-5D, the EQ-5D-3L (7, 8). However, the EQ-5D-3L has been questioned due to its low sensitivity and the lack of descriptive richness, which has been shown following THR in several studies (9, 10). In response to this critisism of the EQ-5D-3L, a five level version of the questionnaire has been developed, the EQ-5D-5L, which expands the range of responses in each of the five dimensions from three to five levels (11). However, the usefulness of the 5L version has not yet been established among Swedish THR patients.

Papers I-III presented and discussed in this thesis aim to use PROMs to explore the outcome following surgery in patients who undergo both THR and LSS and to investigate differences in patient-reported outcomes depending on the order in which surgeries were performed. Paper IV aims to investigate whether PROMs one year postoperatively are able to predict the patients who run a higher risk of reoperation. The last paper (V) compares the new version of the PROM instrument, the EQ-5D-5L, with the EQ-5D-3L in a Swedish total hip replacement population.

Background

Total hip replacement

Hip osteoarthritis (OA) is a common degenerative disease primarily affecting the aging population. In Sweden, the prevalence has been estimated at 10% in those over 85 years but only at 1% in patients under 55 (12). Other reports indicate a significantly higher prevalence of hip OA; 27% in individuals over 45 on plain radiographs (13). The natural course of hip OA is progressive with the loss of cartilage in both the caput femoris and acetabulum. As the chronic and irreversible degenerative progress continues, subchondral cysts and osteophytes may develop. Typical symptoms of hip OA are pain on activity and stiffness of the affected hip. However, pain generated from the hip may present in different ways, such as groin pain, radiating pain down the leg towards the knee, buttock pain, or pain radiating towards the back. The appearance of pain can also differ. Some patients experience only pain on movement, while others have pain at rest, or even sleep-depriving pain. The majority of patients also often suffer from reduced mobility, caused by pain and stiffness.

Diagnostics

Since hip OA presents with different symptoms, diagnosing needs to be individualized to some extent. Symptoms of hip OA may for instance be present with or without minimal radiographic findings. On the other hand, radiographic findings may be present without causing symptoms. Different sources of information must therefore be considered for the assessment. They include the anamnestic information on symptoms, plain radiographs and/or other imaging technology. There are several other disorders, such as degenerative lumbar diseases or knee OA that can mimic hip OA symptoms, and this should be taken into account before making a diagnosis of hip OA.

Treatment

The first line of treatment is non-surgical including physiotherapy, analgesics and information. If non-surgical treatment fails, the alternative is surgery. In 2016, 17,000 THRs were performed in Sweden, and the vast majority were due to OA. This surgical treatment of hip OA consists of irreversible replacement of the femoral head and the acetabulum with an artificial ball-and-socket joint. Sir John Charnley pioneered this procedure in the 1960s. The excellent post-operative results and the cost effectiveness of THR, this procedure has been regarded as "the operation of the century" (14, 15). Several studies and arthroplasty registers have reported the survival of some prostheses at above 95% at 10 years (16, 17). Even if it is called "the operation of the century", it is not a risk-free procedure. A systematic review concluded that the average 90-day mortality after THA was 0.7% (18). THR for hip OA is an elective procedure to relieve pain and improve mobility and HRQoL. As a result, expectations of the outcome are reasonably high. Hip OA is not a life-threatening diagnosis, THR should therefore only be offered to those who will most likely benefit from the procedure.

Reoperation of total hip replacement surgery

Although the majority of THR patients will live the remainder of their lives without requiring further surgery, some patients will need a reoperation due to early or late complications. These complications could be loosening, infection, fracture or dislocation of the prosthesis (16). Every year in Sweden, about 2200 reoperations are performed on patients with THR (16). The SHAR defines a reoperation as any further surgery performed on the hip. A revision is a reoperation in which any implant components are exchanged, removed or added. Examples of reoperations that are not revisions are open reduction, soft-tissue repair, debridement without exchanging implant parts, the removal of heterotopic bone formation and the relief of hemorrhage. Generally, reoperations result in impaired function and disability and constitute a risk factor for repeat surgical interventions (3–5). The result following revision surgery are less likely to be as successful as the first operation (19). In addition, these events are very costly, in terms not only of medical costs but also of the costs of loss of productivity related to patients' loss of working capacity. It is therefore of the utmost importance to minimize the risk of these events.

The need for routine follow-ups and prediction of reoperation

As the incidence of primary THRs is rising and complications are uncommon following THRs, few patients need a reoperation following a standard THR. The increasing numbers of THRs produces an increasing number of follow-ups, at an increasing cost. Those complications that do occur following THRs are often of an acute nature and cannot be foreseen on a return visit. The need for follow-ups after standard THRs for all patients has therefore been questioned (20, 21). As a result, many

health-care providers have abandoned routine follow-ups after standard THRs. However, some complications, such as loosening of the prosthesis, may be symptomatic and could possibly be detected at follow-up visits. Some complications require less extensive interventions if they are detected at an early stage. Follow-up visits may also constitute an important function in identifying issues such as degenerative spinal conditions, contralateral hip disease, poor strength, limited hip range of motion and impaired walking ability eligible for physiotherapy or further surgical interventions. Although routine follow-ups for all patients are not justifiable, it is desirable to develop measures to identify patients running a higher risk of complications, so they can be called to follow-ups. Considering the extensive research on risk factors for reoperation following THR, it is feasible to establish methods to identify high-risk patients. These instruments could potentially include patient-related factors (22–25), implant- and surgical procedure-related factors (24, 25) and PROMs (26–28). Automated and individualized assessment of variables associated with the risk of reoperations could be used to detect patients that would potentially benefit from monitoring. However, no models that have a specificity high enough to be used in a clinical setting are as yet available.

Low back surgery

Lumbar spinal stenosis, spondylosis/spondylolisthesis and segment-related pain are degenerative low back diseases primarily affecting the aging population. LSS is the most common of these diagnoses and its prevalence has been estimated at up to 60% among patients over the age of 60 on magnetic resonance imaging (MRI) (29). The prevalence of these diagnoses is increasing in Sweden, just as it is in the rest of the developed countries. The reason for this increasing trend is probably that these diagnoses are being more commonly diagnosed among the population. This is probably due to multiple reasons. In part, it could reasonably be explained by a change in the demographic situation, with an older age structure among the population, and that symptoms of these diagnoses are not accepted as before, since the population imposes increasingly higher demands on physical activity at an older age. Another reason for the increasing trend for these diagnoses could perhaps be the increasing availability of MRI. In some cases, lumbar spinal stenosis will require surgical intervention as a final treatment (30). In Sweden, the annual rate of surgery due to these diagnoses is close to 55–60 per 100,000 inhabitants and in the past decade there has been a yearly increase of 5–10% according to the Swedish Spine Register, Swespine (2, 31). In the US, 14 per 10,000 inhabitants over the age of 65 undergo lumbar spinal stenosis surgery (LSSS) each year, which represents a fourfold increase since 1985. LSSS has become the most common indication for spinal surgery in Sweden and in other European countries (31–34).

Symptoms and diagnosis

The symptoms of lumbar spinal stenosis are caused by a narrowing of the spinal canal, compressing the neural structures as the nerve roots leaving the spinal cord. This narrowing is caused anteriorly by a bulging disc, dorsally by a thickening of ligamentum flavum and laterally by osteophytes derived from osteoarthritic changes in the joint facets (35, 36). Another contributory factor to stenosis can be degenerative spondylolisthesis. This is caused by an ongoing degenerative process of the lumbar spine segments that can lead to a forward slip of the adjacent upper vertebra (37). The symptoms of lumbar spinal stenosis and other degenerative disorders affecting the lumbar spine are characterized by back pain, numbness, or radiating pain to the buttocks and lower extremities, as well as muscle weakness. At a later stage, walking disability may also appear (38, 39). The symptoms are often referred to as pseudoclaudicatio or neurogenic claudication, and need to be distinguished from genuine claudicatio or claudicatio intermittens caused by arterial insufficiency. Lumbar spinal stenosis symptoms may mimic pain caused by hip and knee joint disorders or polyneuropathy. These differential diagnoses should be taken into consideration when determining the cause of symptoms. As the conditions causing lower limb pain often coincide and contribute individually to the range of symptoms a patient may experience, it is a diagnostic challenge to differentiate the origin of the different pain components. While anamnestic information is of the greatest importance in diagnosing these disorders, a diagnosis of lumbar spinal stenosis requires image-technology confirmation. MRI is now the method of choice and should be used, taking absolute and relative contraindications (for example a pacemaker, ear implant, or claustrophobia) into consideration. The grade of lumbar spinal stenosis can be determined by using the Schizas 7-grade classification which is based on the morphology of the dural sac as observed on MRI based on the rootlet/cerebrospinal fluid ratio (40). The grade of lumbar spinal stenosis can also be measured with a cross section of neural structures of the spinal canal were 75mm^2 or less has been shown to correlate with clinical symptoms, and is considered a confirmation of lumbar spinal stenosis (41). If MRI is contraindicated a combined examination with CT (computed tomography) and myelography can be performed to make a correct diagnosis of lumbar spinal stenosis.

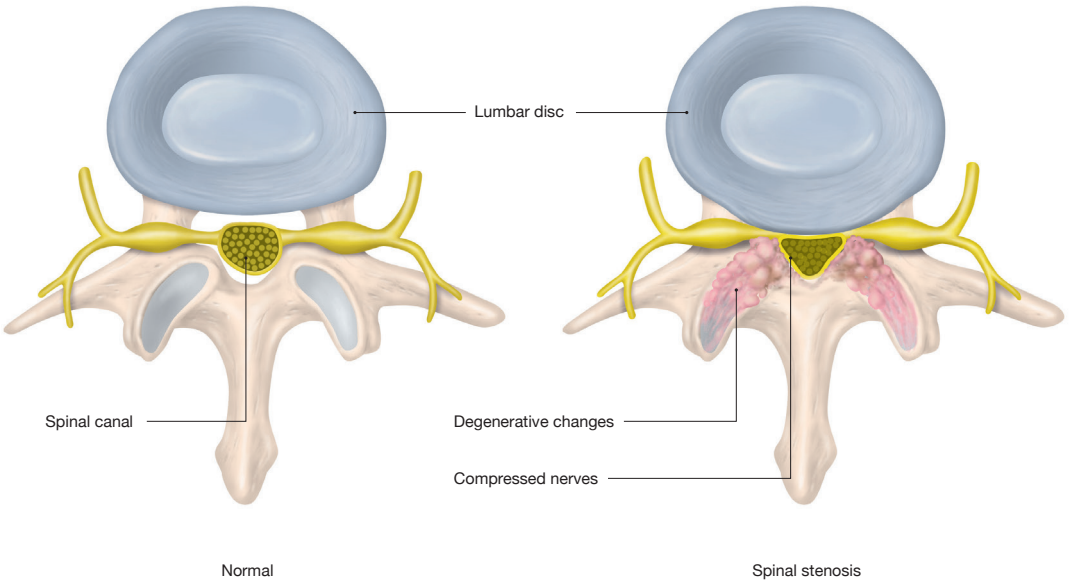


Figure 1. Pictures presenting normal spinal canal and spinal stenosis.

Surgical and non-surgical treatment

The treatment of degenerative diseases of the lumbar spine such as spinal stenosis may consist of physical activity and patient education, epidural joint injections, or surgical intervention. There is no strong evidence of any long-term effects of steroid epidural joint injections (42). Physiotherapy has been shown to postpone surgery by four to six months (43, 44), but there are no studies presenting physical treatment as a long-term solution. There is evidence that surgery is a better long-term alternative compared with non-surgical treatment (45–48). The surgical treatments of these degenerative diagnoses of the lumbar spine is decompression or decompression and fusion of the affected segment. Decompression aims to ease pressure on the neural elements in the stenotic spinal canal. Since the description of pedicle screws by Roy-Camille et al. in 1970 (49), the use of the pedicle instrumentation of affected segments to achieve fusion has gradually increased and it is now used routinely in spinal surgery.

Fusion vs non-fusion

The significance of instrumentation with pedicle screws in relation to the healing rate of spinal fusion has been a subject of debate. Two studies reported no differences in healing rates of instrumented and non-instrumented fusions (50, 51). However, other research reported significant increases in fusion healing for instrumented fusions in clinical and animal studies (52–54). A Cochrane review from 2006 claimed strong evidence of higher fusion rates for instrumented fusion compared with non-instrumented fusion (55). It has been debated whether decompression causes instability of the spine (56, 57). To prevent instability, it has therefore been customary to perform fusion as a complement to decompression, particularly in the presence of degenerative spondylolisthesis. However, according to a recent randomized clinical trial by Försth et al., fusion as a complement to decompression does not lead to better post-operative results or cost-effectiveness compared with decompression alone. These findings were true even in the presence of degenerative spondylolisthesis preoperatively (58, 59). In a study of biomechanics, Försth et al. found that the potential instability caused by decompression was minimal and removal laminectomy did not result in increased instability compared with bilateral laminectomy (60). They suggested that the main principle of LSSS should consist of decompression alone, even if degenerative spondylolisthesis is present pre-operatively.

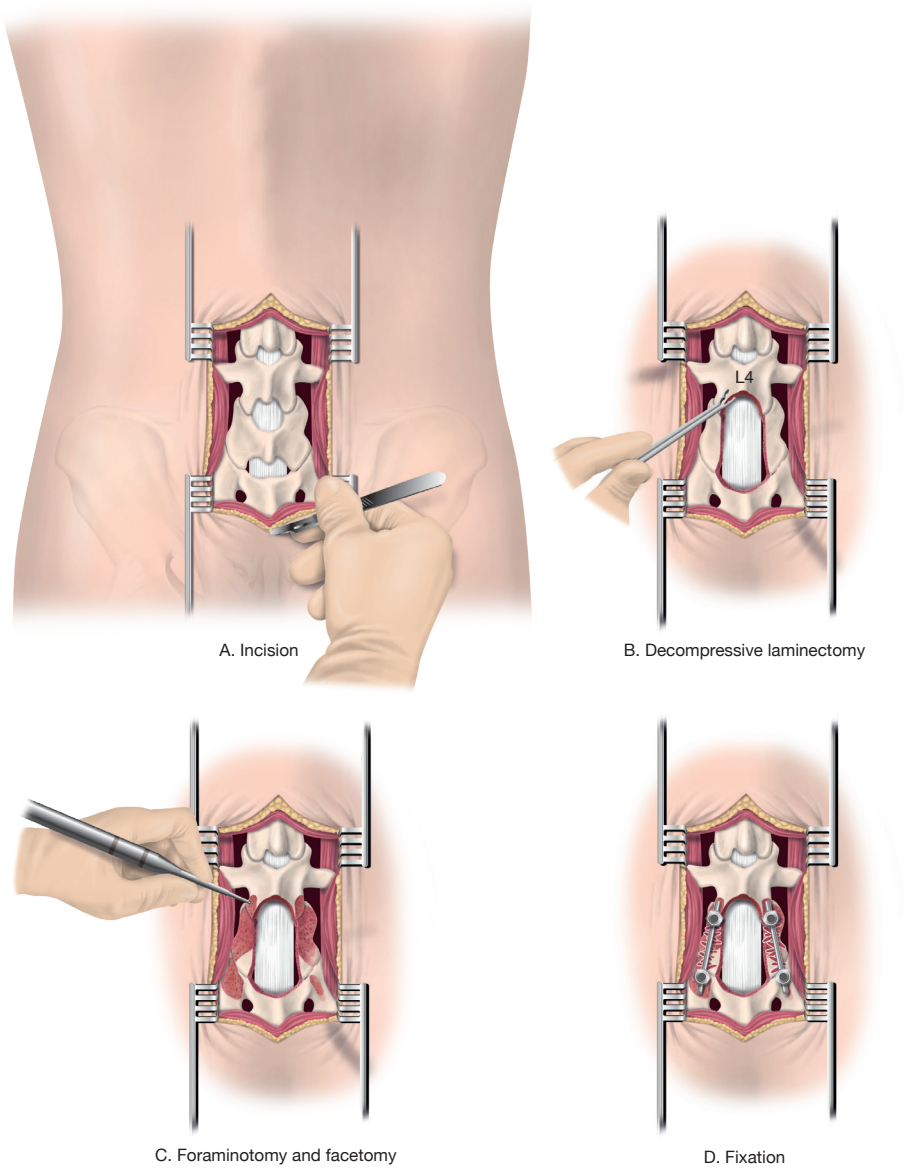


Figure 2. Pictures presenting decompressive and fusion surgery.

Complications following LSSS

Surgical procedures for lumbar spinal stenosis are considered safe, with a reported mortality within 90 days of 0.3–0.4% (61–63). However, there are other risks following LSSS. In a systematic review, the risk of surgical complications (nerve root injury, cauda equinae damage, bleeding in the spinal canal, dura lesion and wound infection) were reported in approximately 5–10% and general medical complications (anaesthesiological, cardiovascular, pulmonary, cerebral, kidney/urinary, and liver/GI) were reported in about 3% of cases (64). A dura tear resulting in cerebral spinal fluid leakage has been reported at even higher levels of 2.1–16% (65–69). Lumbar spinal stenosis surgery is not a lifesaving procedure, the goal is to maintain or increase activity levels, relieve pain and restore health-related quality of life (HRQoL). The decision to proceed with surgery should therefore only be made if the patient has a substantial impairment and conservative treatment fails to control symptoms.

Hip-spine syndrome

Up to 27% of patients over 45 years have signs of hip OA on plain radiographs (13) and 60% of patients over 60 have signs of lumbar spinal stenosis on magnetic resonance imaging (MRI) (29). Due to the high prevalence of these degenerative diseases of the hip and lumbar spine, it is not surprising that the prevalence of coexisting degenerative lumbar spine disorders has been estimated at up to 18% among a THR-population (70). Similarly, among patients eligible for lumbar back surgery, the prevalence of osteoarthritis of the hip or knee has been reported at 10% (71). The combination of degenerative disorders of the hip and lumbar spine is known as the "hip-spine syndrome" and was first described by Ofierski et al. in 1976 (72–75). These degenerative diseases may cause similar symptoms, which make determining the origin of pain in clinical practice and assessing of how these conditions contribute to symptoms problematic, as well as differentiating them from other diseases with similar symptoms, such as arterial insufficiency and polyneuropathy.

Surgical outcome

In general, lumbar spine surgery and hip replacement are well-investigated interventions and the evidence of their effectiveness in reducing pain and restoring mobility is comprehensive. However, there is some variation in outcomes and a great deal of research has focused on exploring factors associated with better and worse results. Increased comorbidities affecting mobility and combinations of degenerative musculoskeletal disorders have been shown to be associated with poorer outcomes following surgery. Comorbidities are defined as patient conditions or diseases not associated with the development or cause of the immediate disease of interest. Comorbidities can be diagnosed at different points in time, which may lead to different associations with the risk of adverse outcomes (76, 77). Since musculoskeletal comorbidity is associated with worse patient-reported outcomes following THR (78), patients with hip-spine syndrome are expected to have poorer outcomes after THR compared with patients with an isolated degenerative hip disorder. There are reports of low back pain prior to THR being associated with poorer outcome and function following surgery (79, 80). Patients with a known degenerative disease in their lumbar spine have worse outcomes in terms of function, physical-status, activity-levels and satisfaction after THR (81). Furthermore, THR patients who had been diagnosed with lumbar spine disorders experienced less improvement in function and pain compared with patients without a history of lumbar spine disorder (5). Similarly, several studies report poorer outcomes following LSS in the presence of preoperative conditions affecting walking capacity, such as hip osteoarthritis (71, 82–85). Reversely, LSS with the absence of comorbidity and disorders affecting walking capacity prior to LSS are associated with better functional outcomes and pain relief (85, 86). However, the knowledge of the outcome following THR and LSS in patients with both procedures performed is limited.

Where to perform surgery first: the hip or the spine?

For years, there has been an ongoing discussion about whether to perform surgery on the hip or spine for patients with hip-spine syndrome. Some argue that THR should be performed first because of its reliable effectiveness (74). One argument in favor of starting with THR is its association with reduced back pain and the fact that residual symptoms may be effectively treated with subsequent lumbar spine surgery (70, 73–74, 87–90). Others favor LSS initially because of the risk of contraction of the spinal nerve roots during the THR procedure, which may cause nerve damage (91, 92). Previous research is therefore inconclusive and somewhat conflicting.

Pain caused by degenerative disease in the hip and lumbar spine

Pain is a complex and subjective experience that could be suspected to affect everyone at some time during a life span. When discussing pain from hip OA and spinal stenosis, both acute and chronic pain needs to be considered, as well as pain arising from nociceptive- and neuropathic pathways.

Acute and chronic pain

Physiologically acute pain is meant to serve as an internal alarm system helping us to react to external dangers in our environment or to internal dangers caused by potentially harmful changes in our bodies. Chronic pain, on the other hand, is always maladaptive and the continuous somatosensory and emotional burden can seriously affect the sufferers quality of life (93). Although chronic pain is a characteristic of many different diseases, hip OA and low back pain as a part of spinal stenosis are two of the most predominant, putting them among the leading causes of disability worldwide (93, 94).

Nociceptive and neuropathic pain

Nociceptive pain is defined as pain arising from actual or threatening damage to non-neural tissue and it is due to the activation of nociceptors (95), or as pain attributable to the activation of the peripheral receptive terminals of primary afferent neurons in response to noxious chemical, mechanical, or thermal stimuli (96). For clinical purposes, the term nociceptive pain can be used when pain is proportional to nociceptive input, and the term is designed to contrast with neuropathic pain. The latter is defined as pain caused by a primary lesion or disease of the somatosensory nervous system (95). Pain in hip OA is mostly caused by nociceptive pain, but up to 23% of patients also have neuropathic pain (97). Within the low back pain population lumbar radiculopathy is a common type of lumbar neuropathic pain, while myofascial tissue (i.e. thoracolumbar fascia) (98) and some lumbar ligaments (99) contain nociceptors capable of generating nociceptive pain. For patients with lumbar spinal stenosis, neuropathic pain have in general been reported to be present in more than one third, and for those patients with radicular pain neuropathic pain has been reported to be present in more than two thirds (100). Because of the high concentration of nociceptors in somatic tissues, chronic somatic pain is typically well localized and often results from degenerative processes (such as arthritis). However, around 15–25% of patients with chronic pain are thought to have neuropathic pain (101).

Pain referral pattern

Pain arising from both osteoarthritis of the hip and lumbar spinal stenosis has complex pain referral patterns. Pain arising from both locations has been shown to be present in several locations other than just the hip or spine. There are several studies describing the pain referral patterns from both the lumbar spine (95, 102) and hip OA (103, 104). The distribution patterns for the pain are similar in, for example, the buttocks, anterior and posterior thigh, groin, low back and knee. Hip OA has previously been thought not to radiate below the knee and that groin pain is associated with hip OA. However, these symptoms have been proved to originate from both locations (104). Due to the difficulty involved in determining the origin of pain, diagnostic tests such as intraarticular injection of the hip joint or spinal nerve root block with local anesthetics have been recommended (75, 91, 102, 105, 106).

Orthopedic registers

National prospective observational registers

National quality registers have three main objectives: to monitor outcomes, stimulate to improvement activities and to facilitate research. Since the SHAR registers type of the prosthesis used in detail, implant surveillance is a fourth important objective. The national quality registers enables studies to determine the demography of the population with certain conditions or undergoing a specific procedure. The opportunity to obtain large sample sizes provides high statistical power. Together with the continuous validation of these registers, this provides for high reliability in the analyses of survival and outcome of implants and techniques. The large sample sizes and repeated validation processes in these registers enable certain confounders to be taken into consideration when determining whether differences

in outcomes are related to the implant or the technique in question. There are naturally data entry errors in all registers, but these have been proven to be minimal (16, 107). Because of prospective collection and continous validation procedures recall bias have been significantly reduced. When the registers are used for prospective observational register studies, the large sample sizes reduce selection bias and significantly reduce confounding bias and heterogeneity.

Stepwise introduction of new implants

Registers monitoring implant survival such as the SHAR also play an important role in the introduction of new prostheses and surgical techniques. It is preferable for the introduction of new technologies or techniques to be performed step-wise, starting with a small cohort which is closely observed to determine eventual early complications. This step is followed by larger multicenter studies and that new technologies or techniques are finally investigated in large scale prospective observational register studies (108). A step-wise introduction of this kind has the potential to eliminate failure at an early stage and prevents the premature introduction of new prostheses, technologies and techniques on a nationwide basis. It is, however, important to consider the last step in the introduction of observational register studies, which are by nature not designed to explain causation. Causation is determined through cohort and randomized controlled trials where causation can be determined.

PROMs and registers

Since their development, observational orthopedic registers have been used to monitor the survival of implants using revision as the endpoint. By doing this, the success of a prosthesis has been based upon the survival of the implant, the functional status performance assessed by the surgeon and plain radiographs. When measuring success in this way, interest focus not on the patient´s opinions of the outcome but on the surgeon's opinion of the outcome following surgery. The opinion of the patient is however most important, since the main indication for the procedure is pain and disability. However, in the last few decades this evaluation approach has shifted to measuring patient-reported outcomes. Ultimately, patients are uninterested in their x-rays, or whether their walking ability as assessed by the surgeon is judged as good, if they are still in pain and dissatisfied with the outcome of surgery. Patient-reported outcome measures (PROMs) provide another dimension to success following orthopedic surgery. PROMs measure not just pain and function but also the patients HRQoL, which can be used to calculate the cost effectiveness of procedures and techniques. PROMs also provide the opportunity to measure outcomes at both group and individual levels. Together with demographic and surgery-specific variables, PROMs enable further register developments aimed at optimizing the care of patients in need of orthopedic surgery.

Linkage of register databases

Personal identity numbers (PIN) are used as a common identifier in most registers in Sweden, in both orthopedic registers, such as SHAR or Swespine, and in other national health data sources, such as Statistics Sweden or the Prescribed Drug Register. This enables the linking of registers, which in turn offer an important opportunity not only to study and adjust for a number of confounders but also to add other outcome measures such as adverse events and sick leave.

The personal identity number

In 1947, the Swedish government introduced the personal identity number (PIN). The personal identity number is a unique 10-digit number. The first six digits contain the birth date (year, month and day). A hyphen separates them from the serial number made up of the three digits, where the third digit identifies the sex, odd numbers for males and an even number for females. The tenth and last digit is a control number. All citizens in Sweden have their own unique PIN. Since this has been used in the majority of health registers, research by register data has been very successful in Sweden. Using a personal identity number makes it possible to link data from different registers at individual level. By doing this, registers complement one another with data by reducing confounding and enabling more complex research questions.

Swedish Hip Arthroplasty Register

The Swedish Hip Arthroplasty Register (SHAR) began in 1979. Its purpose was to gather prospective observational data on all hip replacement surgery in Sweden at both publicly and privately funded hospitals. The data that are collected are used to compare results across providers and to monitor longitudinally outcomes of the procedures with the emphasis on implant types, surgical techniques, and complications. As the SHAR collects PROMs data continuously on the Swedish THR population both before and at one, six, and ten years after surgery, the register is able to attain a higher statistical power than a randomized controlled trial or data collected at a single hospital. Due to the large size and complete coverage, the register is also able to quickly identify complications associated with both implants and surgical techniques. Since 1992, all orthopedic clinics, both public and private, have reported their primary surgeries and subsequent reoperations to the SHAR. In the SHAR coverage is 100%, and the completeness of THR registrations has been reported as 98.1 % (16, 107).

PROMs in SHAR

In 2002, the SHAR launched a nationwide PROMs program for elective THR patients. The program reached full participation among Swedish orthopedic hospitals in 2008. The purpose of the program was to complement the traditional outcome variables, such as implant survival, with patient-reported outcomes relating to pain, function and health-related quality of life (6, 77). The PROMs program invites all patients scheduled for elective THR to participate. Patients are asked to complete a short questionnaire at their pre-operative visit. A follow-up survey to be answered manually is mailed to patients at one, six, and ten years post-operatively. Every month, the SHAR centrally distributes lists of patients that are to receive follow-up questionnaires to the orthopedic departments where specially trained secretaries at the departments are responsible for sending out questionnaires and reminders and entering data in the on-line PROM database. Response frequencies have been reported as 86% pre-operatively, and 90% at the one-year follow-up (6). The PROMs program comprises the EQ-5D health status questionnaire (109), a hip pain visual analog scale (VAS) (110) and at follow-up a VAS addressing outcome satisfaction. Additionally, the patient's musculoskeletal comorbidity is determined using the Charnley classification (111). The PROMs program in the SHAR is the voice of all patients operated with a THR. This information provides an excellent opportunity for developing improved healthcare and providing better outcomes for patients operated with a THR.

Swespine

The Swedish Spine Register (Swespine) was started in 1993. Its aim was to prospectively gather observational data on all surgical procedures on the spine performed in Sweden from both publicly and privately funded hospitals. As in the SHAR, the collected data are used to compare results across providers and to monitor longitudinally the outcomes of the procedure, focusing on surgical techniques and complications. The surgeon's contribution to the register is to make the diagnosis and classification, together with details of the surgical technique, implants and perioperative complications. The completeness of registrations to the Swespine has been reported as 85% (2). The unique personal identity numbers (PIN) given to all inhabitants in Sweden are used as identifiers.

PROMs in the Swespine

The PROMs included in the Swespine comprises questionnaires containing the EQ-5D-3L (112), the Oswestry Disability Index (ODI) (113), back and leg pain according to a visual analog scale (VAS) (110), and until recently the Short Form 36 (abbreviated health survey, SF-36) (114). Questionnaires are filled out at the pre-operative visit, or sent to patients prior to surgery. The same questionnaire, together with a questionnaire regarding satisfaction with the treatment, is filled out at follow-ups one, two, five, and ten years following surgery. The questionnaires are unrelated to any hospital visit, and are completed without the assistance of the surgeon or any other person involved in the treatment. The Swespine distributes lists of patients due to receive

follow-up questionnaires to the orthopedic departments and specially trained secretaries at the departments are responsible for sending out questionnaires and reminders and entering data in the online Swespine database.

Importance of register data quality

The quality of a register analysis or prospective register studies using register data depends largely on the quality of the data in the current registers database. There are five dimensions in particular that need to be take into consideration; validity and reliability, coverage and completeness and response rates. Both the SHAR and Swespine are continuously working on data validation. The SHAR does this by examining medical records from all reoperations. Once a year, all orthopedic departments are also requested to compare the register´s numbers with each local hospitals' patient administration system. The register online entry application also has a built-in warning system for incorrect entries such as the wrong PIN, paired side and implants. When it comes to the reliability of a register it is important that the variables that are included have high consistency or precision of the measuring instrument. The coverage of a register is simply calculated as the proportion of participating units compared with all units, where a high number is good. There are pitfalls to take into consideration, if the coverage is calculated as a possible coverage and not an actual coverage. The coverage is misleading and not a "true coverage", that should be on an individual procedure level. Completeness depends on that the respective participating unit's report at individual level. Both the SHAR and Swespine collaborate with the Swedish National Board of Health and Welfare which operates the National Patient Register based on PINs. Departments are required by law to report all medical interventions to the Patient Register. Each year a linkage between the Swedish Hip Arthroplasty Register and the Swespine respectively with the National Patient Register is performed. In this way registers completeness can be calculated at both departmental and individual level. The figures are published each year in respective registers Annual Reports and this has led to some out-liers rapidly improving their registration. Poor completeness may lead to flawed analyses and feedback will then be misleading, so, if some departments have low completeness they have usually improved their registration.

Prospective observational studies

Prospective observational studies such as register studies obtain data from groups who have or have not been exposed to the subject of interest. In these studies there are no interventions exposure by the researcher or anyone else. Prospective register studies are preferable when investigating the effects of predictive risk factors on an outcome. To study the effects of an intervention, randomized clinical trials (RCT) are the gold standard. In an RCT, the participants are assigned to either intervention or control/placebo, preferably using a blinded random selection. There are advantages and disadvantages to both types of study. In an RCT the advantages are the unbiased distribution of confounders, the opportunity to blind the researcher, and the fact that randomization enables statistical analyses. The advantages of observational studies are that they are ethically safe, less expensive, and require less administration than an RCT. RCTs often includes too few observations to investigate rare events. The larger amount of data is a strength of register studies together with the opportunity to match study groups. Register studies also investigate the performance or effect of an intervention in everyday practice, and not only in a specific clinical or laboratory environment. They therefore prevent performance biases and the results can often be generalized. The disadvantages of register studies are that there are no controls and that there may be hidden confounders. In observational studies such as register studies, there is also always the risk of bias: selection bias, detection bias, reporting bias and so on (115). There can also be problems achieving completeness and response rates that are needed for sufficient analyses. It has previously been stated that randomization is not possible in register studies, but there are now studies in which randomization occurs at registration and cluster randomization studies that also use registers. A well-performed example of a register RCT is the TASTE-study by the Swedish Coronary Angiography and Angioplasty Registry (116).

PROMs

PROs

A patient-reported outcome (PRO) is a patient's direct self-reported health status at any time, without external interpretation. However, outcomes do not necessarily have to be reported directly after an intervention: PROs can be presented at any time and represent the individual's valued feelings, functional ability, pain, and so on with respect to their health status at that particular moment.

PROMs

A patient-reported outcome measure (PROM) is a standardized instrument to measure PROs such as HRQoL, pain, functional impairment, or activity level. A PROM can be either generic or specific. A generic PROM

measures PROs not specific to treatment or disease and can be used to compare results across different populations and study groups, such as between different registers. The EQ-5D is an example of a generic PROM (7, 8). Specific PROMs measure constructs of health specific to a defined treatments or interventions, a disease or conditions, or specific body regions. These are important when investigating a specific outcome for a particular disease or following a treatment, but they cannot be used across areas other than those investigated. The Oxford Hip Score (117) is an example of a specific PROM.

Important factors of PROMs design

To analyze outcomes, PROMs must be valid and reliable. Other requirements for the instrument are a design providing for the highest possible response rate but at the same time sensitive enough to detect even small changes following a treatment or intervention. There is always the risk of floor or ceiling effects if patients choose to answer in the extreme when using scales such as a VAS or EQ-5D. It is therefore important that the instrument has enough levels to prevent these effects. Implementing PROMs to investigate any changes following a treatment or intervention is a delicate task. If the applied instrument is unable to detect changes, no reliable analyses are possible. However, if there are too many questions, the response rate will also be too low for a reliable analysis.

Interpreting PROMs

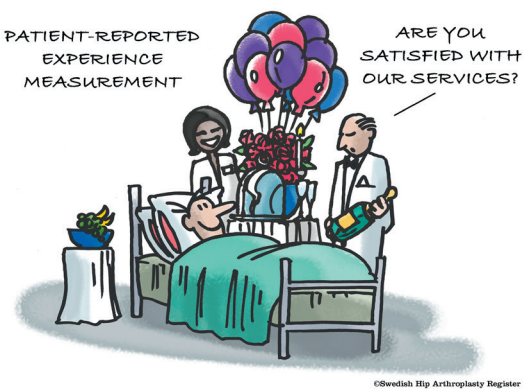
There are also several considerations when interpreting PROMs, besides the risk of floor or ceiling effects. Scores from the same instrument may vary between populations. For instance, there are several national value sets for the EQ-5D index, which is a weighted measure. These value sets are specific to the nation's cultural norms and are based on studies of the general population using time trade-off or VAS studies. Populations may value measured areas differently because of cultural differences. To account for these differences, national value sets weight the patient's responses differently. As a result, comparisons of PROMs such as the EQ-5D between nations are difficult, and imply that trends, rather than exact values, need to be taken into account. It may also be difficult to decide whether changes measured following a treatment or an intervention actually are big enough to represent a clinically relevant difference.

Minimal important difference

As PROMs have become a tool that is frequently used by both clinicians and decision makers in the assessment and comparison of treatments and interventions, there is a need to determine the level of change that constitutes a minimal important difference (MID). Several methods with similar denominations (e.g. minimal clinical important difference, MCID and minimal detectable change, MDC) confirm clinical relevance and its usefulness for implementation in clinical practice (118). However, since these MID tools are specific to different PROMs, conditions, interventions and populations, there are no standard MIDs. MIDs therefore needs to be interpreted with caution and should take account of measurement error for the PROM. One example of this is the MDC90, which is an MDC estimate with a confidence level of 90% (119, 120). Further, MIDs calculated from individual responses may not be able to be translated into changes measured at population level. One example is, if an MID value is established at patient level and the average change for a population is below that MID value, the distribution of change is then more important than the average change. A distribution with a narrow change probably indicates ineffective treatment. However, a broad distribution of change indicates that treatment was probably either beneficial or harmful to some portion of the population (121). MID values can be difficult to interpret and misunderstandings of their implications for a population level compared with a patient level occur frequently. Small changes at population level are easily dismissed as clinically irrelevant when they may actually show significant differences following the treatment of a group within the larger population (122).

PREMs

Patient-reported experience measurements (PREMs) are not to be confused with PROMs. PREMs represent the patient experience of their care, not the outcome following an intervention. PREMs can provide a patient perspective on care and thus be useful for improvements at a single clinic (123), but their usefulness for national quality registers can be questioned. PREMs have not been used in any of the studies in this thesis.



The EQ-5D

One of the most commonly used health-related quality of life (HRQoL) instruments is the original three-level form of the EQ-5D, the EQ-5D-3L (7, 8). This is a short survey and it is recognized as valid in many populations and conditions, including THR populations (8, 112). The EQ-5D descriptive system includes five dimensions of health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is covered by one question with three levels of severity: no problems, moderate and severe problems. The descriptive system yields 243 possible health states. By applying weights from a specific value set, each health state can be transformed into a single index, which serves as an overall measure of HRQoL. There are different index value sets for different countries to reflect response norms for a given population.

Strengths and weaknesses of the EQ-5D

The EQ-5D questionnaire is short, making it easy to complete, thus contributing to high response rates. The nature of the EQ-5D makes it useful not only for comparing HRQoL between populations but also for calculating cost effectiveness between treatments or interventions. There are, however, limitations to the EQ-5D. The national value sets are specific to a nation's cultural norms based on studies of the general population using time trade-off or VAS studies. Populations may value measured areas differently because of cultural differences. To account for these differences, national value sets weight patient responses differently. As a result, comparisons of PROMs such as the EQ-5D between nations are difficult and this implies that trends rather than exact values should be taken into consideration. Moreover, when measuring a change over time or after an intervention, floor or ceiling effects may appear. If an individual has a high EQ-5D index prior to an intervention, there is little room for improvement, resulting in a ceiling effect. However, an individual with a low EQ-5D would have a much higher capacity for improvement. This creates strong dependence on the patient's status prior to an intervention to measure change the intervention brings about in the patient's HRQoL. Clustering has also been observed in the indices. For example, in the Swedish OA-population eligible for THR using the British value set, indices of 0.088 and 0.69 are very common (6).

There was no Swedish value set until 2014 when Burström et al. developed a Swedish value set using the time-trade off method (TTO) (124). For this reason, the register used the British value set. The index ranges from a minimum value of -0.594 to a maximum value of 1.0. Negative values through 0 represent the worst possible health state and 1 represents the best possible health state. Following a study in 2015 by Nemes et al. in which they stated that the Swedish value set was better suited to a Swedish THR population than the Brittish value set (125), the SHAR changed to the Swedish value set in 2016.

The survey also comprises a vertical visual analog scale (EQ VAS), where the patient describes their total health from 0 (worst) to 100 (best). The briefness and simplicity of the survey makes it a popular instrument for assessment (7). The EQ-5D-3L is a part of the standard follow-up procedures for patients both pre- and postoperative in several arthroplasty registries (6, 8, 9, 11, 126, 127). In 2002, the SHAR started to register PROMs using the EQ-5D-3L survey (16, 107).

EQ-5D 5L

The original version of the EQ-5D, the EQ-5D-3L, has been questioned, due to profound ceiling effects, low sensitivity and the lack of descriptive richness. As it has a limited ability to measure small yet clinically relevant changes in the outcome following interventions, its usefulness in assessing interventions has been debated (128–130). These limitations have been reported for both the general population and specific patient groups (128–132), including THR-populations (9, 10). Among THR patients, the EQ-5D-3L exhibits particularly difficulty in assessing outcome in the mobility dimension, where the options "no problems", "some problems" and "confined to bed" limits its use in describing the limitations in mobility commonly experienced by patients with hip disorders. These patients typically experience limping, a limited range of hip joint motion, impaired walking capacity and often require different aids for mobility, but they are seldom confined to bed. Similarly, the response levels of self-care and usual activities ("no problems", "some problems" and "unable") limit the range of responses for individuals with moderate to severe disability (10, 133, 134).

So, the EuroQol group has developed a new version of the questionnaire, the EQ-5D-5L, offering respondents five levels of responses instead of three: no, some, moderate, severe and extreme problems (11). In the three-level survey, a response of "no problems" in all dimensions would be notated as 11111 and "severe problems" as 33333. For the five-level survey, "no problems" in all dimensions would also be notated as 11111, but a response of "extreme problems" in all

five dimensions would be notated as 55555 to reduce the floor and ceiling effects. This gives the new five-level version 3,125 unique health states instead of 243 in the three-level version. The idea is that the increased number of response levels will provide a better profile of the patient's health. The EQ-5D-5L instrument has been compared with the 3L version in several studies and been reported to be valid, to reduce ceiling effects and to increase discriminatory power in several populations (132, 135–137), as well in THR populations (9, 10). For those populations (for example Sweden's) where no five-level value sets are available to calculate an index score, "crosswalk"-algorithms are available from 3L to 5L (11). The 5L version is yet to be tested and validated in a Swedish THR-population.

EQ-VAS

The second part of the EQ-5D contains a VAS addressing general health (EQ VAS) (112), where 0 and 100 represent the worst and best possible health state, respectively. The floor or ceiling effects and the multimodal distribution of indices have made the EQ-5D subject to criticism (138–144). These facts need to be taken into consideration when performing statistical analyses of the EQ-5D. Despite this, the EQ-5D is a useful tool for measuring patient HRQoL pre- and post THR surgery.

Pain VAS

The pain VAS (110) ranges from 0 to 100, where 0 represents no pain and 100 the worst possible pain. In the SHAR, the hip pain VAS is registered pre- and postoperatively at one, six and ten years (16, 107). In the Swespine the leg and back pain VAS is registered pre- and postoperatively at one, two, five, and ten years (2).

Oswestry Disability Index

The Oswestry Disabilty Index (ODI) is frequently used to measure the degree of disability and estimate quality of life in a patient with low back pain. The self-completed questionnaire contains ten topics concerning intensity of pain, lifting, ability to care for oneself, ability to walk, ability to sit, sexual function, ability to stand, social life, sleep quality, and the ability to travel. Each topic's category is followed by six statements describing potential scenarios in the patient's life relating to the topic. Each question is scored on a 0–5 scale with zero indicating the least disability and five indicating the most severe. The scores for all questions are then summarized and multiplied by two to obtain the index, ranging from 0 to 100. Zero is equated with no disability and 100 is the maximum possible disability (113). In the Swespine the ODIs are registered pre- and postoperatively at one, two, five, and ten years (2).

Other measurements used in these studies

Satisfaction

In the SHAR satisfaction with the outcome following THR was measured by the satisfaction VAS. This scale ranges from 0 to 100, where 0 represents very satisfied and 100 very dissatisfied. In the SHAR, satisfaction VAS is registered postoperatively at one, six and ten years (16, 107). In the Swespine outcome satisfaction following LSS is measured by the patient rating the experienced outcome using a three-level questionnaire: 1. Satisfied, 2. Uncertain, 3. Dissatisfied. Satisfaction is registered at one, two, six and ten years following surgery (2).

Charnley class

The Charnley classification is a patient-reported survey in the SHAR, but was originally developed to be assessed by an observer, such as the orthopedic surgeon. The classification determines the musculoskeletal comorbidity status of the patient according to: Class A, corresponding to a unilateral hip disorder, Class B, a bilateral hip disorder, and Class C, a walking impairment due to multiple joint involvement or other medical comorbidities (111). The question of whether to divide Class B into two groups, those with one side or the other already treated, has been discussed (145). However, the evidence for this is not yet strong enough for a new fourth class. In the SHAR, the Charnley classification is registered preoperatively (16, 107).

Aims

The overall objective of the studies presented in this thesis was to investigate the clinical utility of PROMs following THR and LSS. Specifically, the aims were to:

- Explore patient-reported outcomes following THR and LSS in patients in whom both procedures have been performed and to compare these results to patients in whom only one of the procedures was performed. (Paper I and II)
- Explore whether the order of THR and LSS procedures in patients in whom both procedures have been performed within a short period of time of two years influences the patient-reported outcome following the last procedure. (Paper III)
- Investigate the opportunity to use PROMs one year following THR in order to predict the risk of a late reoperation following THR. (Paper IV)
- Calculate for the 3L and 5L-verions of the EQ-5D an estimate for the different response options by dimension using the EQ VAS. To assess the measurement properties of the EQ-5D-5L and investigate any differences compared with the EQ-5D-3L, preoperatively and one year postoperatively in a Swedish THR-population. (Paper V)

Patients and methods

Patients

The data used for papers I, II and III were retrieved from the SHAR and the Swespine for patients undergoing surgery from 2002–2012. These years were selected since the SHAR first started to collect PROMs in 2002. After linking of the registers using the PIN as a common identifier, selections were made based on predefined selection criteria specific to the respective studies. For each study, a separate dataset was compiled. In paper IV, demographic, surgical and PROMs data were retrieved from the SHAR covering patients undergoing primary THR in 2002–2015. In order to reduce confounding, patients included in the analysis were selected according to preset criteria. In paper V, all patients were recruited from one of the seven publicly funded hospitals in western Sweden in 2015. A separate database was established for the EQ-5D-5L versions of the surveys while the EQ-5D-3L versions of the survey were retrieved from the regular PROMs database. All the data sets that were used have been stored within the highly protected IT infrastructure of the SHAR at the Register Centre of Västra Götaland Region.

Table 1 summarizes the number of patients included in the different studies. A clarification is needed to explain the differences regarding patients and procedures between Papers I and II-III. Due to a misunderstanding between authors and statisticians in Paper I the SHAR dataset was expanded until 2013 and the Swespine dataset from 1998 to 2014. However, only patients with LSS prior to THR were included. As a result, only 86 patients with surgery outside the selected years, 2002–2013 were included in the study population in Paper I. This mistake was discovered after publication. These extra patients did not affect the outcome or analysis of the studies. This has been carefully investigated and results without these 86 patients are presented in Table 5.

Table 1

	Tot. no of procedures	Tot. no of patients	Year of surgery	Comments
Paper I				Study and control group following selection Fig 3
SHAR	139,697	109,306	2002–2013	
Swespine	47,433	43,767	1998–2014	
Study group		997		
Matched group		997		
Paper II				Study and control group following selection Fig 5
SHAR	159,247	126,752	2002–2012	
Swespine	34,559	25,394	2002–2012	
Study group		220		
Control group		220		
Paper III				Study group following selection Fig 6
SHAR	159,247	126,752	2002–2012	
Swespine	34,559	25,394	2002–2012	
Study group		255		
Paper IV				All THRs in Sweden 2002–2014, study population selection Fig 7
SHAR		141,300	2002–2014	
Study population		75,899		
-number reoperated		1,405		
Paper V				All patients eligible for THR in western Sweden in 2015 were intentionally invited to take part in the study
THRs		1,567	2015	
Preop 3L		1,182	2015	
Preop 5L		767	2015	
Postop 3L		1400	2016	
Postop 5L		508	2016	

Ethical considerations

According to the Patient Data Act (SFS2008:355), the collection of data in Swedish national quality registers does not require written or oral consent from patients. The law obliges the health-care provider to inform patients that data will be registered and used for quality improvement and research and that they may opt out at any time and have their data deleted from the register. Written information about the collection of data for quality registers is normally provided before or at the preoperative visit. Ethical review board approval is required for all research using national quality register data. Information on ongoing research projects is provided by the respective registers and is ideally posted on the register webpages.

For Paper V, patients were recruited from all public hospitals performing THRs in the Västra Götaland Region in 2015. Information about the study was provided before or at the pre-operative visit by each participating unit. Repeat study information was included when follow-up questionnaires were sent out. The return of questionnaires was regarded as consent to participate. Information about the study was also available at the SHAR website.

For all studies presented in this thesis, ethical review board approval was obtained from the Regional Ethical Review Board in Gothenburg, Sweden (Papers I-III entry number 236-13, Paper IV entry number 368-17, and Paper V, entry number 516-14).

Methods

Papers I and II

Papers I and II generally had a similar study structure. Following linkage of the SHAR and the Swespine a set of predefined step-wise selection criteria was applied in both studies (Figures 3 and 5). Following these steps a study population containing a study group and control group was created. In Paper I the influence of a previous LSS on PROMs one year following THR compared with a group with only THR was investigated. In Paper II the opposite, PROMs one year following LSSS in patients with and without a THR prior to LSSS, was investigated.

In Paper I there was an additional investigation were the prevalence of a prior LSS among patients with THR due to hip OA during 2012 was calculated (Figure 4).

Both studies are prospective observational register studies presenting the outcome without drawing conclusions on causality.

Paper III

Paper III is similar to Papers I and II in terms of study structure. As in the previous papers, the SHAR and Swespine were linked and a set of predefined selection criteria was then applied in a step-wise fashion (Figure 6). The study group consisted of patients who had undergone both THR and LSSS within a two-year period. We investigated whether the order of surgery influenced PROMs (EQ-5D and EQ VAS) one year after the last procedure.

As for Papers I and II, this study is a prospective observational register study presenting the outcome without drawing any conclusions on causality.

Paper IV

For Paper IV data from SHAR were obtained and a set of predefined step-wise selection criteria was applied (Figure 7). From the selected study group a study population of those patients with a late reoperation was identified. The outcome was reoperation for all reasons and all types of surgical procedures later than one year after the index surgical procedure. An investigation was then made of the opportunity to predict the risk of late reoperation. The predictors of reoperation were age, sex and PROMs collected from the PROMs program in the SHAR (146), which includes the EQ-5D health status questionnaire (109), a hip pain visual analogue scale (VAS) (110) and, at follow-ups, satisfaction with the outcome using a VAS. A patient-reported Charnley classification used to determine patient-reported musculoskeletal comorbidity was also included (111).

Paper V

In order to study the aim and research questions in Paper V, the aim was to invite all patients eligible for THR in 2015 on the basis of primary hip osteoarthrosis at any of the seven publicly funded hospitals performing THRs in the western region of Sweden (Västra Götalandsregionen). During the standard preparatory preoperative visit prior to the THR procedure patients regularly completes the EQ-5D-3L questionnaire as part of the routine PROMs program of the SHAR (147). Two weeks prior to this visit, invitation letters including preoperative information are sent to the patients by each hospital's waiting list coordinators. During the study period, these letters also included the 5L version

of the EQ-5D questionnaire and a pre-addressed return envelope to the SHAR. After the 5L version of the questionnaire had been completed, it was sent directly to the SHAR and registered in a separate EQ-5D-5L database. No reminders were sent to patients regarding the preoperative 5L versions (Figure 8). One year following the index-procedure, the postoperative 3L surveys are sent to all patients by the SHAR-affiliated secretary at each hospital. The postoperative 3L versions were returned to the hospitals and registered into the SHAR PROMs database. This is general practice within the SHAR PROMs program. Non-responders were reminded after one month. Two weeks following registration of the 3L version, the 5L version was sent out together with information about the study and a pre-addressed envelope to the SHAR. After the survey was returned to the SHAR, the answers were entered into the 5L database at the SHAR (Figure 8).

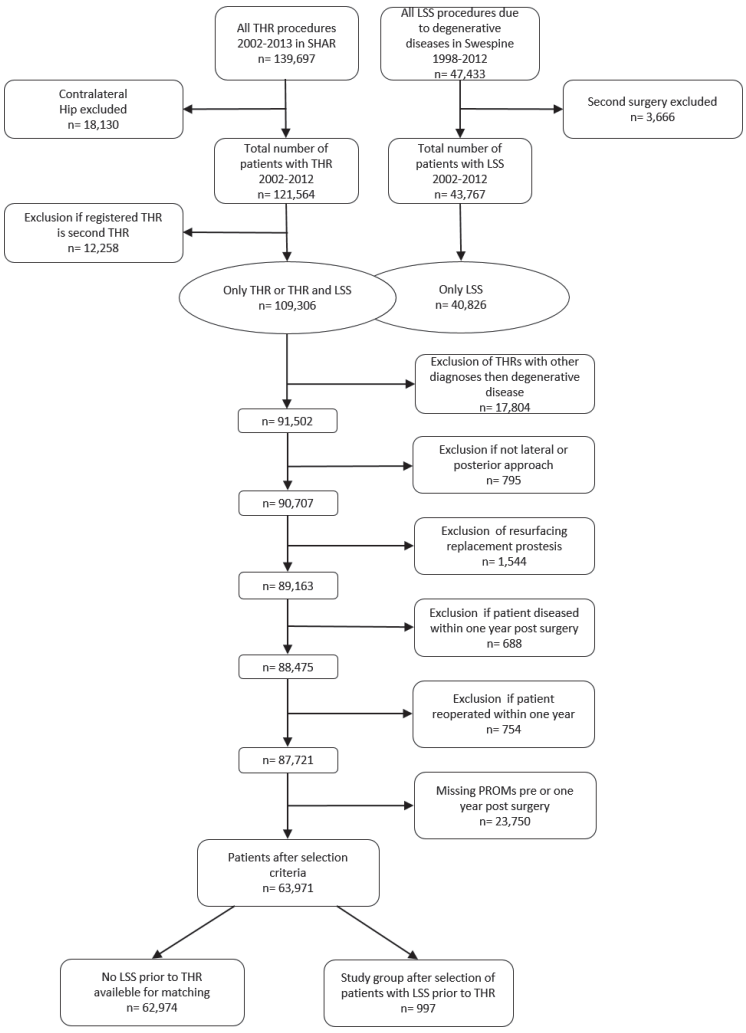


Figure 3. Selection of patients undergoing THR with or without previous LSS.

LSS = Lumbar spine surgery,
THR = Total hip replacement,
SHAR = Swedish Hip Arthroplasty Register,
Swespine = Swedish Spine Register

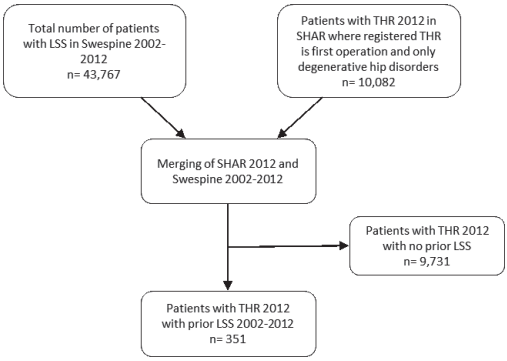


Figure 4. Flow diagram showing the prevalence of previous LSS in patients undergoing THR in 2012.

LSS = Lumbar spine surgery,
THR = Total hip replacement,
SHAR = Swedish Hip Arthroplasty Register,
Swespine = Swedish Spine Register

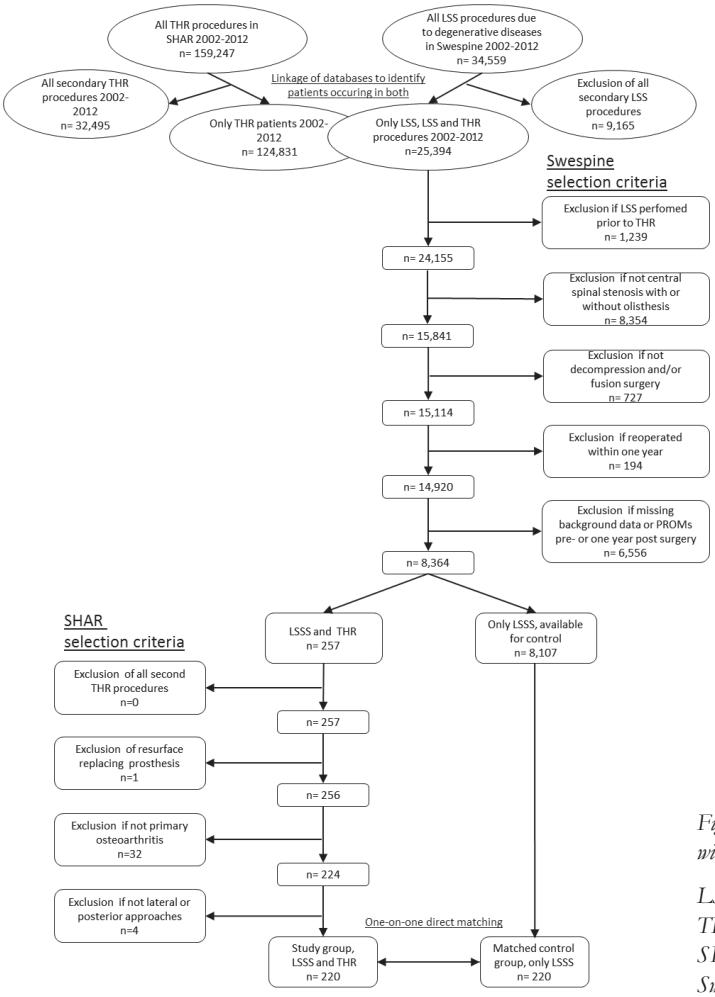


Figure 5. Selection of LSSS patients with and without previous THR.

LSSS = Lumbar spinal stenosis surgery,
THR = Total hip replacement,
SHAR = Swedish Hip Arthroplasty Register,
Swespine = Swedish Spine Register

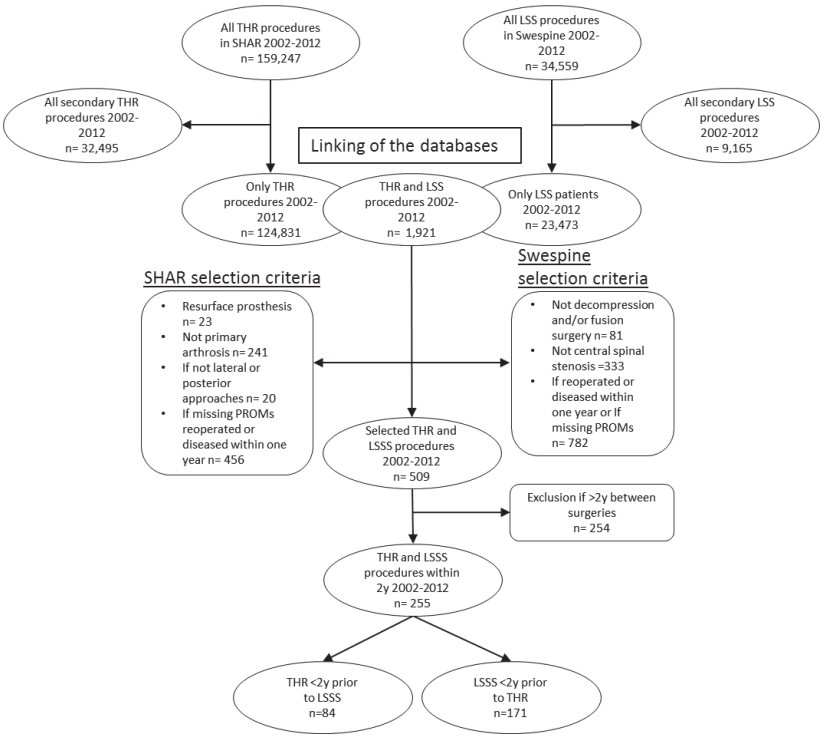


Figure 6. Selection of patients with THR and LSSS performed within two years.

LSS = Lumbar spine surgery,
LSSS = Lumbar spinal stenosis surgery,
THR = Total hip replacement,
SHAR = Swedish Hip Arthroplasty Register,
Swespine = Swedish Spine Register

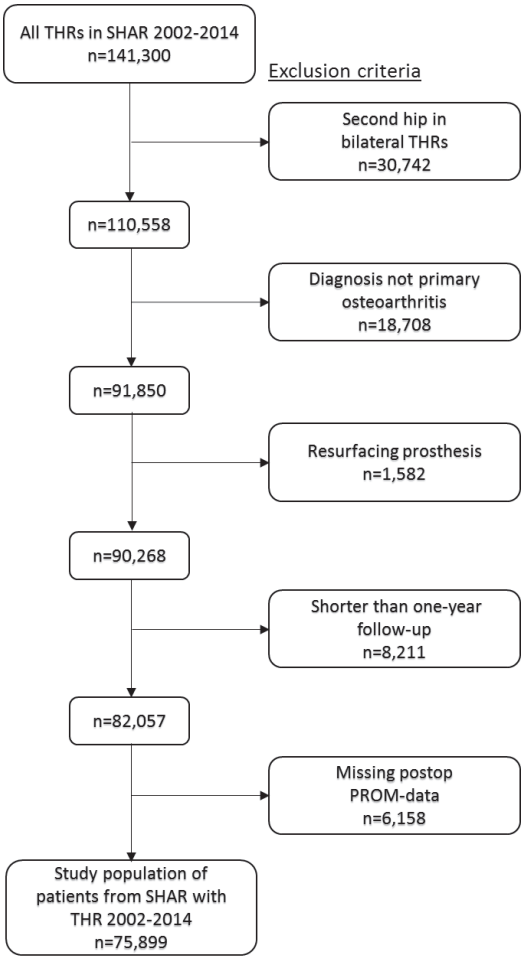


Figure 7. Flowchart describing the selection process

SHAR = Swedish Hip Arthroplasty Register,
THR = Total hip replacement,
PROM = Patient-reported outcome measures

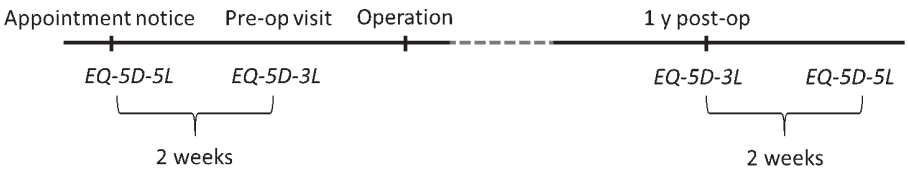


Figure 8. Preoperative and one-year postoperative procedures for collecting the EQ-5D-3L and -5L questionnaires.

Statistical methods

Descriptive statistics

Throughout the thesis data on categorical variables are presented using frequencies and proportions. Moreover, data on continuous variables are presented using means and standard deviations (SD).

Comparing means or proportions

Raw data were summarized as frequencies for categorical data and means and associated standard deviations for continuous data. The group comparisons were conducted using the Chi-square test for categorical variables and a t-test for continuous variables.

P value below 0.05 represent significant differences.

Matching procedures

In Papers I and II, the one-to-one matching was performed with a non-parametric matching method, nearest-neighbor matching (148).

Regression models

Papers I and II

Post-operative PROMs data were modeled with linear regression analysis with the post-operative value as the outcome and LSS as exposure in Paper I, and THR as exposure in Paper II. In Paper II, satisfaction was modelled with logistic regression analysis. To enable this response, option 2 (uncertain) and 3 (dissatisfied) were merged. All models were adjusted for age, sex, and pre-operative PROM values. For both Paper I and II a separate linear regression analyses were conducted to investigate whether the time between surgeries had any association with the outcome. In Paper II, a sub-analysis was conducted in which an investigation was made to determine whether the influence of type of surgery (decompression, decompression with fusion or fusion alone) had any association with the outcomes.

In Paper I and II the pre-operative values were modeled in piecewise-linear regression splines that corrects to a certain extent the ceiling effect and with predicted post-operative values more likely in appropriate range (146).

Paper III

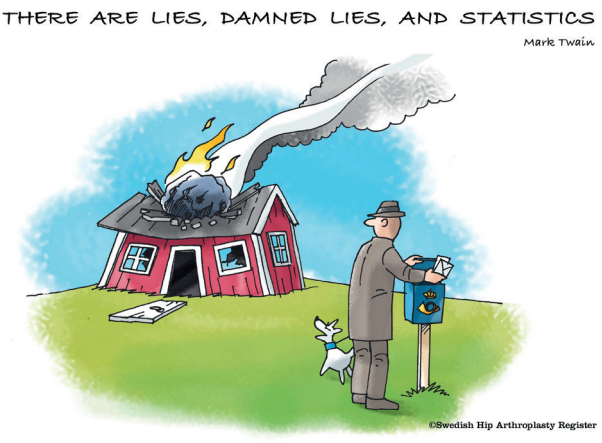
Any association with previous surgery was investigated using linear regression for the EQ-5D index and the EQ VAS score. Logistic regression models were applied after unifying answers 2 and 3 for the separate EQ-5D dimensions. The regression models were adjusted for sex, age, preoperative PROM scores and time between surgeries.

Paper IV

Cox regression analysis was used to investigate the association between postoperative PROMs, Charnley class, age and sex with reoperation, the model was adjusted for postoperative PROMs, age and sex. Investigation was made up to eight years following THR, after this there were too few reoperations to perform accurate analyses.

Paper V

Univariable ordinary least squares (OLS) regression models were used to estimate EQ VAS values for the different levels of severity of each dimension. For the preoperative EQ-5D-3L estimate, the preoperative EQ VAS score was regressed onto the preoperative EQ-5D-3L dimensions. For the preoperative EQ-5D-5L



estimate, the preoperative EQ VAS score was regressed onto the preoperative EQ-5D-5L dimensions. This calculation with use of postoperative data was repeated for estimation of the postoperative values.

Prevalence calculation

In Paper I, prevalence of an LSS prior to THR was calculated as the ratio of patients identified with previous LSS surgery divided by the total number of patients with osteoarthritis operated with THR in 2012.

Prediction models

In Paper IV the predictive power of PROMs one year postoperatively was evaluated by the concordance index (C) (149) (Figure 9). This value ranges from 0.5 to 1, with values closer to 1 representing a better score. A value of 0.5 means that PROMs are unable to predict the risk of reoperation, while a value of 1 indicates that reoperation could be completely predicted by the model.

Concordance index
The concordance index is a value ranging from 0.5 to 1; the higher, the better. Interpretations of its absolute value are subjective, but the following limits have been suggested for applications in medicine:

0.0 – 0.5	poorer than random
0.5 – 0.7	poor
0.7 – 0.8	good
0.8 – 0.9	excellent
0.9 – 1.0	"too good to be true"

Figure 9. Concordance index

Reoperation probabilities

In Paper IV, Kaplan-Meier curves were used to summarize reoperation probabilities

Response rates

In Paper V, response rates were calculated for the pre- and postoperative 3L and 5L versions of the surveys for the whole group of patients and for individual hospitals. Differences in response rates were then compared between the 3L and 5L questionnaires, both pre- and postoperatively. For those patients who completed both questionnaires (pre- and/or one year postoperatively), the 3L and 5L responses were compared by dimension. The definition of responses was determined as the same, new or inconsistent (inconsistent was regarded as a change by two levels or more between the surveys (150) (Figure 10).

Ceiling and floor effects

In Paper V, ceiling effects were investigated by calculating the proportion of responses of "no problems" in individual dimensions. Overall ceiling effects were investigated by calculating the proportion of patients reporting "no problems" in all dimensions. An investigation of floor effects was made by calculating the proportion of patients with "extreme problems" in individual dimension and overall. Ceiling and floor effects were considered present if > 15% of patients reported the best (ceiling) or worst (floor) response option (151).

Correlations

In Paper V, Spearman´s rank correlation coefficient (r_s) was used to determine the convergence of the two EQ VAS survey scores. The correlation strength between the two surveys was defined as absent ($r_s < 0.20$), weak ($0.20 \leq r_s < 0.35$), moderate ($0.35 \leq r_s < 0.50$), or strong ($r_s \geq 0.50$) (152).

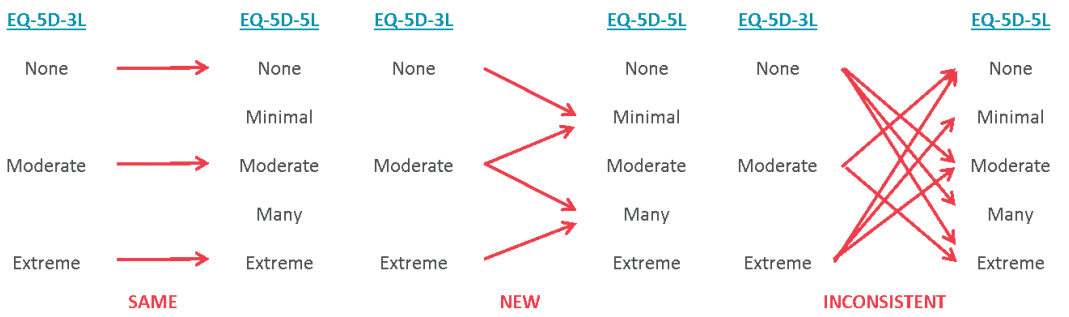


Figure 10. Possible distribution of responses between 3L and 5L versions of the EQ-5D.

Summary of papers

Paper I

The linkage involved 121,564 patients in the SHAR operated on from 2002–2013 and 43,767 patients in Swespine operated on from 1998–2014. Patients common in both registers were identified using the PIN. Following a stepwise selection process a study group of 997 patients and a matched control group of 997 patients were obtained. One year after THR, patients with a previous LSS reported more pain, worse EQ-5D index, worse health status according to the EQ VAS and less satisfaction (all $p<0.001$). This relationship was confirmed with regression analyses (Table 2). We found no association with time between surgeries and PROs one year after THR adjusting for sex and age ($r=0.11$, $p=0.0001$).

Among patients with hip osteoarthritis who underwent THR in 2012, the prevalence for a previous LSS was 3.5%. Of these patients 40% had their LSS less than two years before THR (Figure 2).

Paper II

From 2002 to 2012, there were 126,752 patients with THRs in the SHAR and 25,394 patients with LSS in the Swespine. Following linkage of the registers common patients were identified using PINs as a common identifier. Following exclusion according to the selection criteria presented in Figure 2, a study group of 220 patients with THR prior to their LSSS was identified. A matched control with no history of a previous THR was successfully identified for each patient in the study group (Table 3). Linear regression confirmed an association with THR prior to LSSS and more back pain one year following LSSS, but no other associations was revealed by linear or logistic regression (Table 4).

In two separate linear regression analyses there were no associations with time between the surgeries or the type of surgery and patient-reported outcomes (Table 5).

Table 2. The effect of prior lumbar surgery on patient reported outcome measures (PROMs) one year after total hip replacement (THR). Crude values are from equations regressing lumbar spine surgery on post-operative PROMs, adjusted values take into consideration pre-operative PROM values, age and gender. The table present regression coefficients and associated 95 % confidence intervals.

	Crude	Adjusted
Pain VAS	4.33 (2.53; 6.12)	4.35 (2.57; 6.12)
EQ-5D Index	-0.08 (-0.11; -0.06)	-0.08 (-0.11; -0.06)
EQ VAS	-6.79 (-8.68; -4.90)	-6.75 (-8.58; -4.92)
Satisfaction VAS	6.04 (4.05; 8.03)	6.04 (4.05; 8.02)

VAS, visual analogue scale

Table 3. Demography and pre-operative LSSS patient-reported outcome measures in the study group and the matched control group.

		Control group (n=220)	Study group (n=220)	p-value
Age, mean (SD)		72.0 (8.7)	72.2 (7.8)	0.81
Sex, n (%)	Female	118 (53.6)	115 (52.3)	0.85
	Male	102 (46.4)	105 (47.7)	
Year of surgery, mean (SD)		2010.4 (1.9)	2010.3 (1.6)	0.70
Type of surgery, n (%)	Decompression	170 (77.3)	171 (77.7)	0.99
	Decompression + fusion	49 (22.3)	48 (21.8)	
	Fusion	1 (0.5)	1 (0.5)	
Diagnosis, n (%)	Central spinal stenosis without olisthesis	158 (71.8)	163 (74.1)	0.67
	Central spinal stenosis with olisthesis	62 (28.2)	57 (25.9)	
EQ-5D index, mean (SD)		0.36 (0.32)	0.38 (0.31)	0.55
Mobility, n (%)	1	20 (9.1)	11 (5.0)	0.15
	2	199 (90.5)	209 (95.0)	
	3	1 (0.5)	0 (0.0)	
ADL/self-care, n (%)	1	188 (85.5)	184 (83.6)	0.86
	2	29 (13.2)	33 (15.0)	
	3	3 (1.4)	3 (1.4)	
Usual activities, n (%)	1	71 (32.3)	81 (36.8)	0.46
	2	124 (56.4)	111 (50.5)	
	3	25 (11.4)	28 (12.7)	
Pain, n (%)	1	2 (0.9)	1 (0.5)	0.80
	2	107 (48.6)	111 (50.5)	
	3	111 (50.5)	108 (49.1)	
Anxiety/depression, n (%)	1	99 (45.0)	122 (55.5)	0.05
	2	109 (49.5)	92 (41.8)	
	3	12 (5.5)	6 (2.7)	
EQ VAS, mean (SD)		49.6 (22.4)	48.8 (22.5)	0.72
Back pain VAS, mean (SD)		60.4 (24.8)	59.0 (25.9)	0.55
Leg pain VAS, mean (SD)		60.0 (25.0)	58.9 (26.0)	0.65
ODI score, mean (SD)		44.1 (15.7)	44.5 (14.8)	0.79

SD; standard deviation, VAS; visual analogue scale, ADL; Activities of daily living, ODI; Oswestry Disability Index,

Table 4. The effect of prior THR on PROMs one year after LSSS surgery. Crude values are from equations regressing LSSS on post-operative PROMs, adjusted values take into consideration pre-operative PROM values, age and gender of the patients.

	Crude	Adjusted
EQ VAS	-3.25 (-7.50; 1.01)	-2.97 (-6.90; 0.97)
Back pain VAS	4.65 (-0.79; 10.08)	5.30* (0.27; 10.33)
Leg pain VAS	1.22 (-4.43; 6.86)	1.52 (-4.00; 6.99)
EQ-5D Index	0.01 (-0.05; 0.07)	0.06 -0.05; 0.06)
ODI-score	2.81 (-0.71; 6.33)	2.58 (-0.47; 5.63)
Satisfaction (OR)	1.07 (0,73; 1.58)	1.07 (0.72; 1.59)

EQ VAS, back and leg pain VAS, EQ-5D index and ODI are performed using linear regression analysis. Satisfaction are performed using logistic regression analyse. THR; Total hip replacement, LSSS; Lumbar spinal stenosis surgery, PROM; Patient-reported outcome measurement, OR=odds ratio. VAS; visual analogue scale, ODI; Oswestry Disability Index.
**A value for linear regression that does not cross 0 is equivalent to significance.*

Table 5. The effect of type of LSSS in comparison with decompression on PROMs one year after LSSS.

	Decompression + fusion		Fusion	
	Crude	p-value	Adjusted	p-value
EQ VAS	2.64 (-2.62;7.89)	0.33	7.75 (-24.39;39.89)	0.64
Back pain VAS	-1.81 (-8.25;4.62)	0.58	-1.09 (-40.44;38.26)	0.96
Leg pain VAS	0.52 (-6.40;7.44)	0.88	-1.52 (-43.84;40.81)	0.94
EQ-5D Index	0.02 (-0.05;0.09)	0.54	0.02 (-0.38;0.42	0.91
ODI-score	-0.15 (-4.33;4.02)	0.94	-3.28 (-28.80; 22.24)	0.80
Satisfaction	-0.04 (-0.20;0.12)	0.60	0.52 (-0.45;1.49)	0.30

The table present regression coefficients and associated 95 % confidence intervals. EQ VAS, back and leg pain VAS, EQ-5D index and ODI are performed using linear regression analysis. Satisfaction are scored using logistic regression analysis. VAS; visual analogue scale, ODI; Oswestry Disability Index

Paper III

A linkage procedure was performed using the same SHAR- and Swespine datasets from 2002 to 2012, as in Paper II. Common patients were identified using PINs. Two study groups were successfully identified with LSSS prior to THR (n=171) and THR prior to LSSS (n=84). Linear regression analysis revealed an association with LSSS prior to THR and a better outcome in the EQ-5D-index and EQ VAS (Table 6). Using logistic regression analysis, LSSS prior to THR also revealed an association with a better outcome for the separate dimensions of "pain" and "anxiety/depression" (Table 7).

Table 6. Linear regression analysis with association of first LSSS with PROMs one year after surgery. Crude values are from equations regressing LSSS on post-operative PROMs, while adjusted values take into consideration pre-operative PROM values, age and sex of the patients and time between surgeries.

	Crude	Adjusted
EQ-5D Index	0.09* (0.02; 0.16)	0.09* (0.03; 0.16)
EQ VAS	5.59* (0.14; 11.05)	5.61* (0.36; 10.86)

*The table present linear regression coefficients and associated 95 % confidence intervals. VAS; visual analog scale, *a value for linear regression that do not cross 0 is equivalent to significance*

Table 7. Logistic regression analysis of the association of first LSSS with PROMs one year after surgery. Crude values are from equations regressing LSSS on post-operative PROMs, while adjusted values take into consideration pre-operative PROM values, age and sex of the patients and the time between surgeries.

	Crude	Adjusted
Mobility	1.53 (0.88; 2.73)	1.52 (0.86; 2.72)
Self-care	1.57 (0.67; 3.56)	0.97 (0.35; 2.59)
Usual activities	1.42 (0.83; 2.42)	1.51 (0.88; 2.62)
Pain	3.00* (1.55; 6.22)	3.01* (1.54; 6.29)
Anxiety/depression	1.99* (1.13; 3.48)	2.26* (1.25; 4.14)

*The table present logistic regression coefficients and associated 95 % confidence intervals, *a value for logistic regression that do not cross 1 is equivalent to significance*

Paper IV

Of the patients included according to the selection criteria, the prosthesis survival rate at the ten-year follow-up was 95.5 % (95.3–95.8). The mean time until reoperation was 1589 days (SD 887 days). Cox regression modelling revealed an association with PROMs for the risk of reoperation with pain (B=1.01, 95% CI: 1.01, 1.02), satisfaction VAS (B=1.02, 95% CI: 1.01, 1.02), and the EQ-5D-index (B=0.64, 95% CI: 0.49, 0.85), but none for the EQ VAS (B=1.00, 95% CI: 0.99, 1.01). The Cox regression also revealed an association for the risk of reoperation with age (B=0.98, 95% CI: 0.97, 0.98), sex (female B=0.71, 95% CI: 0.64, 0.79), and Charnley class B (B=0.75, 95% CI: 0.62, 0.91), and C (B=0.83, 95% CI: 0.73, 0.94) (Table 8). Satisfaction VAS (C=0.650) and pain VAS (C=0.649) had the highest predictive powers (Table 8). It was possible to construct a model for predicting the risk of future reoperation, with a concordance index of 0.68. There was only a marginally difference between observed reoperations and predicted reoperations using the predictive model. If further information were put into the model, it could possibly be used to construct an automatized system for the detection of patients running a higher risk of reoperation following THR. The way different levels of PROMs affect the probability of being reoperated following THR is presented in Figure 11.

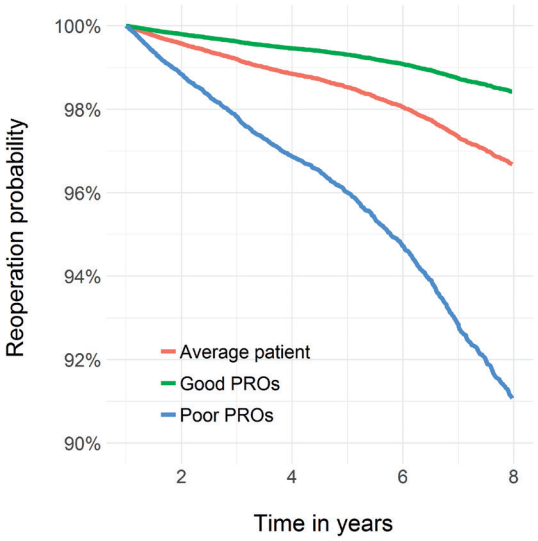


Figure 11. Probability of being reoperated.

Cox regression survival estimates for the average patient (average baseline characteristics and one-year PROMs), a patient with good PROs (no hip VAS pain, full satisfaction, EQ mobility=1 EQ pain/discomfort=1) and a patient with poor PROs (hip VAS pain=50, satisfaction VAS=50, EQ mobility=2, EQ pain/discomfort=2).

Table 8. Association of postoperative PROMs, Charnley class, age and sex with reoperation using Cox regression adjusted for age, sex and postoperativ PROMs. Predictive power of postoperative PROMs, Charnley class, age and sex with reoperation.

Variables	HR	95% CI lower	95% CI upper	C
Charnley class A	Ref			0.539
Charnley class B	0.752	0.623	0.909	
Charnley class C	0.829	0.728	0.943	
Pain VAS	1.014	1.011	1.017	0.649
EQ VAS	1.001	0.998	1.005	0.602
Satisfaction VAS	1.016	1.013	1.018	0.650
EQ-5D index	0.643	0.489	0.846	0.607
Age	0.975	0.970	0.980	0.566
Male	Ref			0.535
Female	0.713	0.641	0.793	

HR = hazard ratio, 95% confidence interval
C =concordance index

Paper V

The response rates were lower than expected for both surveys both pre- and postoperatively (Table 9).

A large proportion of the patients used new response options preoperatively in the mobility (61%), self-care (41%), usual activities (46%), and pain/discomfort (54%) dimensions in the 5L version compared with the 3L version (Figure 12). One year postoperatively most patients reported no problems in all dimensions for both versions of the survey, (3L 32%, 5L 25%). Inconsistent answers were most frequently reported preoperatively and then in the separate dimensions on self-care (17%) and usual activities (20%) (Figure 12).

There were limited ceiling effects in each version preoperatively. Postoperatively, all dimensions in both versions presented ceiling effects but to a lesser degree in the 5L version. The overall ceiling effect differed by seven percentage units postoperative. Floor effects were only present in the preoperative pain/discomfort dimension of the 3L survey.

The correlations between the 3L and 5L EQ VAS values were strong: preoperatively $r_s = 0.71$ and postoperatively $r_s = 0.87$.

The EQ VAS estimates for different severity levels of each dimension conformed well to the expected pattern (Figure 13 and 14), with the exception for preoperative mobility. Because of the rarity of level 4 and 5 responses in the EQ-5D-5L questionnaire, these two levels were merged.

Table 9. Total hip replacements performed in 2015 and preoperative response rate for the EQ-5D 3L and 5L surveys

	Preoperative				Postoperative			
Clinic	Tot.	3L	5L	3L and 5L	Tot.	3L	5L	3L and 5L
All, n (%)	1567	1182 (75)	767 (49)	524 (33)	1554	1400 (90)	508 (33)	508 (33)

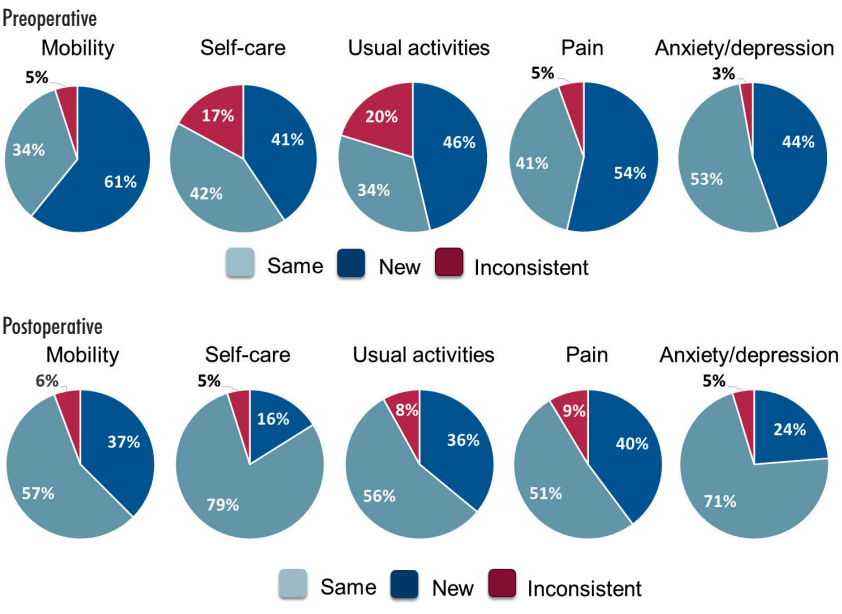


Figure 12. Distributions of answers between 3L and 5L-surveys for all patients

Same is the same answer option between 3L and 5L. New is one step from 3L to 5L. Inconsistent is two or more steps from 3L to 5L.

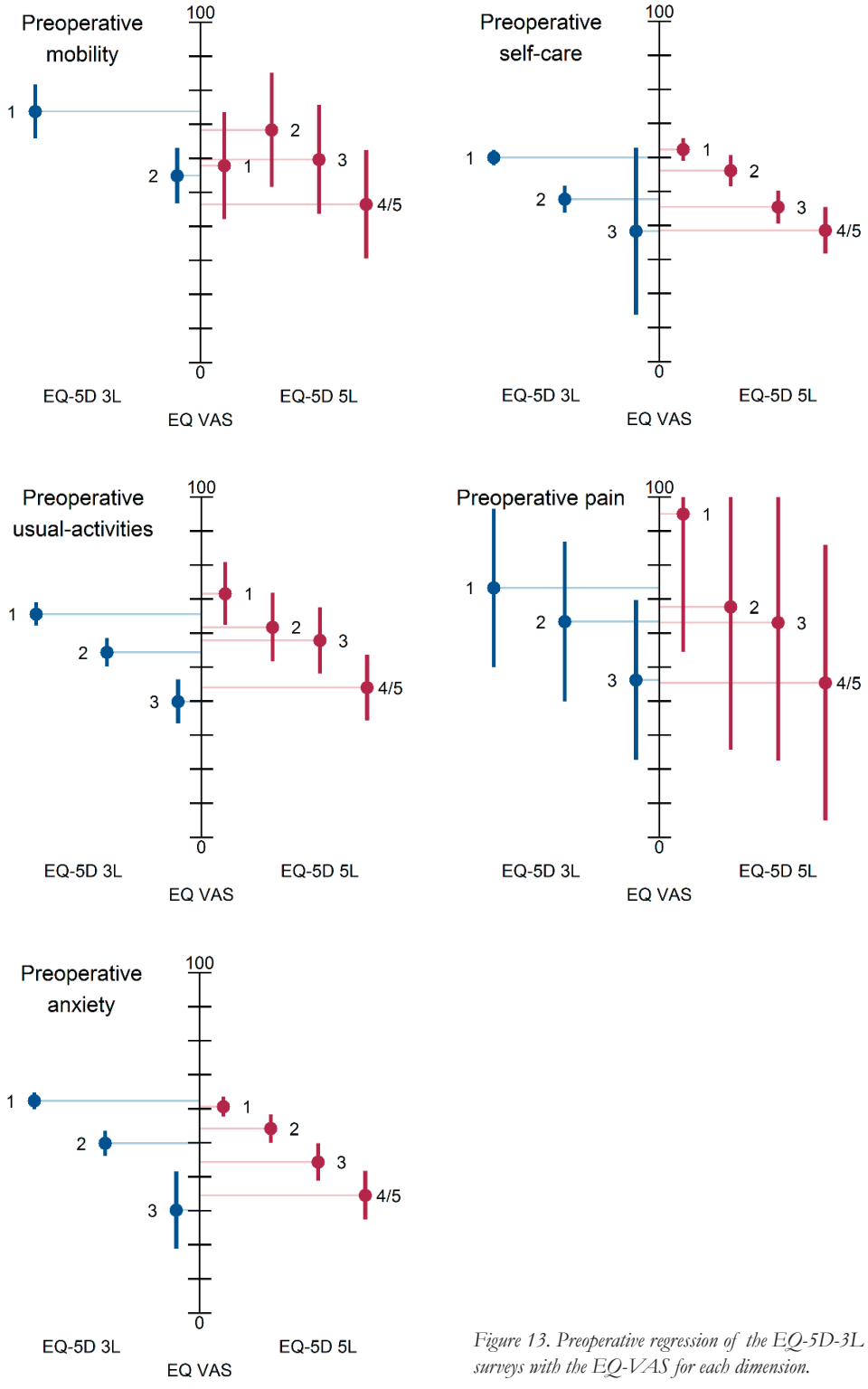


Figure 13. Preoperative regression of the EQ-5D-3L and -5L surveys with the EQ-VAS for each dimension.

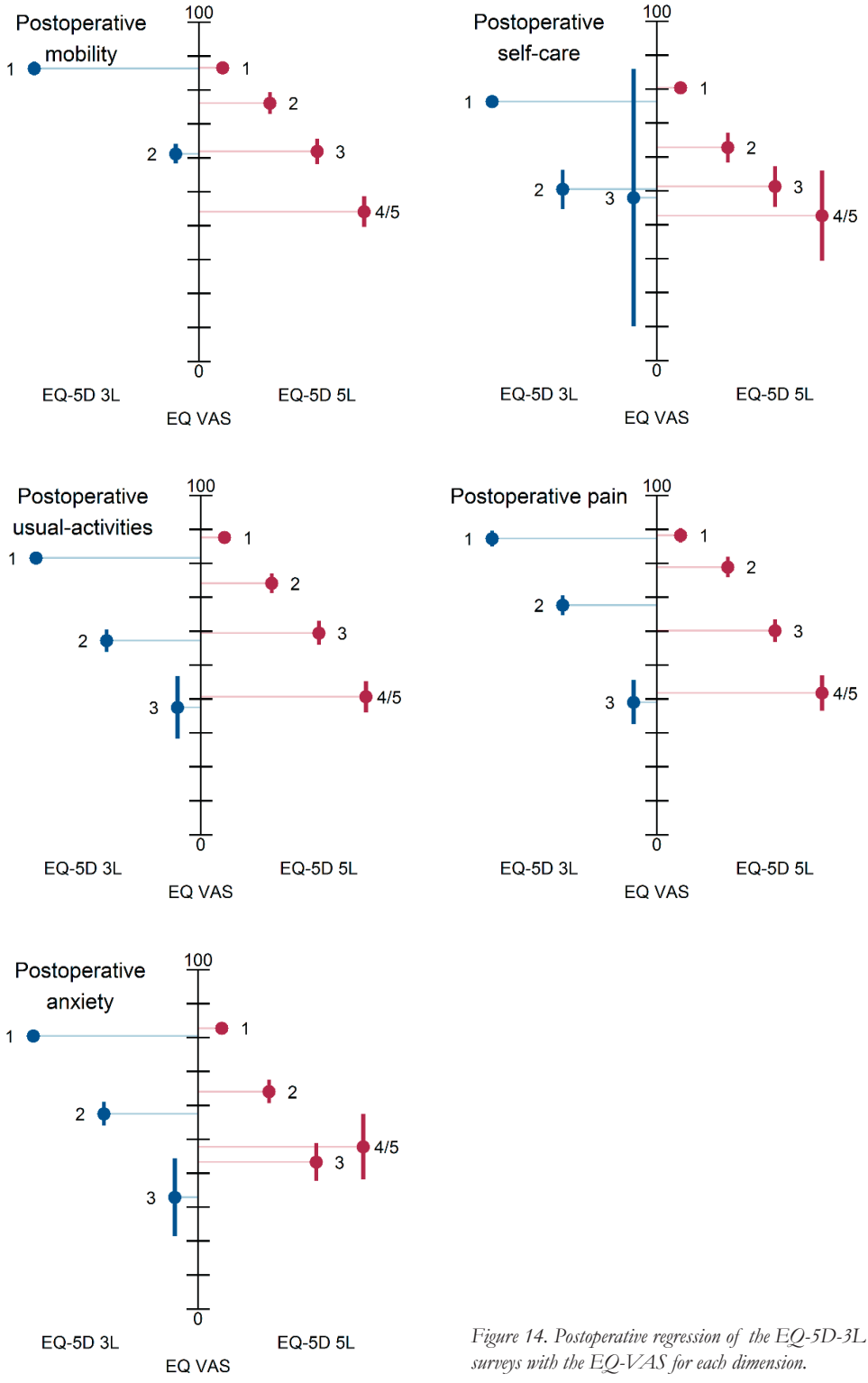


Figure 14. Postoperative regression of the EQ-5D-3L and -5L surveys with the EQ-VAS for each dimension.

Additional results

This section contains analyses and results of the papers included in this thesis that have not been or are not intended to be included in the publications.

Paper I

In addition to the published results, ceiling effects of EQ-5D-3L pre- and postoperative THR for both groups were investigated. The method used was the same as in paper V. As expected and in agreement with earlier reports, both groups presented profound ceiling effects at the follow-up (Table 10).

An additional regression analysis was also performed following the exclusion of the patients with LSS performed prior to 2002 (n=86). The association with worse PROMs following THR in patients with a previous LSS did not change (Table 11).

Table 10. Ceiling effects preoperative and one-year postoperative THR in patients with and without a previous LSSS.

Survey dimension	Preoperative		Postoperative	
	Only THR (n=997)	LBS and THR (n=997)	Only THR (n=997)	LBS and THR (n=997)
Mobility	3.5 %	2.9 %	51.1 %	34.8 %
Self-care	67.6 %	68.2 %	89.1 %	87.1 %
Usual activities	30.8 %	25.0 %	72.5 %	59.7 %
Pain/discomfort	0.7 %	0.7 %	35.6 %	26.3 %
Anxiety/depression	48.9 %	48.9 %	73.5 %	66.1 %
Overall	0.3 %	0.1 %	28.2 %	18.8 %

Table 11. Adjusted effect of prior lumbar surgery on patient reported outcome measures (PROMs) one year after total hip replacement (THR) following the exclusion of the 86 patients with LSSS prior to 2002. Crude values are from equations regressing lumbar surgery on post-operative PROMs, while adjusted values take into consideration pre-operative PROM values, age and gender. The table present regression coefficients and associated 95 % confidence intervals.

	Crude	Adjusted
Pain VAS	4.30 (2.54; 6.19)	4.30 (2.49; 6.11)
EQ-5D index	-0.08 (-0.10; -0.06)	-0.08 (-0.10; -0.06)
EQ VAS	-6.69 (-8.61; -4.77)	-6.68 (-8.54; -4.82)
Satisfaction VAS	6.11 (4.12; 8.14)	6.14 (4.12; 8.16)

VAS, visual analogue scale

Paper II

As for Paper I an additional calculation for this thesis were made investigating the ceiling effects of the EQ-5D-3L pre- and postoperative LSSS for both groups. Postoperative ceiling effects were present in the only LSSS group for all dimensions except "pain" and "overall". For the group with both THR and LSSS ceiling effects were present in all dimension except for "mobility", "pain" and "overall" (Table 12).

Table 12. Ceiling effects preoperative and one-year postoperative THR in patients with and without a previous LSS.

Survey dimension	Preoperative		Postoperative	
	Only LSSS (n=220)	LHR and LSSS (n=220)	Only LSSS (n=220)	THR and LSSS (n=220)
Mobility	4.1 %	2.3 %	18.2 %	12.7 %
Self-care	38.6 %	38.2 %	38.6 %	38.6 %
Usual activities	14.5 %	16.8 %	27.3 %	25.9 %
Pain/discomfort	0.5 %	0 %	7.3 %	6.4 %
Anxiety/depression	20.5 %	25.0 %	29.5 %	28.2 %
Overall	0 %	0 %	5.9 %	5.0 %

Paper III

The change in health-related quality of life was investigated over time by analyzing differences from before to one year after the first procedure, one year after first procedure to before second procedure, and before and one year after the second procedure. Due to the fact that the preoperative measurement for the second procedure had to occur after the postoperative measurement following the first procedure, the number of included patients was reduced to 67 (first hip) and 69 (first spine). The largest improvement occurred from before to after the second procedure (Table 13 and 14). This corroborates the results in paper III where preoperative first procedure to preoperative second procedure and pre- and postoperative second procedure was investigated.

A calculation was also made that presents the way the distribution of time between the procedures takes place for the patients with both procedures performed within two years. Of the patients with first an LSSS, 68 % (n=150) had their THR within one year. For the patients with first THR, it was 37 % (n=81) who had their LSSS within one year (Figure 15).

Table 13. Differences in PROMs for EQ-5D index and EQ VAS between interventions.

Period	PROM	First procedure	Diff. (mean)	p-value
1	EQ-5D	Hip (n=67)	0.23	0.000
		Spine (n=69)	0.20	0.000
2	EQ-5D	Hip	-0.18	0.000
		Spine	-0.25	0.000
3	EQ-5D	Hip	0.27	0.000
		Spine	0.37	0.000
1	EQ VAS	Hip	9.30	0.034
		Spine	11.91	0.000
2	EQ VAS	Hip	-9.57	0.006
		Spine	8.06	0.017
3	EQ VAS	Hip	17.27	0.000
		Spine	19.03	0.000

Period 1 = pre and postoperative first procedure,
2 = postoperative first procedure and preoperative second procedure,
3 = pre- and postoperative second procedure

Table 14. Differences in PROMs for the separate dimensions of the EQ-5D between interventions.

Dimension	Period	first	Diff. mean	p-value
Mobility	1	Hip (n=67)	-0.239	0.000
		Spine (n=69)	-0.130	0.022
	2	Hip	0.224	0.000
		Spine	0.174	0.001
	3	Hip	-0.284	0.000
		Spine	-0.319	0.000
Self-care	1	Hip	-0.149	0.013
		Spine	0.058	0.336
	2	Hip	0.090	0.145
		Spine	0.145	0.072
	3	Hip	-0.090	0.145
		Spine	-0.203	0.003
Usual activities	1	Hip	-0.254	0.013
		Spine	-0.232	0.010
	2	Hip	0.254	0.004
		Spine	0.319	0.001
	3	Hip	-0.328	0.002
		Spine	-0.478	0.000
Pain	1	Hip	-0.478	0.000
		Spine	-0.420	0.000
	2	Hip	0.403	0.000
		Spine	0.449	0.000
	3	Hip	-0.522	0.000
		Spine	-0.725	0.000
Anxiety/ depression	1	Hip	-0.060	0.564
		Spine	-0.101	0.133
	2	Hip	0.060	0.362
		Spine	0.072	0.236
	3	Hip	-0.075	0.261
		Spine	-0.188	0.030

Period 1 = pre and postoperative first procedure,
2 = postoperative first procedure and preoperative second procedure,
3 = pre- and postoperative second procedure

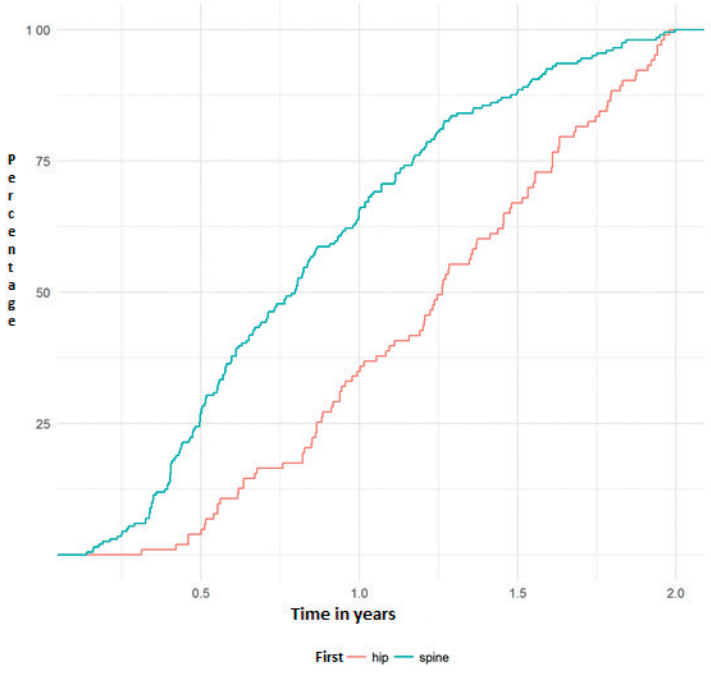


Figure 15. Percentage of patients with both procedure performed within one-year.

Strengths and limitations

General limitations of studies based on register data

A register study can never be more valid than the register data it is based upon. Furthermore, the validity of a register is dependent on the completeness and the coverage of the investigated variable in the register. In the SHAR the coverage is 100%, and the completeness of THR registrations has been reported as 98.1 % (16, 107), for the Swespine the coverage is 98% and the completeness of registrations has been reported as 85% (2). Nevertheless, it is still important to remember that an observational register study can be used to investigate, explore and present correlations between exposure and outcomes, but it does not allow for the possibility of determining causality. This is due to the fact, that in register studies there are no outside controls, there can always be hidden confounders and the risk of bias. There are many possible confounders that could influence both the exposure and the outcome. Confounding factors can be patient related such as PROs, BMI, smoking, education, medical and psychiatric comorbidity or surgery related, such as surgery time, bleeding, implant (type, fixation, positioning) and so on. In all surgery such as orthopedic surgery, the surgeon may also have an influence on the outcome. There are also many possible biases in observational studies such as register studies. Examples of different types of bias are selection bias, detection bias, reporting bias, performance bias, and attrition (115). Despite these limitations, register studies have an important role when clinical trials are not possible to conduct due to high costs, necessary number of patients and length of observation period.

Specific strengths and limitations regarding paper I-III

The large number of patients in the study population and the precise matching procedure of patients add to the strengths of Paper I-II. The thorough selection procedure in all studies was also designed to reduce confounding bias and heterogeneity. In Papers I and II, matching procedures was based not only on demographic variables, year of surgery and details of the surgical method but also on the patients´ self-reported pain level, health-related quality of life and in Paper I also Charnley class. The data for all three studies comes from two well-established and thoroughly validated national quality registers. They could therefore be considered to reflect the general orthopedic practice in Sweden and this limits performance bias and increases generalizability.

Paper III only investigated outcomes common in both registers (EQ-5D and EQ VAS), which restricts the possibilities of comprehensive analyses. It was not possible to investigate pain (except for the separate "pain" dimension of the EQ-5D) or satisfaction with the outcome. Both these outcome variables are of course important since pain and satisfaction with the outcome is of utmost importance in this type HRQoL improvement procedures.

The observational nature of the data from these two national quality registers prevents the drawing of conclusions relating to causality. The analyses were restricted to investigating the outcomes in patients with both THR and LSS compared with matched controls with no documented history of LSS or THR due to a degenerative spinal disorder and or hip OA and patients with both THR and LSS within a short period of time. In Paper III the assumption was made that the patients had degenerative diseases in both locations prior to surgery due to the short time between surgeries, but this is not known. Another limitation applicable for Papers I-III, is the possible influence of other musculoskeletal conditions such as knee osteoarthritis or presence of joint replacement in other locations. Other non-musculoskeletal comorbidities such as diabetes or cardiovascular diseases were not adjusted for and this could be regarded a limitation. The follow-up period of one year is also relatively short, it is possible that the differences will adjust over time. Analyses were restricted to the data available in registries. Other clinical measures, such as radiographic severity or abnormalities were not available.

There are differences between the three studies regarding the inclusion of spinal diagnoses. In all three studies we included central and lateral spinal stenosis with and without olistehsis. However, in Paper I we also included spondylolisthesis/spondylolysis and segment related pain. Discussion within the research group following the completion of Paper I resulted in the decision to exclude spondylolisthesis/spondylolysis and segment related pain in the further studies as these diagnoses differ in origin, symptoms and progress and in relationship with hip OA. However, the inclusion of these diagnoses in Paper I did not have any practical consequences for the interpretation of results since these two diseases were present in only 8% of the population.

Specific considerations regarding paper IV

In comparison with earlier studies investigating the predictive power of different patient-reported variables, a substantially larger number of patients were included in the calculation of this study. In contrast to most previous studies, several PROMs have been taken into consideration when performing the analysis. Patients were selected in order to reduce confounding biases and provide a homogenous group to investigate. The previously described studies presenting patient-related factors (22–25) and PROMs (26–28) to predict the risk of future revision following THR have used OR (odds ratio) and HR (hazard ration) to predict the risk of revision. However, these methods have been declared unsuitable for these conclusions since they lack predictive strength (153). Together with a Cox regression analysis, an analysis using the concordance index method was conducted in paper IV. This provides a substantially higher power to the predictive power of the analyses than earlier reports.

There are limitations to this study. Factors other than poor PROMs, such as high BMI and long surgery time, contribute to the risk of reoperation (22–25). These confounders have not been analysed or adjusted for in this model, simply due to the lack of such information. The models presented in this study only included one-year PROMs and before the construction of a model to scan the register in order to detect these patients there is a need to add further patient data, surgical data and longer follow-ups. Furthermore, patients not returning the PROMs questionnaires might also have a poorer outcome and there are also of course patients in the model with an estimated low risk who will need a future reoperation, but these will not be detected by a system of this kind.

Specific considerations regarding paper V

Time span of two weeks between the distributions of the surveys could be considered a limitation. The most commonly used method to investigate differences between the three- and five-level surveys of the EQ-5D is to administer both surveys at the same sitting, commonly with other surveys in-between the two versions (132, 136, 154). However, it has been shown that patients have a tendency to avoid using the intermediate options in the five level survey if the three level version is administered first in the same sitting (150). In an attempt to avoid this possible bias, we decided to administer the two surveys with a two-week time-span in between. Due to the natural changes in hip symptoms the time span likely contributed to the inconsistency in the responses in the EQ-5D dimensions of "mobility" and "pain".

Another limitation is the various response rates between the different hospitals. There are no explanations for this since demographic do not differ and no other reasons are apparent. At all hospitals except one, both the preoperative- and postoperative response rate for the three level version are close to the average response rate of the EQ-5D 3L in the Swedish Hip Arthroplasty Register, above 90% (16, 107). This is a considerably higher response rate of the survey than in similar studies (9, 10). When comparing to a study investigating preoperative differences in the three- and five level versions of EQ-5D in a THR and knee replacement population the preoperative response frequency of the five level version is similar (10).

Another limitation of this study is that in comparison with other studies that constructs value sets, is the low number of included patients. However, since the purpose of this study was to construct a provisional estimation regarding a Swedish THR-population, the number of included patients is acceptable for its purpose.

The calculated estimate between the EQ-5D-3L and 5L with EQ VAS that is developed in this study is only applicable to a Swedish total hip replacement population. Therefor, these results are limited for this use and cannot be applied in other diagnoses or populations.

Discussion

General discussion

The common feature for all the papers in this thesis is the assessment of the clinical utility of PROMs in total hip replacement surgery, and for Papers I-III in lumbar spine surgery. PROMs have been used and investigated in several different ways, using different methods.

In general, all patients in Paper I to III reports better outcome following surgery, in HRQoL, pain or satisfaction with the outcome, regardless of whether this relates to LSS/LSSS or THR. It is however apparent that patients undergoing surgery in both the hip and spine due to degenerative disorders have a poorer outcome than patients with only surgery in one of the locations. It appears that patients in whom both surgeries are performed within a short time are better off starting with LSSS. It is also apparent that PROMs can be used to detect patients running a higher risk for reoperation. Moreover, the knowledge that the new five level version of the EQ-5D better assesses the outcome following THR adds to a possible improved detection of changes in the care of the THR-population.

The results presented from the studies in this thesis add to the knowledge regarding patients with THR and LSS procedures performed. Moreover, this knowledge can be used for investigations for better planning for time of surgery, to prevent or detect complications and to provide a better understanding of the expected outcome of surgery. Potentially, this may help reduce suffering and pain among patients with degenerative diseases eligible surgical interventions to hip and lumbar spine.

The clinical assessment of PROMs following THRs and LSSs

The numbers of patients with need for both THRs and LSSs will continue to increase for many years to come (1, 2). In time this will also contribute to an increase in the number of patients undergoing both procedures and also contribute to a larger number of patients requiring late reoperations. All these circumstances will increase the pressure on health-care resources, not only in Sweden but also internationally.

Patient-reported outcome measures following surgery in patients with both total hip replacement and lumbar spine surgery

In Papers I and II, patient-reported outcomes following THR and LSS are worse for patients with both procedures performed compared to patients with only one of the procedures performed. Musculoskeletal comorbidity has been reported to be associated with worse patient-reported outcomes following both THR (78, 155) and LSS (83, 84). It is therefore not surprising that patients with surgery-dependent degenerative diseases in both the hip and lumbar spine had poorer outcomes following THR and LSS compared to patients with an isolated total hip replacement or lumbar spine surgery. Furthermore, when comparing the results between Paper I and II, LSS prior to THR appeared to have worse outcomes than the controls for all outcome variables, as opposed to those with LSS after a previous THR who "only" had worse outcomes in back pain. When the two studies are compared in more detail, the emphasis is on the postoperative EQ-5D index and EQ VAS values, as these are the comparable outcome measures between the two studies, similar to what was done in paper III. The investigation of the preoperative variables for EQ-5D index and EQ VAS reveals differences between Paper I and II. Prior to THR in Paper I, the scores for EQ-5D index and EQ VAS were 0.29 and 47.9, respectively, and for Paper II the preoperative values prior to LSS were 0.38 and 48.8 (Tables 2 and 5). The postoperative results for Paper I showed a mean EQ-5D index of 0.66 and EQ VAS of 66.3 (Δ 0.37 and 18.4) and for Paper II 0.62 and 61.8 respectively (Δ 0.24 and 13) (Tables 3 and 6). Comparing these studies, the LSS prior to THR group from Paper I had better outcomes than the THR prior to LSS group from Paper II, but worse preoperative scores and less improvement when compared to patients with only THR and LSS respectively.

Paper I and II contributes to the knowledge of the influence of previous surgery due to degenerative diseases in the lower back and hip. Importantly, the combination of spine and hip problems prior to LSS or THR surgery predispose worse patient-reported outcomes regardless of surgical order. However, patients with LSS prior to THR appear to have a less favorable result compared to patients with THR prior to LSS. However, it is important

to mention that there is a difference in the type of pain originating from degenerative diseases from the hip and lumbar back. The majority of the pain from hip OA is nociceptive while pain from lumbar spinal stenosis (which is the majority of the patients with LSS performed) is neuropathic. This difference in pain mechanism may partly explain why patients with lumbar condition to a larger extent develop chronic pain. Likely, the instruments used are less do not detect such differences. Therefore, the pain measured is somewhat different in its presentation and could probably reflect the differences in outcome in some aspect.

However, patients likely benefit from being informed about the possibility that they might require two different operations to treat their combined symptoms (91). This knowledge about the risk of less improvement in the expected outcome in patients with a known comorbidity should be considered in the shared decision-making process in patients eligible for THR and LSS procedures, and it may help communication in order to set proper expectations for the outcome following total hip replacement and lumbar spine surgery.

Ceiling effects following lumbar spinal surgery and total hip replacement

Ceiling effects are a known limitation of the EQ-5D-3L following several procedures (156). In the papers included into this thesis this has been investigated in Paper V. In this thesis investigation has also been conducted if this limitation is also apparent in Papers I and II. As predicted in Paper I there are ceiling effects with the outcome for all dimensions of the EQ-5D. In paper II on the other hand the ceiling effects are less apparent but still in a majority of the dimensions. In the group with both THR and LSSS it is not surprising that there is less observed ceiling effect in the "mobility" dimension since patients with degenerative disease in multiple locations could be considered to have greater walking impairment. Nevertheless, the presence of ceiling effects presented in paper I, II and V points at this complication with the EQ-5D instrument that reduces the possibility to detect changes of care following orthopedic surgical interventions such as total hip replacement and lumbar spine surgery. The reduction of ceiling effects presented with the use of EQ-5D 5L version in Paper V could be expected to be present in Paper I if used there as well. This could possibly also be expected if implemented into the Swespine in the future.

In addition, the results in Paper V reveal that the use of the EQ-5D-5L reduces not only ceiling effects, it is also more sensitive and provides a deeper descriptive richness following THR. It also demonstrates a strong correlation of the EQ VAS tool administered in the two surveys and that the valuation of the different response option from the two versions follow a consistent pattern. The results indicate that the new version of the EQ-5D provides more accurate information of the outcome following THR. This may facilitate the assessment of health care interventions and improvements in care processes and provides a more fine-granular tool to identify areas to improve. This is especially important since THR is an elective procedure with the main purpose to reduce pain, gain mobility and improve HRQoL.

Shifting to the EQ-5D-5L may improve the assessment of clinical outcomes following both total hip replacement and lumbar spine surgery.

PROMs as predictors of the risk of late reoperation

As presented in Paper IV, PROMs collected one-year after THR can predict the risk of future reoperation. This has a substantial possibility to improve the clinical care of this group of patients running an increased risk of future revision. This knowledge could be used to monitor these patients intensively and deal with their symptoms and complications following THR at an earlier stage, thereby shortening their suffering. This has the potential not only to reduce patient suffering, but also to save health-care resources that could be used elsewhere. The model in our study can also be used to estimate individualized reoperation probabilities at different time intervals. This could be used in the process of developing a warning system to indicate patients running a high risk of future revision following THR. Since the completeness of the register is about 98.1% (16, 107) almost all patients at increased risk for reoperation could be detected. To do so, future studies need to be performed with an increased input of data to the model. A delicate challenge of that work will be to determine the threshold for acceptable and not acceptable levels of increased risks.

The hip-spine syndrome -where to start with surgery, the hip or the spine?

Since the "hip-spine syndrome" was defined by Ofierski et al in the late 1970s, there has been an ongoing discussion were to perform surgery first in patients with known symptomatic degenerative disease in both the hip and lumbar spine.

The results from Paper III suggested, for patients who receives both THR and LSSS procedures within a short

period of time, that those who first receives a LSSS have better final HRQoL outcomes compared to the opposite order. The results also demonstrated that the most improvement occurred between the pre- and postoperative time points for the second procedure, regardless of in which location the first surgery was performed. However, a higher improvement was seen for the group where LSSS where performed as the first procedure. This implies that both surgeries were indicated and needed in order to gain improvement in HRQoL and pain measurements. Only considering the results from paper III, one may conclude that it is preferable to start with LSSS if surgery is indicated in both locations. However, there are other aspects that are needed to be taken into consideration before such a conclusion can be drawn.

Firstly, we looked at the number of patients treated. In Paper III, it is twice as common to start with LSSS and then go on with a THR (n=171) than to start with THR and then receive a LSSS (n=84). This difference was also observed when considering the number of patients in the study groups of Paper I and II. In Paper I there were 997 patients with LSSS prior to THR compared to 220 patients with THR before LSSS in Paper II. Some of these differences in number of procedures might be explained by the different time-periods of inclusion between paper I and II-III. In Paper I, the included years from Swespine was 1998–2012 compared to 2002–2012 in Paper II and III. More spinal diagnoses was also included in Paper I than in Paper II and III. After adjustments of the 86 patients in paper I with LSS prior to 2002 (central spinal stenosis with and without olistesis n=64, lateral spinal stenosis n=12, lumbar spondylosis/spondylolisthesis n=5, and segment related pain n=5), and the patients with lateral spinal stenosis (12%, n=120), lumbar spondylosis/spondylolisthesis (4%, n=38) and segment related pain (4%, n=41), in total 285 patients, there are 712 patients with THR following LSSS. Even after this adjustment, there were almost three times as many patients that received a THR following LSSS than the opposite.

Secondly, we looked at time between surgeries. In Paper III there is a difference in time between surgeries, where the time-period between LSSS first and THR second is significantly shorter than the opposite. Of those with both procedures performed within one year, around 68% of the patients with first LSSS had their THR performed within one year, in contrast to those with first THR where only about 37% received their LSSS within the first year (Figure 16). However, this could be due to that THRs have been more accessible in Sweden the last decades. There is also a time difference between the surgeries between Paper I and II, with 3.27 years between surgeries if LSSS first and 3.0 years if THR first, a difference of almost four months. So, the time differences between hip first and spine first appears to be reduced over time. However, there were differences in these studies where there were patients with LSSS procedures performed from 1998 that could affect this time. Despite these comparisons, it is also important to note that there were no significant differences in postoperative PROs when time between surgeries was investigated separately in any of the Paper I-III, so these time differences between surgeries less likely play any major role for the result obtained.

Thirdly, we compare the outcomes in the two groups in Paper III with the outcomes of the study groups in Paper I and II. Again, only EQ-5D index and EQ VAS were compared since these are the only common PROMs between the three studies. In Paper III, there were no significant difference between the groups preoperatively. Postoperatively, there were significant differences where LSSS prior to THR had an outcome at EQ-5D index of 0.72 and EQ VAS 72.2, compared with THR prior to LSSS with 0.63 and 65.6. If these results are compared with the previous Paper I and II, we can see that the preoperative values for LSSS prior to THR in Paper III are similar to those for LSSS prior to THR in Paper I, and the values for THR prior to LSSS in Paper III are slightly higher than THR prior to LSSS in Paper II. However, the postoperative values for the LSSS prior to THR in Paper III are almost the same as the group with only THR in Paper I. So, this group with LSSS prior to THR performed within a short period of time almost have the same outcome in EQ-5D index and EQ VAS as a group with only THR procedure. For both groups in Paper III the improvement occurred in the time period between pre- and postoperative measurements of the second procedure. If the delta values of EQ-5D index and EQ VAS between before and after the second procedure from these groups were compared to those in the groups with both THR and LSS/LSSS from Paper I and II, we see an interesting relationship. In Paper I, the delta value pre and post THR in the LBS prior to THR group was Δ0.37 for EQ-5D index and Δ18.4 for EQ VAS. These values are very similar to the difference in the LSSS prior to THR group in paper III, with a pre- to postoperative difference of Δ0.37 in EQ-5D index and Δ19.3 in EQ VAS. In Paper II, the THR prior to LSSS group had pre- and post LSSS EQ-5D index changes of 0.24 and for EQ VAS 13 units. This was a slightly less improvement compared to Paper III where the THR prior to LSSS group had a change EQ-5D index of 0.27 and in EQ VAS of 17.27. Comparing results of these studies, all groups had improvement

following their last procedure but LSS prior to THR had a better improvement overall in both EQ-5D and EQ VAS. It is important to mention that these comparisons cannot be determined to be significant or not, just generally compared. However, the observations could be due to that the surgery of the hip and lumbar spine alone respectively had less effect on the symptoms, hence these patients strongly benefit by the following THR or LSS procedure and reflects that the patients were in the need of both procedures due to combination of degenerative diseases.

Lastly, we searched the literature for reports of complications following surgery in patients with known LSS and THR performed. The literature presents several studies reporting that complications following THR increases if there is a previous lumbar spinal fusion performed (157–162). There is also one study presenting that the risk is higher for complication after THR if spinal fusion is performed after THR (161). However, there are no reports of complications following spinal surgery in patients with previous THR. Not surprisingly, these reports take account of the change occurring in pelvic position and less flexibility following lumbar spinal fusion. In a seated position, the pelvic assumes a more (posterior) pelvic tilt. On average this increases by 22º (176), which would result in approximately 15° increase in acetabular anteversion. This increase in anteversion reduces the risk of dislocation due to improved posterior coverage of the femoral head, and also by preventing anterior femoro-acetabular impingement. Spinal fusion to the pelvis prevents the lumbar spine from reducing lordosis and thereby increasing (posterior) pelvic tilt (171). Similarly, a patient with increased pelvic tilt due to spinal deformity will have less change in the postural variation in pelvic tilt. Since spinal deformity correction aims to increase lumbar lordosis, and reduce pelvic tilt with fixation and fusion. As a consequence, changes in spinal alignment will cause a change in acetabular anteversion. A decrease in pelvic tilt is accompanied by a decrease in acetabular anteversion, a change in the anterior pelvic plane by 1° changes acetabular anteversion by 0.7° (163). This imply a higher risk for dislocation of the hip prosthesis following a lumbar spinal fusion. If a spinal fusion is performed prior to THR, this changes in alignment and reduction in the flexibility of the pelvis, which could be taken into consideration when positioning the acetabular cup.

It is probably impossible to create a golden rule for were to begin with surgery in patients with "hip-spine syndrome". However, if we take the knowledge acquired from the studies in this thesis and the literature, an algorithm could be made as a help or guide in the decision-making process relating to the order in which to start, the hip or the spine, in the case of degenerative disease in both locations. This algorithm is presented in Figure 16. Firstly, if the patient has a location with more severe symptoms, it is logical to start with surgery in this location, even if no strict scientific evidence for this exists. If this is the hip and it is suspected that the patient will need a spinal fusion in the future in order to achieve spinal realignment, this needs to be taken into consideration when positioning the acetabular cup, or else fusion of the spine for realignment should be performed first. If the location of pain is inconclusive or both are suspected to generate pain, diagnostic tests with intraarticular injection to the hip joint or spinal nerve root block if unclear foraminal stenosis with local anesthetics can be motivated in order to better determine whether pain derives from the lumbar spine, the hip, or both (75, 91, 102, 105, 106). Since the evidence is somewhat stronger and the procedure is simpler starting with intraarticular injection with local anesthetics to the hip joint is recommended. If the location that is most painful is still inconclusive, the need for spinal fusion for realignment or other reason needs to be determined. If spinal fusion is needed the recommendation is to start with this procedure. This since to start with the spine have a better outcome following THR than the opposite and that the risk for complications, firstly and foremost with dislocation of the THR are somewhat reduced. If there is no need for a fixation, the type of back pain needs to be considered. If it is predominately back pain, starting with THR could be considered since back pain often reduces after THR, a relationship demonstrated in several studies (70, 87–90). However, those patients with radiating sciatic pain could more frequently be in the need of a following lumbar spine surgical procedure. Further, THR improves the patients walking capacity significantly, their mobility increases and can with this reduce their pain from spinal stenosis and possibly postpone the need for a following LSSS. If the patient has radiating pain in the lower limb and hip pain from hip OA, the recommendation is to start with spinal surgical procedure due to better outcome and reduction for risk of complication following THR.

Importantly, the combination of spine and hip problems prior LSSS or THR surgery predispose worse patient-reported outcomes regardless of surgical order, and these patients have a risk for future surgery in the other locations. This much debated issue of where to start with surgery will not end with this thesis. This work contributes to the knowledge about the complicated treatment and assessment of this group of patients with

"hip-spine syndrome", and the influence of previous surgery due to degenerative diseases in the lower back and hip. With this thesis, new knowledge has been provided to the surgeon and patient in order to make better decisions in the shared decision-making process prior to surgery of the hip or lumbar spine.

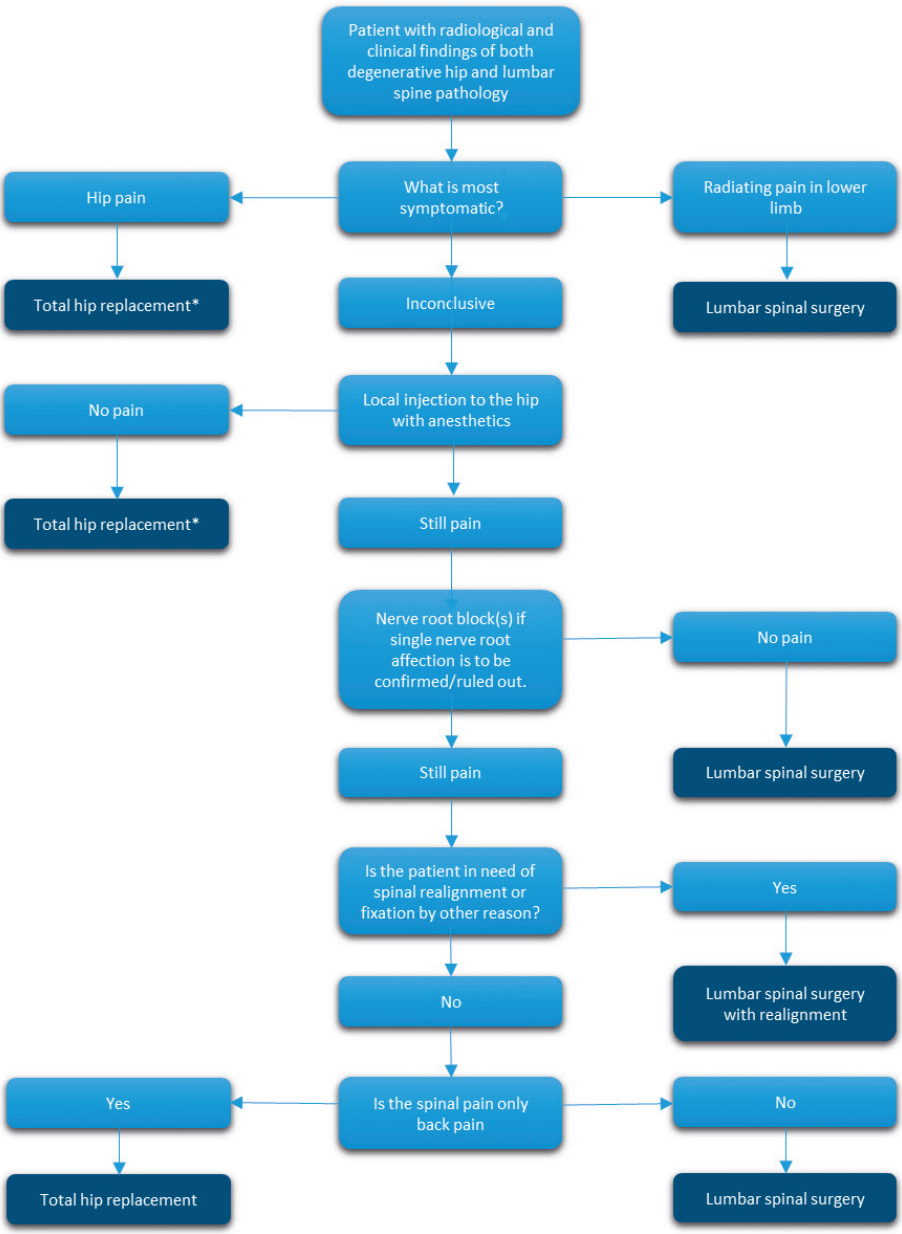


Figure 16. Algorithm presenting decision making tool to decide whether to start with total hip replacement or lumbar spine surgery when degenerative diseases are present in both locations.

**If a need for future spinal fusion is suspected, this needs to be taken into consideration when positioning the acetabular cup, or the decision to begin with realignment of the lumbar spine prior to THR.*

Conclusions

Paper I

3.5% of all patients in whom a THR procedure was performed in 2012 had undergone an LSS procedure during an 11 years period prior to their hip surgery. This estimation could however be considered low, since patients with LSS performed prior to 2002 were not included into the calculation.

Patients who had undergone an LSS prior to their THR generally experienced less pain reduction, worse health-related quality of life and less satisfaction one year after their THR procedure compared to patients with only a THR performed. There was no association of time between surgeries with the outcome following THR. This knowledge is important to communicate in the shared decision-making process prior to a THR and may help set proper expectations for the outcomes following the procedure.

Paper II

Patients undergoing a THR prior to their LSSS generally experience more back pain one year after LSSS compared with patients who had no previous history of THR. No significant differences in health-related quality of life, leg pain, disability and patient satisfaction at one year were reported following the LSSS procedure. There was no association of time between surgeries or type of LSSS procedure with the outcome following the LSSS procedure. This knowledge is important to communicate to patients eligible for LSSS with a known history of previous THR in order to set appropriate expectations for the outcome of surgery.

Paper III

In patients in whom both THR and LSSS procedures have been performed within two years, patients who had an LSSS first had a better outcome following their THR in the EQ-5D index and EQ-VAS than patients who started with THR following their LSSS. It is important to take into consideration that it was twice as common and that there was a significant shorter time between surgeries in those patients that first did LSSS. It is also important to note that this study reflects the outcomes of routine care in Sweden. As such, the decision on the order of surgery can be assumed to be the result of a thorough clinical assessment and shared-decision making. The decision on where to begin should be individualized and balance a number of important factors.

Paper IV

PROMs collected one year after THR are able to predict future reoperations. PROMs one year following THR are stronger predictors of reoperation than age and sex. The model presented is able to estimate individualized reoperation probabilities at different time points. This could be used in order to develop a warning system to indicate those patients running a high risk of reoperation. Including other baseline information in the model could increase its predictive power.

Paper V

The derived value sets conforms well with one an-other and the EQ VAS. This could be used to create a standardized value set for transformations between the 3L and 5L versions in a Swedish total hip replacement population. The results also indicate that the EQ-5D-5L better describes HRQoL in a Swedish total hip replacement-population. Consequently, the new version has been adopted for routine follow-ups in the Swedish Hip Arthroplasty Register.

Future projects

The "hip-spine syndrome"

There are several aspects that needs to be taken into consideration when planning for surgery in patients with known degenerative diseases in both the hip and lumbar spine, and even if this thesis highlights some of them, it is a long way from answering them all. For instance, no information is available today in either of the SHAR or Swespine regarding patients with known degenerative disease but without surgery. It would be very interesting to investigate those patients that for various reasons do not proceed with surgery. For patients with hip OA, they might need to be identified in an early stage in the primary health care and then included into the registry, or to use the information in the BOA-registry (Better management of patients with OsteoArthritis). For the spine patients, it would be possible to include those when referred to the spinal surgical department for an evaluation of whether or not to perform surgery. If these patients could be registered, a much clearer picture of this combination of degenerative disease could be achieved.

There is also the influence of several comorbidities that have not been investigated in these studies such as smoking, BMI, prescriptions of different drugs, socioeconomics and other diseases affecting the outcome such as pulmonary disease (chronic obstructive pulmonary disease), cardiovascular disease or psychiatric disorders. Smoking and BMI have been introduced in the SHAR recent years so those could in a future study be taken into consideration. The knowledge of other comorbidities would need to be taken from the Swedish patient registry. Socioeconomics and prescribed medications could be retrieved following linkage with the Statistics Sweden and Swedish Precribed Drug Registry.

The answer to where to start with surgery in the case of degenerative hip and spine disease has not been fully answered in this thesis. To answer this, a RCT would probably be needed. As the results presents in our studies, there are a substantial number of these patients that are in need of surgery in both location. Following thorough clinical investigation, patients who presents with symptoms from both locations that are in the need of surgical intervention, an RCT could possibly be performed. To achieve enough patients would probably require a multicenter design.

There is reports about the risk for complications following THR in patients with a previous LSS or patients with a LSS following the THR. Further studies on this subject with use of data from the SHAR and the Swespine are planned. In these studies diagnoses of the spine leading to surgery will be considered, but also numbers of segments included in the spine, fusion or non-fusion and involvement of sacrum.

The "hip-knee syndrome"

Another known combination of degenerative disease that are related to the "hip-spine syndrome" is the "hip-knee syndrome". It is not seldom that patients with degenerative diseases in the hip also have degenerative disease in the knee. And as with the "hip-spine syndrome" it is in these cases sometimes difficult to know the origin of pain or were to start with surgery, in the knee or hip. More focus regarding this dilemma have been presented recent years with articles produced. To do similar linkage studies between the Swedish Knee Arthroplasty register and the Swedish Hip Arthroplasty register as those in between the SHAR and Swespine in paper I to III is of course possible and could probably expand the knowledge regarding this dilemma.

Detection of patients with a high risk of reoperation

Following the results in Paper IV the next step would be to construct an automatized algorithm that scans the SHAR in order to detect patients with a high risk for reoperation. This system would then automatically signal the patient's orthopedic department in order to present the possibility for extra follow-ups. To create such an algorithm, the work would be needed to expand beyond clinical sciences and work together with external collaborator with knowledge in computer science and possibly machine learning.

This type of model for detection of complications following THR could possibly be expanded to include patients with degenerative diseases in multiple

locations such as the "spinal stenosis" or "knee OA". For this purpose, there would be a need for inclusion of parameters regarding both knee and spine into the SHAR. This could be accomplished in different ways. One would be to gather more background information in SHAR were the patient state that they have a condition. Or maybe the registers should be annually linked, exchanging information. By doing so those patients with a risk for complication following orthopedic procedures could be identified and counter measures made earlier.

Sammanfattning på svenska

Målsättningen med det här avhandlingsarbetet är att undersöka den kliniska användbarheten av patient-rapporterat utfallsmått (PROMs) hos patienter som är opererade med höftproteskirurgi och ländryggskirurgi.

Avhandlingen baseras på fem delarbeten. I de tre första studierna undersöks utfallet efter kirurgi hos patienter som opererats med *både* höftproteskirurgi och ländryggskirurgi, baserat på data från Svenska Höftprotesregistret och Swespine (Svenska Rygg-registret). Syftet med undersökningarna är att beskriva utfallet efter kirurgi i både höft och rygg samt att undersöka om det finns skillnader i utfall baserat på kirurgins ordning. I studie IV undersöks möjligheten att med patientrapporterade utfallsmått identifiera de patienter som har en ökad risk för omoperation efter höftproteskirurgi. I studie V undersöks om en ny version av det patientrapporterade utfallsmåttet EQ-5D har en bättre förmåga att mäta hälsorelaterad livskvalitet före och efter höftproteskirurgi, samt möjligheten att skapa en mall för att översätta den gamla versionen av EQ-5D till den nya.

Både höftproteskirurgi som utförs på grund av artros och ländryggskirurgi som utförs på grund av spinal stenos är normalt framgångsrika ingrepp med förbättrad hälsorelaterad livskvalitet, minskad smärta och nöjda patienter efter respektive operation. Det finns en grupp av patienter som både har symptom av artros i höften och spinal stenos, det så kallade ”rygg-höftdilemmat”. Dessa patienter kan behöva genomgå ingrepp både med höftprotes- och ländryggskirurgi, dock är resultatet för den här patientgruppen relativt obeforskat. Det är också debatterat var det är bäst att börja med kirurgi, i höften eller ländryggen, hos de patienter som har besvär från både höften och ländryggen.

I studie I undersöktes det patientrapporterade utfallet efter höftproteskirurgi hos patienter som tidigare opererats i ländryggen, det utfallet jämfördes sedan med patienter som enbart opererats med höftproteskirurgi. De patienterna som opererats med både ländryggskirurgi och höftproteskirurgi hade sämre hälsorelaterad livskvalitet, mer smärta och mindre nöjdhet efter höftproteskirurgin jämfört med de patienter som enbart opererats med höftproteskirurgi. Dessa samband verifierades med hjälp av regressionsanalys.

I studie II undersöktes det omvända, det vill säga utfallet efter ländryggskirurgi hos patienter som tidigare hade opererats med höftproteskirurgi, och jämfördes med patienter som enbart opererats med ländryggskirurgi. Patienterna som opererats med först höftproteskirurgi och sedan ländryggskirurgi hade mer smärta i ryggen efter ländryggskirurgin, men det var ingen skillnad i övriga utfallsmått som hälsorelaterad livskvalitet, bensmärta eller nöjdhet med ländryggsoperationen jämfört med de patienter som bara opererats med ländryggskirurgi.

Resultaten från studie I och II talar för att patienter som opereras med både höftproteskirurgi och ländryggskirurgi riskerar att inte förbättras i den omfattning som patienter som bara opererats med antingen höftproteskirurgi eller ländryggskirurgi. Denna kunskap är viktig att förmedla till patienterna i den gemensamma diskussionen inför en eventuell operation för att ge korrekta förväntningar på resultatet av kirurgin.

I studie III undersöktes det patientrapporterade utfallet hos patienter som opererats med både höftproteskirurgi och ländryggskirurgi inom en kort tidsperiod på två år. Den korta tidsperioden valdes för att öka sannolikheten att patienterna hade besvär från både höften och ryggen vid tillfället för första operationen. De patienter som först opererats med ländryggskirurgi hade ett bättre utfall efter den efterföljande höftprotesoperationen än det omvända. Dock är det vanligare att patienterna börjar med ländryggskirurgi och fortsätter med höftproteskirurgi än omvänt vilket kan vara en signal om att höftproteskirurgi kan ha en skyddande effekt på behovet av framtida operation i ländryggen. Det går sannolikt inte att skapa en gyllene regel för att avgöra var det är bäst att börja med kirurgi. En algoritm som beslutsstöd har skapats för att underlätta i beslutet var kirurgi skall påbörjas. Det är dock viktigt att informera dessa patienter att de har en risk för framtida behov av kirurgi i både höften och ländryggen.

Komplikationer efter höftproteskirurgi är ovanligt och således behöver få patienter omopereras efter en höftprotesoperation. Som en konsekvens av detta och att antalet höftprotesoperationer successivt ökar, har behovet för uppföljning efter samtliga höftprotes-operationer börjat ifrågasättas. Resultatet har blivit

att många vårdgivare, både i Sverige men också internationellt, börjat överge rutinmässiga uppföljningar efter höftprotesoperationer. Det finns dock en liten andel patienter som behöver opereras om på grund av olika orsaker, till exempel infektion, att protesen lossnar eller att protesen går ur led. Tidigare studier som har undersökt vilka faktorer som kan förutsäga vilka patienter som har en ökad risk för omoperation har framförallt visat att det är patientrelaterade och kirurgiska faktorer såsom ålder, kön och implantattyp som har störst betydelse. På senare tid har det kommit några studier som visar att även patientrapporterade utfallsmått efter operation kan förutsäga risken för omoperation.

I studie IV undersöktes om patientrapporterade utfallsmått ett år efter höftprotesoperationen kan prediktera risken för framtida behov av omoperation. Studien visade att graden av höftsmärta och nöjdhet var de starkaste prediktiva faktorerna. Den modell som konstruerades hade en måttlig förmåga att bestämma risken för framtida omoperation. Det finns möjlighet att öka modellens prediktiva förmåga genom att tillföra ytterligare variabler. Med hjälp av en sådan modell är det möjligt att skapa en applikation som automatiskt avläser registerdata och identifierar patienter som löper en ökad risk att behöva omopereras. Dessa patienter skulle kunna erbjudas uppföljning och tätare kontakter med sin ortopedklinik. På så sätt skulle förebyggande åtgärder kunna sättas in tidigare, lidande för patienten kan minskas och samhällsresurser sparas.

Sedan Svenska Höftprotesregistret började registrera patientrapporterade utfallsmått 2002 har instrumentet EQ-5D-3L använts. Detta instrument är spritt i stora delar av världen och används för att mäta utfallet efter flera olika interventioner. Instrumentet har dock kritiserats för att det inte förmår beskriva lindrig påverkan på hälsotillståndet; stora delar av populationen anger att de inte har några problem i de fem dimensioner som frågorna avser även om deras hälsotillstånd kan vara påverkat. Det brukar kallas för takeffekt och märks tydligt bland dem som genomgått höftprotesoperation. Därför är de svårt att med EQ-5D-3L skilja mellan dem som blir helt bra och dem som har kvarvarande symptom eller andra hälsoproblem. Därför har ett nytt instrument, EQ-5D-5L tagits fram för att mer nyanserat kunna beskriva utfallet efter en intervention.

I studie V har ett antal patienter fått fylla i både den nya och gamla versionen av EQ-5D före och efter höftproteskirurgi. Studien visar att utfallet blir mer nyanserat beskrivet och takeffekterna minskar med den nya versionen. Det var också möjligt att skapa en mall för att översätta de gamla resultaten till den nya versionen, vilken möjliggör analyser över tid.

Konklusioner från avhandlingen:

- Patienter som är opererade med både ländryggskirurgi och höftprotes har ett sämre patientrapporterat utfall än de patienterna som enbart opereras med ett ingrepp.
- De patienter som först opereras med ländryggskirurgi före höftproteskirurgi har bättre patientrapporterat utfall efter sista operationen jämfört med dem som opereras med höftproteskirurgi följt av ländryggskirurgi.
- Med hjälp av patientrapporterade utfallsmått ett år efter höftproteskirurgi kan man förutsäga risken för framtida omoperation.
- Den nya versionen av EQ-5D med fem svarsalternativ för varje fråga är bättre på att beskriva hälsorelaterad livskvalitet hos patienter som genomgår höftprotesoperation än den gamla versionen med tre svarsalternativ. Korrelationen mellan självskattad hälsa mätt med en VAS-skala av besvär för de olika hälsodimensionerna i de två olika versionerna av EQ-5D följer ett logiskt mönster.

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References

1. Nemes S, Gordon M Fau - Rogmark C, Rogmark C Fau - Rolfson O, Rolfson O. Projections of total hip replacement in Sweden from 2013 to 2030. Acta orthopaedica.85:3:238–43.

2. Strömqvist B, Frizell P, Hägg O, Knutsson B, Gerdhem P, Abbot A, et al. Follow-up of spine surgery in Sweden, Annual register report 2014. 2015.

3. Espehaug B, Havelin LI, Engesaeter LB, Langeland N, Vollset SE. Patient satisfaction and function after primary and revision total hip replacement. Clinical orthopaedics and related research. 1998(351):135–48.

4. Lie SA, Vollset LI, Havelin ON, Furnes LB, Engesæster SE. Failure rates for 4762 revision total hip arthroplasties in the Norwegian arthroplasty register. Journal of Bone and Joint Surgery - Series B. 2004;86(4):504–9.

5. Lübbeke A, Katz JN, Perneger TV, Hoffmeyer P. Primary and revision hip arthroplasty: 5-year outcomes and influence of age and comorbidity. The Journal of rheumatology. 2007;34(2):394.

6. Rolfson O, Karrholm J, Dahlberg LE, Garellick G. Patient-reported outcomes in the Swedish Hip Arthroplasty Register: results of a nationwide prospective observational study. The Journal of bone and joint surgery British volume. 2011;93(7):867–75.

7. EuroQol - a new facility for the measurement of health-related quality of life. Health policy (Amsterdam, Netherlands). 1990;16(3):199–208.

8. Devlin NJ, Krabbe PFM. The development of new research methods for the valuation of EQ-5D-5L. The European journal of health economics : HEPAC : health economics in prevention and care. 2013;14 Suppl 1:S1.

9. Greene ME, Rader KA, Garellick G, Malchau H, Freiberg AA, Rolfson O. The EQ-5D-5L Improves on the EQ-5D-3L for Health-related Quality-of-life Assessment in Patients Undergoing Total Hip Arthroplasty. Clinical orthopaedics and related research. 2015;473(11):3383.

10. Conner-Spady BL, Marshall DA, Bohm E, Dunbar MJ, Loucks L, Al Khudairy A, et al. Reliability and validity of the EQ-5D-5L compared to the EQ-5D-3L in patients with osteoarthritis referred for hip and knee replacement. Qual Life Res. 2015;24(7):1775–84.

11. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2011;20(10):1727.

12. Danielsson L, Lindberg H. Prevalence of coxarthrosis in an urban population during four decades. Clinical orthopaedics and related research. 1997(342):106–10.

13. Dagenais S, Garbedian S, Wai EK. Systematic review of the prevalence of radiographic primary hip osteoarthritis. Clinical orthopaedics and related research. 2009;467(3):623–37.

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

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

16. Rolfson O, Kärrholm J, Rogmark C, Nemes S, Lindahl H, Malchau H, et al. Swedish Hip Arthroplasty Register, Annual Report 2016. Report. 2017.

17. 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;Dec;87(6):546–553.

18. Singh JA, Kundukulam J, Riddle DL, Strand V, Tugwell P. Early Postoperative Mortality Following Joint Arthroplasty: A Systematic Review. The Journal of rheumatology. 2011;38(7):1507–13.

19. 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.

20. Bolz KMD, Crawford RW, Donnelly B, Whitehouse SL, Graves N. The Cost-effectiveness of Routine Follow-up After Primary Total Hip Arthroplasty. The Journal of arthroplasty. 2010;25(2):191–6.

21. Sethuraman V, McGuigan J, Hozack WJ, Sharkey PF, Rothman RH. Routine follow-up office visits after total joint replacement: Do asymptomatic patients wish to comply? The Journal of arthroplasty. 2000;15(2):183–6.

22. Dy CJ, Bozic KJ, Pan TJ, Wright TM, Padgett DE, Lyman S. Risk Factors for Early Revision After Total Hip Arthroplasty. Arthritis Care & Research. 2014;66(6):907–15.

23. Paxton EW, Inacio MCS, Khatod M, Yue E, Funahashi T, Barber T. Risk calculators predict failures of knee and hip arthroplasties: findings from a large health maintenance organization. Clinical orthopaedics and related research. 2015;473(12):3965.

24. Wright EA, Katz JN, Baron JA, Wright RJ, Malchau H, Mahomed N, et al. Risk factors for revision of primary total hip replacement: Results from a national case–control study. Arthritis Care & Research. 2012;64(12):1879–85.

25. Prokopetz JJZ, Losina E, Bliss RL, Wright J, Baron JA, Katz JN. Risk factors for revision of primary total hip arthroplasty: a systematic review. BMC Musculoskeletal Disorders. 2012;13:251-.

26. Singh JA, Schleck C, Harmsen S, Lewallen D. Clinically important improvement thresholds for Harris Hip Score and its ability to predict revision risk after primary total hip arthroplasty. BMC Musculoskeletal Disorders. 2016;17(1):<xocs:firstpage xmlns:xocs="&#;/>.

27. Rothwell AG, Hooper GJ, Hobbs A, Frampton CM. An analysis of the Oxford hip and knee scores and their relationship to early joint revision in the New Zealand Joint Registry. The Journal of bone and joint surgery British volume. 2010;92(3):413–8.

28. Devane P, Horne G, Gehling D. Oxford Hip Scores at 6 Months and 5 Years Are Associated With Total Hip Revision Within the Subsequent 2 Years. Clinical orthopaedics and related research. 2013;471(12):3870–4.

29. Borenstein DG, O'Mara JW, Boden SD, Lauerman WC, Jacobson A, Platenberg C, et al. The Value of Magnetic Resonance Imaging of the Lumbar Spine to Predict Low-Back Pain in Asymptomatic Subjects. A Seven-Year Follow-up Study. 2001;83(9):1306–11.

30. Lurie JD, Tosteson TD, Tosteson A, Abdu WA, Zhao W, Morgan TS, et al. Long-term outcomes of lumbar spinal stenosis: eight-year results of the Spine Patient Outcomes Research Trial (SPORT). Spine (Phila Pa 1976). 2015;40(2):63–76.

31. Stromqvist B, Fritzell P, Hagg O, Jonsson B, Swedish Society of Spinal S. The Swedish Spine Register: development, design and utility. Eur Spine J. 2009;18 Suppl 3(1432-0932 (Electronic)):294–304.

32. Ciol MA, Deyo RA, Howell E, Kreif S. An assessment of surgery for spinal stenosis: time trends, geographic variations, complications, and reoperations. J Am Geriatr Soc. 1996;44(3):285–90.

33. Deyo RA, Mirza Sk Fau - Martin BI, Martin Bi Fau - Kreuter W, Kreuter W Fau - Goodman DC, Goodman Dc Fau - Jarvik JG, Jarvik JG. Trends, major medical complications, and charges associated with surgery for lumbar spinal stenosis in older adults. JAMA. 2010;303(13):1259–65.

34. Du Bois M, Szpalski M, Donceel P. A decade's experience in lumbar spine surgery in Belgium: sickness fund beneficiaries, 2000–2009. Eur Spine J. 2012;21(12):2693–703.

35. Hansson T, Suzuki N, Hebelka H, Gaulitz A. The narrowing of the lumbar spinal canal during loaded MRI: the effects of the disc and ligamentum flavum. Eur Spine J. 2009;18(5):679–86.

36. Lurie J, Tomkins-Lane C. Management of lumbar spinal stenosis. BMJ. 2016;352.

37. Newman PH. Spondylolisthesis, its cause and effect. Annals of the Royal College of Surgeons of England. 1955;16(5):305–23.

38. Katz JN, Dalgas M, Stucki G, Katz NP, Bayley J, Fossel AH, et al. Degenerative lumbar spinal stenosis. Diagnostic value of the history and physical examination. Arthritis Rheum. 1995;38(9):1236–41.

39. Watters WC, 3rd, Baisden J, Gilbert TJ, Kreiner S, Resnick DK, Bono CM, et al. Degenerative lumbar spinal stenosis: an evidence-based clinical guideline for the diagnosis and treatment of degenerative lumbar spinal stenosis. The spine journal : official journal of the North American Spine Society. 2008;8(2):305–10.

40. Schizas C, Theumann N, Burn A, Tansey R, Wardlaw D, Smith FW, et al. Qualitative grading of severity of lumbar spinal stenosis based on the morphology of the dural sac on magnetic resonance images. Spine (Phila Pa 1976). 2010;35(21):1919–24.

41. Schonstrom N, Lindahl S, Willen J, Hansson T. Dynamic changes in the dimensions of the lumbar spinal canal: an experimental study in vitro. J Orthop Res. 1989;7(1):115–21.

42. Friedly JL, Comstock BA, Turner JA, Heagerty PJ, Deyo RA, Sullivan SD, et al. A randomized trial of epidural glucocorticoid injections for spinal stenosis. N Engl J Med. 2014;371(1):11–21.

43. Kovacs FM, Urrutia G, Alarcon JD. Surgery versus conservative treatment for symptomatic lumbar spinal stenosis: a systematic review of randomized controlled trials. Spine (Phila Pa 1976). 2011;36(20):E1335–51.

44. Nord T, Kornerup U, Gronlund P, Reuterwall C. [Exercise reduced the need for operation in lumbar spinal stenosis. Circulatory load in the form of cycling gave good effect]. LID - C7XP [pii]. Lakartidningen. 2015(112:C7XP).

45. Atlas SJ, Keller RB, Robson D, Deyo RA, Singer DE. Surgical and nonsurgical management of lumbar spinal stenosis: four-year outcomes from the maine lumbar spine study. Spine (Phila Pa 1976). 2000;25(5):556–62.

46. Amundsen T, Weber H, Nordal HJ, Magnaes B, Abdelnoor M, Lilleas F. Lumbar spinal stenosis: conservative or surgical management?: A prospective 10-year study. Spine (Phila Pa 1976). 2000;25(11):1424–35; discussion 35–6.

47. Malmivaara A, Slatis P, Heliovaara M, Sainio P, Kinnunen H, Kankare J, et al. Surgical or nonoperative treatment for lumbar spinal stenosis? A randomized controlled trial. Spine (Phila Pa 1976). 2007;32(1):1–8.

48. Weinstein JN, Lurie JD, Tosteson TD, Tosteson AN, Blood EA, Abdu WA, et al. Surgical versus nonoperative treatment for lumbar disc herniation: four-year results for the Spine Patient Outcomes Research Trial (SPORT). Spine (Phila Pa 1976). 2008;33(25):2789–800.

49. Roy-Camille R. R-C, M.,, Demeulenaere C. Osteosynthesis of dorsal, lumbar, and lumbosacral spine with metallic plates screwed into vertebral pedicles and articular apophyses. Presse Med. 1970;Jun;78(32):1447–8.

50. Bernhardt M, Swartz DE, Clothiaux PL, Crowell RR, White AA. Posterolateral Lumbar and Lumbosacral Fusion with and without Pedicle Screw Internal-Fixation. Clinical orthopaedics and related research. 1992(284):109–15.

51. Thomsen K, Christensen FB, Eiskjaer SP, Hansen ES, Fruensgaard S, Bunger CE. 1997 Volvo Award winner in clinical studies. The effect of pedicle screw instrumentation on functional outcome and fusion rates in posterolateral lumbar spinal fusion: a prospective, randomized clinical study. Spine (Phila Pa 1976). 1997;22(24):2813–22.

52. Fischgrund JS, Mackay M, Herkowitz HN, Brower R, Montgomery DM, Kurz LT. 1997 Volvo Award winner in clinical studies – Degenerative lumbar spondylolisthesis with spinal stenosis: A prospective, randomized study comparing decompressive laminectomy and arthrodesis with and without spinal instrumentation. Spine. 1997;22(24):2807–12.

53. Yuan HA, Garfin SR, Dickman CA, Mardjetko SM. A Historical Cohort Study of Pedicle Screw Fixation in Thoracic, Lumbar, and Sacral Spinal Fusions. Spine (Phila Pa 1976). 1994;19(20 Suppl):2279S-96S.

54. Kanayama M, Cunningham Bw - Sefter JC, - Goldstein JA, - Stewart G, - Kaneda K, - McAfee PC, et al. Does spinal instrumentation influence the healing process of posterolateral spinal fusion? An in vivo animal model. Spine. 1999;24(11:1058–65.

55. Gibson JN, Grant IC, Waddell G. The Cochrane review of surgery for lumbar disc prolapse and degenerative lumbar spondylosis. Spine (Phila Pa 1976). 1999;24(17):1820–32.

56. Johnsson KE, Redlund-Johnell I, Uden A, Willner S. Preoperative and postoperative instability in lumbar spinal stenosis. Spine (Phila Pa 1976). 1989;14(6):591–3.

57. Hasegawa K, Kitahara K, Shimoda H, Ishii K, Ono M, Homma T, et al. Lumbar Degenerative Spondylolisthesis Is Not Always Unstable: Clinicobiomechanical Evidence. Spine. 2014;39(26).

58. Forsth P, Michaelsson K Fau - Sanden B, Sanden B. Does fusion improve the outcome after decompressive surgery for lumbar spinal stenosis?: A two-year follow-up study involving 5390 patients. The bone & joint journal. 2013;95-B:960–5.

59. Forsth P, Olafsson G, Carlsson T, Frost A, Borgstrom F, Fritzell P, et al. A Randomized, Controlled Trial of Fusion Surgery for Lumbar Spinal Stenosis. N Engl J Med. 2016;374(15):1413–23.

60. Försth P. On Surgery for Lumbar Spinal Stenosis. 2015.

61. Juratli SM, Mirza SK, Fulton-Kehoe D, Wickizer TM, Franklin GM. Mortality after lumbar fusion surgery. Spine (Phila Pa 1976). 2009;34(7):740–7.

62. Deyo RA, Mirza SK, Martin BI, Kreuter W, Goodman DC, Jarvik JG. Trends, major medical complications, and charges associated with surgery for lumbar spinal stenosis in older adults. JAMA. 2010;303(13):1259–65.

63. Faciszewski T, Winter RB, Lonstein JE, Denis F, Johnson L. The surgical and medical perioperative complications of anterior spinal fusion surgery in the thoracic and lumbar spine in adults. A review of 1223 procedures. Spine (Phila Pa 1976). 1995;20(14):1592–9.

64. Steiger F, Becker HJ, Standaert CJ, Balague F, Vader JP, Porchet F, et al. Surgery in lumbar degenerative spondylolisthesis: indications, outcomes and complications. A systematic review. European Spine Journal. 2014;23(5):945–73.

65. Smorgick Y, Baker KC, Herkowitz H, Montgomery D, Badve SA, Bachison C, et al. Predisposing factors for dural tear in patients undergoing lumbar spine surgery. Journal of neurosurgery Spine. 2015;22(5):483.

66. Sin AH, Caldito G, Smith D, Rashidi M, Willis B, Nanda A. Predictive factors for dural tear and cerebrospinal fluid leakage in patients undergoing lumbar surgery. Journal of neurosurgery Spine. 2006;5(3):224.

67. Cammisa FP, Jr., Girardi FP, Sangani PK, Parvataneni HK, Cadag S, Sandhu HS. Incidental durotomy in spine surgery. Spine (Phila Pa 1976). 2000;25(20):2663–7.

68. Guerin P, El Fegoun AB, Obeid I, Gille O, Lelong L, Luc S, et al. Incidental durotomy during spine surgery: incidence, management and complications. A retrospective review. Injury. 2012;43(4):397–401.

69. Khan MH, Rihn J, Steele G, Davis R, Donaldson WF, 3rd, Kang JD, et al. Postoperative management protocol for incidental dural tears during degenerative lumbar spine surgery: a review of 3,183 consecutive degenerative lumbar cases. Spine (Phila Pa 1976). 2006;31(22):2609–13.

70. Prather H, Van Dillen LR, Kymes SM, Armbrecht MA, Stwalley D, Clohisy JC. Impact of coexistent lumbar spine disorders on clinical outcomes and physician charges associated with total hip arthroplasty. The spine journal : official journal of the North American Spine Society. 2012;12(5):363–9.

71. Jonsson B, Annertz M, Sjoberg C, Stromqvist B. A prospective and consecutive study of surgically treated lumbar spinal stenosis. Part II: Five-year follow-up by an independent observer. Spine (Phila Pa 1976). 1997;22(24):2938–44.

72. Offierski CM, MacNab I. Hip-spine syndrome. Spine (Phila Pa 1976). 1983;8(3):316–21.

73. Bohl WR, Steffee AD. Lumbar spinal stenosis. A cause of continued pain and disability in patients after total hip arthroplasty. Spine (Phila Pa 1976). 1979;4(2):168–73.

74. McNamara MJ, Barrett KG, Christie MJ, Spengler DM. Lumbar spinal stenosis and lower extremity arthroplasty. The Journal of arthroplasty. 1993;8(3):273–7.

75. Devin CJ, McCullough KA, Morris BJ, Yates AJ, Kang JD. Hip-spine syndrome. The Journal of the American Academy of Orthopaedic Surgeons. 2012;20(7):434–42.

76. Mnatzaganian G, Ryan P, Norman PE, Hiller JE. Accuracy of hospital morbidity data and the performance of comorbidity scores as predictors of mortality. Journal of clinical epidemiology. 2012;65(1):107–15.

77. Greene ME, Rolfson O, Gordon M, Garellick G, Nemes S. Standard Comorbidity Measures Do Not Predict Patient-reported Outcomes 1 Year After Total Hip Arthroplasty. Clinical Orthopaedics and Related Research®. 2015:1–10.

78. Gordon M, Frumento P, Skoldenberg O, Greene M, Garellick G, Rolfson O. Women in Charnley class C fail to improve in mobility to a higher degree after total hip replacement. Acta orthopaedica. 2014;85(4):335–41.

79. Quintana JM, Escobar A, Aguirre U, Lafuente I, Arenaza JC. Predictors of Health-related Quality-of-life Change after Total Hip Arthroplasty. Clinical Orthopaedics and Related Research®. 2009;467(11):2886.

80. Bischoff-Ferrari HA, Lingard EA, Losina E, Baron JA, Roos EM, Phillips CB, et al. Psychosocial and geriatric correlates of functional status after total hip replacement. Arthritis Rheum. 2004;51(5):829–35.

81. Jauregui JJ, Banerjee S, Issa K, Cherian JJ, Mont MA. Does Co-Existing Lumbar Spinal Canal Stenosis Impair Functional Outcomes and Activity Levels after Primary Total Hip Arthroplasty? The Journal of arthroplasty. 2015;30(9):1569–73.

82. Airaksinen O, Herno A, Turunen V, Saari T, Suomlainen O. Surgical outcome of 438 patients treated surgically for lumbar spinal stenosis. Spine. 1997;22(19):2278.

83. Hurri H, Slätis P, Soini J, Tallroth K, Alaranta H, Laine T, et al. Lumbar spinal stenosis: assessment of long-term outcome 12 years after operative and conservative treatment. Journal of spinal disorders. 1998;11(2):110.

84. Katz JN, Stucki G, Lipson SJ, Fossel AH, Grobler LJ, Weinstein JN. Predictors of surgical outcome in degenerative lumbar spinal stenosis. Spine. 1999;24(21):2229.

85. Aalto JT, Malmivaara JA, Kovacs JF, Herno JA, Alen JM, Salmi JL, et al. Preoperative Predictors for Postoperative Clinical Outcome in Lumbar Spinal Stenosis: Systematic Review. Spine. 2006;31(18):E648-E63.

86. Foulongne E, Derrey S - Ould Slimane M, - Leveque S, - Tobenas AC, - Dujardin F, - Freger P, et al. Lumbar spinal stenosis: which predictive factors of favorable functional results after decompressive laminectomy? Neurochirurgie. 2013;Volume 59, Issue 1, :Pages 23–9.

87. Ben-Galim P, Ben-Galim T, Rand N, Haim A, Hipp J, Dekel S, et al. Hip-spine syndrome: the effect of total hip replacement surgery on low back pain in severe osteoarthritis of the hip. Spine (Phila Pa 1976). 2007;32(19):2099–102.

88. Redmond JM, Gupta A, Hammarstedt JE, Stake CE, Domb BG. The hip-spine syndrome: how does back pain impact the indications and outcomes of hip arthroscopy? Arthroscopy : the journal of arthroscopic & related surgery : official publication of the Arthroscopy Association of North America and the International Arthroscopy Association. 2014;30(7):872–81.

89. Parvizi J, Pour AE, Hillibrand A, Goldberg G, Sharkey PF, Rothman RH. Back pain and total hip arthroplasty: a prospective natural history study. Clinical Orthopaedics and Related Research®. 2010;468(5):1325–30.

90. Hsieh PH CY, Chen DW, Lee MS. Pain distribution and response to total hip arthroplasty: a prospective observational study in 113 patients with end-stage hip disease. J Orthop Sci. 2012;17:213–8.

91. Fogel GR, Esses SI. Hip spine syndrome: management of coexisting radiculopathy and arthritis of the lower extremity. The spine journal : official journal of the North American Spine Society. 2003;3(3):238–41.

92. Pritchett JW. Lumbar decompression to treat foot drop after hip arthroplasty. Clinical orthopaedics and related research. 1994(303):173–7.

93. March L, Smith EUR, Hoy DG, Cross MJ, Sanchez-Riera L, Blyth F, et al. Burden of disability due to musculoskeletal (MSK) disorders. Best Pract Res Cl Rh. 2014;28(3):353–66.

94. Becker A, Held H, Redaelli M, Strauch K, Chenot J, Leonhardt C, et al. Low Back Pain in Primary Care Costs of Care and Prediction of Future Health Care Utilization. SPINE. 2010;35(18):1714–20.

95. Nijs J, Apeldoorn A, Hallegraeff H, Clark J, Smeets R, Malfliet A, et al. Low back pain: guidelines for the clinical classification of predominant neuropathic, nociceptive, or central sensitization pain. Pain Physician. 2015;18(3):E333–46.

96. Smart KM, Blake C, Staines A, Doody C. Clinical indicators of 'nociceptive', 'peripheral neuropathic' and 'central' mechanisms of musculoskeletal pain. A Delphi survey of expert clinicians. Manual Therapy. 2010;15(1):80–7.

97. French HP, Smart KM, Doyle F. Prevalence of neuropathic pain in knee or hip osteoarthritis: A systematic review and meta-analysis. Seminars in Arthritis and Rheumatism. 2017;47(1):1–8.

98. Schilder A, Hoheisel U, Magerl W, Benrath J, Klein T, Treede R-D. Sensory findings after stimulation of the thoracolumbar fascia with hypertonic saline suggest its contribution to low back pain. Pain. 2014;155(2):222–31.

99. Tsao JH, Tucker WK, Coppieters WM, Hodges WP. Experimentally induced low back pain from hypertonic saline injections into lumbar interspinous ligament and erector spinae muscle. Pain. 2010;150(1):167–72.

100. Park SY, An HS, Moon SH, Lee HM, Suh SW, Chen D, et al. Neuropathic Pain Components in Patients with Lumbar Spinal Stenosis. Yonsei Medical Journal. 2015;56(4):1044–50.

101. Cohen SP, Mao J. Neuropathic pain: mechanisms and their clinical implications. BMJ : British Medical Journal. 2014;348.

102. Sembrano JN, Polly DW, Jr. How often is low back pain not coming from the back? Spine. 2009;34(1):E27-32.

103. Lesher JM, Dreyfuss P, Hager N, Kaplan M, Furman M. Hip joint pain referral patterns: a descriptive study. Pain medicine (Malden, Mass). 2008;9(1):22–5.

104. Khan AM, McLoughlin E, Giannakas K, Hutchinson C, Andrew JG. Hip osteoarthritis: where is the pain? Annals of the Royal College of Surgeons of England. 2004;86(2):119–21.

105. Pateder DB, Hungerford MW. Use of fluoroscopically guided intra-articular hip injection in differentiating the pain source in concomitant hip and lumbar spine arthritis. American journal of orthopedics (Belle Mead, NJ). 2007;36(11):591–3.

106. Brown MD, Gomez-Marin O, Brookfield KFW, Li PS. Differential Diagnosis of Hip Disease Versus Spine Disease. Clinical orthopaedics and related research. 2004;419:280–4.

107. Garellick G, Kärrholm J, Lindahl H, Malchau H, Rogmark C, Rolfson O. Swedish Hip Arthroplasty Register, Annual report 2014. 2015.

108. Malchau H. On the importance of stepwise introduction of new hip implant technology : assessment of total hip replacement using clinical evaluation, radiostereometry, digitised radiography and a national hip registry. 2008.

109. Williams A. Euroqol – a New Facility for the Measurement of Health-Related Quality-of-Life. Health policy (Amsterdam, Netherlands). 1990;16(3):199–208.

110. Scott J, Huskisson E. Graphic representation of pain. Pain. 1976;2(2):175–84.

111. Charnley J. The long-term results of low-friction arthroplasty of the hip performed as a primary intervention. Journal of Bone & Joint Surgery, British Volume. 1972;54(1):61–76.

112. Rabin R, Charro Fd. EQ-SD: a measure of health status from the EuroQol Group. Annals of medicine. 2001;33(5):337–43.

113. Fairbank JC, Pynsent PB. The Oswestry Disability Index. Spine. 2000;Volume 25(22) 2940–53.

114. Jenkinson C Fau - Wright L, Wright L Fau - Coulter A, Coulter A. The SF 36 health survey questionnaire. ...if used within its limits. 1993;307:449.

115. 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.

116. Fröbert O, Lagerqvist B, Olivecrona GK, Omerovic E, Gudnason T, Maeng M, et al. Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction. The New England Journal of Medicine. 2013;369(17):1587–97.

117. Dawson J, Fitzpatrick R, Carr A, Murray D. Questionnaire on the perceptions of patients about total hip replacement. Journal of Bone and Joint Surgery-British Volume. 1996;78b(2):185–90.

118. 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 RegistriesPart II. Recommendations for selection, administration, and analysis. Acta orthopaedica. 2016;87(Suppl 1):9–23.

119. Kennedy DM, Stratford PW, Wessel J, Gollish JD, Penney D. Assessing stability and change of four performance measures: a longitudinal study evaluating outcome following total hip and knee arthroplasty. BMC Musculoskelet Disord. 2005;6(1471–2474):3.

120. Kovacs FM, Abraira V, Royuela A, Corcoll J, Alegre L, Tomas M, et al. Minimum detectable and minimal clinically important changes for pain in patients with nonspecific neck pain. BMC Musculoskelet Disord. 2008;9(1471–2474):43.

121. Brozek JL, Guyatt GH, Schunemann HJ. How a well-grounded minimal important difference can enhance transparency of labelling claims and improve interpretation of a patient reported outcome measure. Health Qual Life Outcomes. 2006;4:69.

122. Greene ME. Who should have total hip replacement? Use of patient-reported outcome measures in identifying the indications for and assessment of total hip replacement. 2015.

123. Bobrovitz N, Santana MJ, Kline T, Kortbeek J, Widder S, Martin K, et al. Multicenter validation of the Quality of Trauma Care Patient-Reported Experience Measure (QTAC-PREM). The journal of trauma and acute care surgery. 2016;80(1):111.

124. Burstrom K, Sun S, Gerdtham UG, Henriksson M, Johannesson M, Levin LA, et al. Swedish experience-based value sets for EQ-5D health states. Qual Life Res. 2014;23(2):431–42.

125. Nemes S, Burstrom K, Zethraeus N, Eneqvist T, Garellick G, Rolfson O. Assessment of the Swedish EQ-5D experience-based value sets in a total hip replacement population. Qual Life Res. 2015;24(12):2963–70.

126. Devlin NJ, Parkin D, Browne J. Patient-reported outcome measures in the NHS: new methods for analysing and reporting EQ-5D data. Health Economics. 2010;19(8):886–905.

127. Lawless B, Greene M, Slover J, Kwon Y-M, Malchau H. Does Age or Bilateral Disease Influence the Value of Hip Arthroplasty? Clinical Orthopaedics and Related Research®. 2012;470(4):1073–8.

128. Brazier J, Roberts J, Tsuchiya A, Busschbach J. A comparison of the EQ-5D and SF-6D across seven patient groups. Health Economics. 2004;13(9):873–84.

129. Johnson AJ, Pickard SA. Comparison of the EQ-5D and SF-12 Health Surveys in a General Population Survey in Alberta, Canada. Medical Care. 2000;38(1):115–21.

130. Sullivan WP, Lawrence FW, Ghushchyan FV. A National Catalog of Preference-Based Scores for Chronic Conditions in the United States. Medical Care. 2005;43(7):736–49.

131. Giesinger K, Hamilton DF, Jost B, Holzner B, Giesinger JM. Comparative responsiveness of outcome measures for total knee arthroplasty. Osteoarthritis and Cartilage. 2014;22(2):184–9.

132. Janssen MF, Pickard AS, Golicki D, Gudex C, Niewada M, Scalone L, et al. Measurement properties of the EQ-5D-5L compared to the EQ-5D-3L across eight patient groups: a multi-country study. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2013;22(7):1717.

133. Fransen M, Edmonds J. Reliability and validity of the EuroQol in patients with osteoarthritis of the knee. Rheumatology. 1999;38(9):807–13.

134. Wolfe F, Hawley DJ. Measurement of the quality of life in rheumatic disorders using the EuroQol. Rheumatology. 1997;36(7):786–93.

135. Hinz A, Kohlmann T, Stöbel-Richter Y, Zenger M, Brähler E. The quality of life questionnaire EQ-5D-5L: psychometric properties and normative values for the general German population. An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation – Official Journal of the International Society of Quality of Life Research. 2014;23(2):443–7.

136. Scalone L, Ciampichini R, Fagiuoli S, Gardini I, Fusco F, Gaeta L, et al. Comparing the performance of the standard EQ-5D 3L with the new version EQ-5D 5L in patients with chronic hepatic diseases. Qual Life Res. 2013;22(7):1707–16.

137. Pickard SA, De Leon CM, Kohlmann CT, Cella CD, Rosenbloom CS. Psychometric Comparison of the Standard EQ-5D to a 5 Level Version in Cancer Patients. Medical Care. 2007;45(3):259–63.

138. Bharmal M, Thomas J. Comparing the EQ-5D and the SF-6D descriptive systems to assess their ceiling effects in the US general population. Value in Health. 2006;9(4):262–71.

139. Brazier J, Roberts J, Tsuchiya A, Busschbach J. A comparison of the EQ-5D and SF-6D across seven patient groups. Health Econ. 2004;13(9):873–84.

140. Gunther OH, Roick C, Angermeyer MC, Konig HH. The responsiveness of EQ-5D utility scores in patients with depression: A comparison with instruments measuring quality of life, psychopathology and social functioning. J Affect Disord. 2008;105(1–3):81–91.

141. Johnson JA, Pickard AS. Comparison of the EQ-5D and SF-12 health surveys in a general population survey in Alberta, Canada. Med Care. 2000;38(1):115–21.

142. Kopec JA, Willison KD. A comparative review of four preference-weighted measures of health-related quality of life. J Clin Epidemiol. 2003;56(4):317–25.

143. Luo N, Johnson Ja Fau - Shaw JW, Shaw Jw Fau - Feeny D, Feeny D Fau - Coons SJ, Coons SJ. Self-reported health status of the general adult U.S. population as assessed by the EQ-5D and Health Utilities Index. Medical care. 2005;Volume 43(11) pp 1078–86.

144. Sullivan PW, Lawrence WF, Ghushchyan V. A national catalog of preference-based scores for chronic conditions in the United States. Med Care. 2005;43(7):736–49.

145. Roder C, Staub LP, Eichler P, Widmer M, Dietrich D, Eggli S, et al. Avoiding misclassification bias with the traditional Charnley classification: rationale for a fourth Charnley class BB. J Orthop Res. 2006;24(9):1803–8.

146. Greene ME, Rolfson O, Garellick G, Gordon M, Nemes S. Improved statistical analysis of pre- and post-treatment patient-reported outcome measures (PROMs): the applicability of piecewise linear regression splines. Qual Life Res. 2015;24(3):567–73.

147. Clement ND, Muzammil A, Macdonald D, Howie CR, Biant LC. Socioeconomic status affects the early outcome of total hip replacement. The Journal of bone and joint surgery British volume. 2011;93(4):464.

148. Stuart EA. Matching methods for causal inference: A review and a look forward. Statistical science : a review journal of the Institute of Mathematical Statistics. 2010;25(1):1–21.

149. Heagerty PJ, Zheng Y. Survival Model Predictive Accuracy and ROC Curves. Biometrics. 2005;61(1):92–105.

150. Janssen MF, Birnie E, Haagsma JA, Bonsel GJ. Comparing the Standard EQ□5D Three□Level System with a Five□Level Version. Value in Health. 2008;11(2):275–84.

151. Lim CR, Harris K, Dawson J, Beard DJ, Fitzpatrick R, Price AJ. Floor and ceiling effects in the OHS: an analysis of the NHS PROMs data set. BMJ Open. 2015;5(7):e007765.

152. Myers JL, Well AD. Research Design and Statistical Analysis (2nd ed.). Lawrence Erlbaum. 2003: p. 508.

153. Pepe MS, Longton G, Leisenring W, Newcomb P, Janes H. Limitations of the odds ratio in gauging the performance of a diagnostic, prognostic, or screening marker. American Journal of Epidemiology. 2004;159(9):882–90.

154. Craig BM, Pickard AS, Lubetkin EI. More Common, but Less Severe: Differences between EQ-5D 3-Level, Youth, and 5-Level Versions. Journal of clinical epidemiology. 2014;67(1):93–9.

155. Ayers DC, Li W, Oatis C, Rosal MC, Franklin PD. Patient-reported outcomes after total knee replacement vary on the basis of preoperative coexisting disease in the lumbar spine and other nonoperatively treated joints: the need for a musculoskeletal comorbidity index. The Journal of bone and joint surgery American volume. 2013;95(20):1833–7.

156. Buchholz I, Janssen MF, Kohlmann T, Feng Y-S. A Systematic Review of Studies Comparing the Measurement Properties of the Three-Level and Five-Level Versions of the EQ-5D. PharmacoEconomics. 2018.

157. Sing DC, Barry JJ, Aguilar TU, Theologis AA, Patterson JT, Tay BK, et al. Prior Lumbar Spinal Arthrodesis Increases Risk of Prosthetic-Related Complication in Total Hip Arthroplasty. The Journal of arthroplasty. 2016;31(9 Suppl):227–32 e1.

158. Gausden EB, Parhar HS, Popper JE, Sculco PK, Rush BNM. Risk Factors for Early Dislocation Following Primary Elective Total Hip Arthroplasty. The Journal of arthroplasty. 2018;S0883-5403(17:31140–3.

159. Esposito CI, Carroll KM, Sculco PK, Padgett DE, Jerabek SA, Mayman DJ. Total Hip Arthroplasty Patients With Fixed Spinopelvic Alignment Are at Higher Risk of Hip Dislocation. 2017;S0883-5403(17)(1532-8406):31093-8.

160. Bedard NA, Martin CT, Slaven SE, Pugely AJ, Mendoza-Lattes SA, Callaghan JJ. Abnormally High Dislocation Rates of Total Hip Arthroplasty After Spinal Deformity Surgery. The Journal of arthroplasty. 2016;31(12):2884–5.

161. Buckland AJ, Puvanesarajah V, Vigdorchik J, Schwarzkopf R, Jain A, Klineberg EO, et al. Dislocation of a primary total hip arthroplasty is more common in patients with a lumbar spinal fusion. Bone & Joint Journal. 2017;99-B(5):585–91.

162. An VVG, Phan K, Sivakumar BS, Mobbs RJ, Bruce WJ. Prior Lumbar Spinal Fusion is Associated With an Increased Risk of Dislocation and Revision in Total Hip Arthroplasty: A Meta-Analysis. Journal of Arthroplasty. 2018;33(1):297–300.

163. Lembeck B, Mueller O, Reize P, Wuelker N. Pelvic tilt makes acetabular cup navigation inaccurate. Acta orthopaedica. 2005;76(4):517–23.