Infection after primary hip arthroplasty

Epidemiology, time trends and risk factors in data from national health registers

The Norwegian Arthroplasty Register

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Scientific environment

The present PhD project was initiated in 2007 while I was working as a consultant at the Department of Orthopaedic Surgery, Haukeland University Hospital, Bergen. Since August 2007 my primary workplaces have been the Department of Orthopaedic Rehabilitation and the Norwegian Arthroplasty Register, Haukeland University Hospital.
Supervision has been given by the staff at the Norwegian Arthroplasty Register and in particular by supervisor Professor Lars Birger Engesæter and co-supervisors Professor Leif I Havelin and Professor Birgitte Espehaug.
Parts of the project have been conducted in cooperation with the Norwegian Institute of Public Health and the Nordic Arthroplasty Register Association.

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Contents

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The thesis at a glance

	Main findings	**Interpretation**
Paper I	The incidence of revision due to infection after primary THA in Norway was 0.6% during the period 1987-2007. The risk of *revision due to infection* increased during the study period. Risk factors associated with increased risk for revision due to infection were male sex, more than 100 minutes duration of surgery, laminar air flow in the operation room, uncemented THAs, and the use of bone cement without antibiotics.	The increased risk of *revision due to infection* after THA possibly reflects a true increase in incidence of *prosthetic joint infection* in Norway during the study period. No single cause for the increased risk of *revision due to infection* was identified among the risk factors assessed. Possible contributing factors as comorbidity, improved diagnostics, changed indications for revision, and awareness of low-grade infection were discussed.
Paper II	We found the incidence of *surgical site infections* after THA to be 3.0%, and *revision due to infection* after THA to be 0.7%, during the 2005-2009. For HA the corresponding incidences were 7.3% and 1.5%. Several risk factors associated with *revision due to infection* and *surgical site infection* after primary hip arthroplasty were identified.	The incidence of *SSI* and *revision due to infection* after HA and THA in Norway was found to be similar to that reported from other countries. There were differences in risk patterns between *surgical site infection* and *revision due to infection* as well as between HA and THA in the three health registers studied. Arthroplasty registers and infection surveillance systems can supply complementary data concerning infection after primary hip arthroplasty.

Paper III	The incidence of *revision due to infection* after primary THA in the dataset of the Nordic Arthroplasty Register Association (NARA) was 0.6% during the period 1995-2009. The risk of *revision due to infection* increased in Denmark, Finland, Norway, and Sweden during the study period. The increase in risk was most prominent the first three postoperative months. Risk factors for *revision due to infection* were male sex, hybrid fixation, cement without antibiotics and THA performed due to inflammatory disease, hip fracture or femoral head necrosis.	The increased risk of *revision due to infection* after THA possibly reflects a true increase in incidence of *prosthetic joint infection* in Denmark, Finland, Norway and Sweden during 1995-2009. The study confirmed that increasing risk of *revision due to infection* is a common feature in the Nordic countries. No single cause for the increased risk of *revision due to infection* was identified among the risk factors studied. Possible causes and contributing factors were discussed.

List of abbreviations

ASA	American Society of Anaesthesiologists
BMI	Body Mass Index
CDC	Centres for Disease Control and Prevention (USA)
CoNS	Coagulase-Negative Staphylococci
CRP	C-Reactive Protein
ESR	Erythrocyte Sedimentation Rate
FDA	Food and Drug Administration (USA)
HA	Hemiarthroplasty of the hip
HELICS	Hospitals in Europe Link for Infection Control through Surveillance
ICD	International Classification of Diseases
LAF	Laminar air flow
MRSA	Methicillin-Resistant Staphylococcus Aureus
MRSE	Methicillin-Resistant Staphylococcus Epidermidis
NAR	Norwegian Arthroplasty Register
NARA	Nordic Arthroplasty Register Association
NHFR	Norwegian Hip Fracture Register
NNIS	National Nosocomial Infections Surveillance (UK)
NOIS	Norwegian acronym for: Norwegian Surveillance System for Healthcare-Associated Infections
NOMESCO	Nordic Medico-Statistical Committee
NPR	Norwegian Patient Register
OA	Osteoarthritis
PCR	Polymerase Chain Reaction
PJI	Prosthetic Joint Infection
SSI	Surgical Site Infection
THA	Total Hip Arthroplasty
WBC	White Blood Cells

Abstract

Every year, more than 10,000 Norwegians undergo hip replacement (7,360 THAs and 3,214 HAs in 2011). This may be due to osteoarthritis (OA), inflammatory joint disease, fractures, fracture sequelae, aseptic femoral head necrosis or sequelae after childhood hip disease. The native hip joint is replaced by a total hip arthroplasty (THA) or a hemiarthroplasty (HA). The implants constitute large foreign bodies that could be predilection spots for adherence of microorganisms, and postoperative infections are a feared complication. Such infections are difficult to treat and impose increased morbidity and mortality on the patients.

To meet the challenge of *prosthetic joint infection, s*everal risk factors have been identified and prophylactic measures have been introduced. The Norwegian Arthroplasty Register (NAR) has had several publications on antibiotic prophylaxis, systemically and in bone cement, for THA, and probably contributed to that Norwegian orthopaedic surgeons changed their routines. The starting point of the present PhD project was to assess whether these changes in antibiotic prophylaxis had changed the risk of *revision due to infection*.

We found that, in spite of the anticipated improved antibiotic prophylaxis, the risk of *revision due to infection* after primary THA had increased threefold from 1987-1992 to 2003-2007 (Paper I). In the Nordic Arthroplasty Register Association's (NARA) dataset from Denmark, Finland, Norway and Sweden, a similar increase in risk of *revision due to infection* after primary THA was found between 1995-1999 and 2005-2009 (Paper III). The reason for this increase could not be explained by any known changes in the risk factors assessed in the two studies (Papers I and III). The possibility of a true increase in *prosthetic joint infection* and other possible explanations were discussed.

In Norway there are no systematic registrations of true *prosthetic joint infection*. *Revisions due to infection* should be reported to the NAR and the Norwegian Hip

Fracture Register (NHFR), and *surgical site infections* should be reported to the Norwegian Surveillance System for Healthcare-Associated Infections (NOIS). In Paper II we assessed risk factors and risk patterns for these two endpoints for both THA and HA. The first-year incidence of *surgical site infection* after primary arthroplasty was found to be nearly five times higher than the first-year incidence of *revision due to infection.* There also seems to be differences in the risk patterns between *surgical site infection* and *revision due to infection* and between HA and THA.

The risk factors associated with increased risk of *revision due to infection* after primary THA were male sex, advanced age (70-90 years when adjusted for comorbidity), comorbidity (ASA class > 1), long duration of surgery (> 100 minutes), uncemented or hybrid fixation, bone cement without antibiotics, laminar air flow in the operation room, NNIS risk index higher than one, and THA performed due to inflammatory disease, hip fracture or femoral head necrosis.

Risk factors of *surgical site infection* after THA was advanced age (> 80 years), comorbidity (ASA class > 2), and short duration of surgery (< 60 minutes).

For primary HAs the only risk factor associated with increased risk of *revision due to infection* was young age (< 60 years), whereas no statistically significant risk factors of *surgical site infection* were identified.

The overall conclusion of this thesis is that the risk of *revision due to infection* after primary THA has been increasing. Definite causes of this increased risk could not be established in the three papers. Considering risk factors and possible confounders we still believe that there might have been a true increase in the incidence of *prosthetic joint infection.*

Norsk sammendrag (Summary in Norwegian)

Hvert år får mere enn 10 000 nordmenn erstattet sitt hofteledd med en hofteprotese (7 360 totalproteser og 3 214 hemiproteser i 2011). Dette kan skyldes «slitasjegikt» (artrose), inflammatorisk leddsykdom, lårhalsbrudd, komplikasjoner etter brudd, aseptisk nekrose av lårbeinshodet eller ettervirkninger etter barnehoftelidelser. Hofteleddet kan erstattes av en total hofteprotese eller en hemiprotese. Hofteproteser utgjør store fremmedlegemer som kan være utsatt for mikroorganismer, og postoperative infeksjoner er en fryktet komplikasjon. Slike infeksjoner er vanskelig å behandle og fører til økt sykelighet og dødelighet for de pasientene som rammes.

For å møte utfordringen med proteseinfeksjoner, har flere risikofaktorer blitt identifisert og forebyggende tiltak er innført. Nasjonalt register for leddproteser (NRL) har hatt flere publikasjoner om antibiotikaprofylakse, systemisk og i beinsementen, ved innsetting av totalprotese i hoften, og har sannsynligvis bidratt til at kirurgene har endret sine rutiner. Utgangspunktet for dette doktorgradsarbeidet var å vurdere om disse endringene i antibiotikaprofylakse hadde endret risiko for *revisjon på grunn av infeksjon*.

Vi fant at til tross for at antibiotikaprofylaksen ved hofteproteseoperasjoner var endret i tråd med funnene, var risikoen for *revisjon på grunn av infeksjon* tredoblet fra 1987-1992 til 2003-2007 (Artikkel I). Vi fant også økning i risikoen for *revisjon på grunn av infeksjon* etter primær total hofteprotese mellom 1995-1999 og 2005-2009 i Nordic Arthroplasty Register Association (NARA) sitt datasett fra Danmark, Finland, Norge og Sverige (Artikkel III). Grunnen til denne økningen kan ikke forklares med registrerte endringer i risikofaktorer vurdert i de to studiene (Artikkel I og III). Muligheten for en sann økning av *proteseinfeksjoner* og andre mulige forklaringer ble diskutert.

I Norge har vi ikke systematisk registrering av sanne *proteseinfeksjoner*. *Revisjoner på grunn av infeksjon* skal rapporteres NRL og Nasjonalt hoftebruddregister

(NHBR), og *postoperative sårinfeksjoner* rapporteres til Norsk overvåkingssystem for antibiotikabruk og helsetjenesteassosierte infeksjoner (NOIS). I Artikkel II vurderte vi risikofaktorer og risikomønstre for *postoperative sårinfeksjoner* og *revisjoner på grunn av infeksjon* for både primær hemi- og totalprotese i hofte. Den samlede forekomst av *postoperativ sårinfeksjon* det første året etter primær protesekirurgi ble funnet å være nesten fem ganger så høy som forekomsten av *revisjon på grunn av infeksjon* det første året postoperativt. Det så også ut til å være forskjeller i risikomønstre mellom *postoperativ sårinfeksjon* og *revisjon på grunn av infeksjon* og mellom hemi- og totalprotese.

Risikofaktorer som var forbundet med økt risiko for *revisjon på grunn av infeksjon* etter primær totalprotese i hofte var menn, høy alder (70-90 år når det justeres for andre sykdommer), andre sykdommer (ASA-klasse> 1), lang varighet av kirurgi (> 130 minutter), usementert eller hybrid fiksering, beinsement uten antibiotika, laminær luftstrøm på operasjonsstuen, NNIS risiko indeks høyere enn én, og totalprotese på grunn av inflammatorisk leddsykdom, hoftebrudd eller aseptisk nekrose av lårbeinshodet.

Risikofaktorer for *postoperativ sårinfeksjon* etter totalprotese i hoften var høy alder (> 80 år), andre sykdommer (ASA-klasse> 2), og kort varighet av kirurgi (<60 minutter).

Ved primær hemiprotese i hoften var bare ung alder (<60 år) forbundet med økt risiko for *revisjon på grunn av infeksjon*, mens vi ikke fant noen statistisk signifikante risikofaktorer for *postoperativ sårinfeksjon*.

Konklusjonen av denne avhandlingen er at risikoen for *revisjon på grunn av infeksjon* har vært økende hos pasienter som har fått innsatt primær totalprotese i hofte. Årsakene til denne økningen ble ikke funnet blant de risikofaktorene som ble studert i denne doktoravhandlingen. Vurdert utfra mulige risikofaktorer og andre faktorer (effektforvekslere) som kan ha påvirket resultatene, tror vi at det har vært en sann økning i forekomsten av infeksjoner etter innsetting av totalprotese i hofte.

List of publications

The thesis is based on the following papers, referred to in the text by their Roman numerals:

I Dale H, Hallan G, Espehaug B, Havelin L I, Engesæter L B. **Increasing risk of revision due to deep infection after hip arthroplasty**. Acta Orthop 2009; 80 (6): 639-45.

II Dale H, Skråmm I, Løwer H L, Eriksen H M, Espehaug B, Furnes O, Skjeldestad F E, Havelin L I, Engesæter L B. **Infection after primary hip arthroplasty**. Acta Orthop 2011; 82 (6): 646-54.

III Dale H, Fenstad A M, Hallan G, Havelin L I, Furnes O, Overgaard S, Pedersen A B, Kärrholm J, Garellick G, Pulkkinen P, Eskelinen A, Mäkelä K, and Engesæter L B. **Increasing risk of prosthetic joint infection after total hip arthroplasty**. Acta Orthop 2012; 83 (5): 449-58.

1 Introduction and background

Every year, more than 10,000 Norwegians undergo surgery to replace their native hip joint with a hip prosthesis, a primary hip arthroplasty or hip replacement (7,360 THAs and 3,214 HAs in 2011) (The Norwegian Arthroplasty Register 2012, The Norwegian Hip Fracture Register 2012). The implanted prostheses constitute large foreign bodies that are predilection areas for adherence of microorganisms, and postoperative infection is a feared complication. Sir John Charnley stated that "postoperative infection is the saddest of all complications" (Waugh and Charnley 1990). Symptoms can vary from pain, sometimes due to loosening of the prosthesis, without other accompanying signs of infection, to fulminant prosthetic joint infections with life-threatening septicaemia. The treatment is multidisciplinary and involves surgery, often repetitive, and prolonged antibiotic treatment.

For the individual patient a prosthetic joint infection imposes extra suffering with extensive surgery and medical treatment often associated with complications, adverse effects and functional loss (Westberg et al. 2012, Aslam and Darouiche 2012). For the healthcare services THA infections imply great medical challenges, long hospital stays and 3-4 times increased costs compared to uncomplicated primary THA (Whitehouse et al. 2002, Kurtz et al. 2007, Aslam and Darouiche 2012).

The Norwegian Arthroplasty Register (NAR) has published studies on antibiotic prophylaxis against infection after THA, and the Norwegian orthopaedic surgeons have complied with the findings and changed their routines accordingly (Espehaug et al. 1997, Engesæter et al. 2003, Engesæter et al. 2006).

The starting point of the present PhD project was to study whether these changes in antibiotic prophylaxis had had an impact on the risk of *revision due to infection* (Dale et al. 2008). We wanted to assess these time trends and possible contributing risk factors.

1.1 Primary hip arthroplasty

Primary hip arthroplasty is a surgical procedure where the whole or part of the hip joint is removed and replaced by a hip prosthesis. Primary refers to the first time a hip prosthesis is implanted in the joint. The most common reasons for hip replacement are osteoarthritis (OA), inflammatory joint disease, fractures, sequelae after hip fracture, aseptic femoral head necrosis or sequelae after childhood hip disease (Figure 1). The hip joint may be replaced by a total hip arthroplasty (THA) or a hemiarthroplasty (HA).

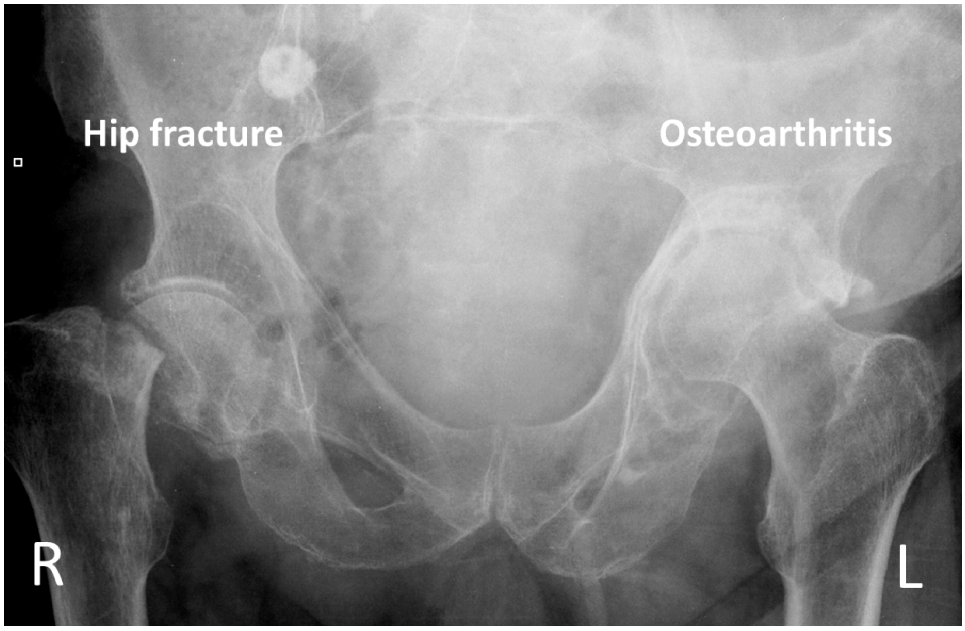

Figure 1: *X-ray of hip joints with a hip fracture in the right hip and osteoarthritis in the left.*

1.1.1 Total hip arthroplasty (THA)

In a *total hip arthroplasty* both the femoral head and neck and the acetabular cartilage are removed and replaced by a femoral component (the head and stem) and an acetabular cup (Figure 2).

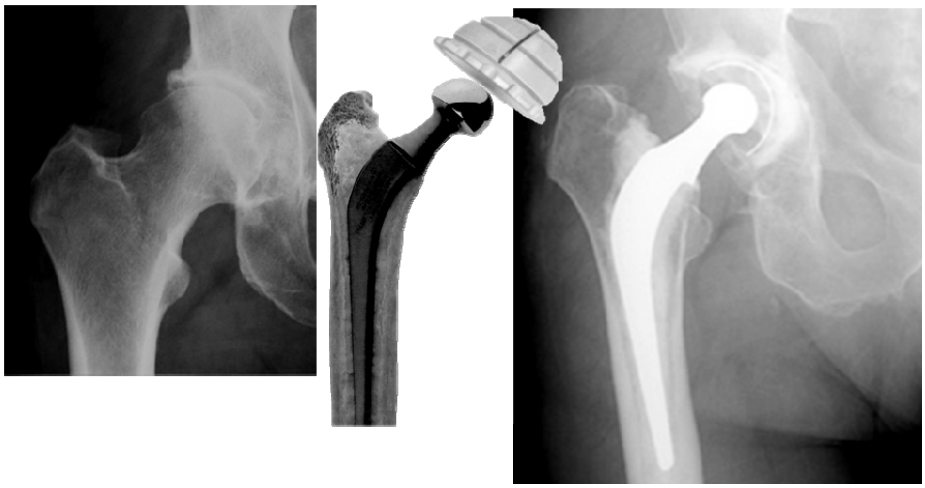

Figure 2: *X-rays of an osteoarthritic hip joint (left), a photo of a cemented Charnley hip prosthesis with plastic acetabular cup (middle), and x-ray of a similar total hip prosthesis after hip replacement (right).*

Figure 3 illustrates basic concepts of total hip prostheses. The femoral component may be produced with head and stem in one piece, as in the previously widely used Charnley prostheses, which are therefore called monoblock prostheses (Figures 2 and 3). The most commonly used femoral components today have separate heads and stems, and are therefore called modular prostheses (Figure 3). The acetabular component (cup) consists either of a single cup (mostly polyethylene) or a metal cup with different sorts of inserts (liners) (Figure 3). The cup and the stem can be fixed with or without cement. If both components are cemented it is known as a cemented THA and if both components are fixed without cement it is called an uncemented (or cementless) THA. A combination of a cemented stem and an uncemented cup is called a hybrid THA, and an uncemented stem combined with a cemented cup is an inverse (or reverse) hybrid THA. There are many different THAs on the market, with different brands and designs, using a variety of materials and articulations. There are also many brands of bone cement for THA fixation, some with and some without antibiotics. New products and procedures are being introduced continuously, and the need for post marketing surveillance led to the inception of the NAR in 1987.

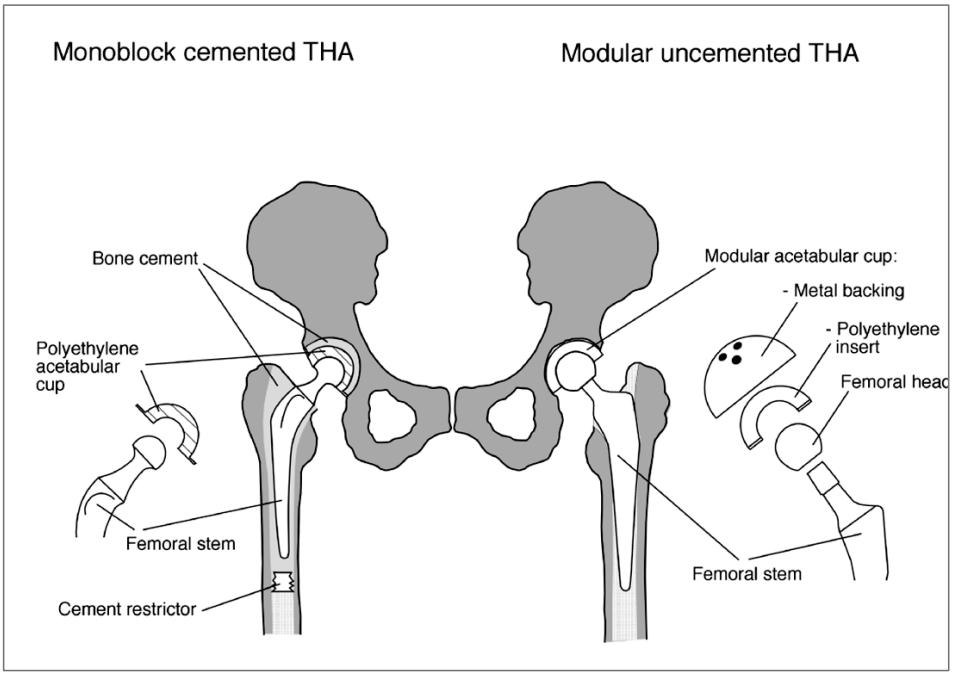

Figure 3: *An illustration of basic concepts of total hip arthroplasty (THA). (Courtesy of Geir Hallan)*

1.1.2 Hemiarthroplasty (HA)

In a *hemiarthroplasty* of the hip, only the femoral part of the hip joint is replaced by a prosthesis. HA stems are usually the same as in THA but with a head equal in size to the native femoral head. In the unipolar prosthesis the head and stem are in one piece, whereas the bipolar prosthesis has an articulation between the head and the stem. HAs can also be either cemented or uncemented, and are predominantly inserted due to hip fractures (Figure 1) as an alternative to osteosynthesis (Figure 4). HA due to hip fractures should be reported to the Norwegian Hip Fracture Register (NHFR), which was established in 2005. HA due to other causes than fracture should be reported to the NAR from 2012.

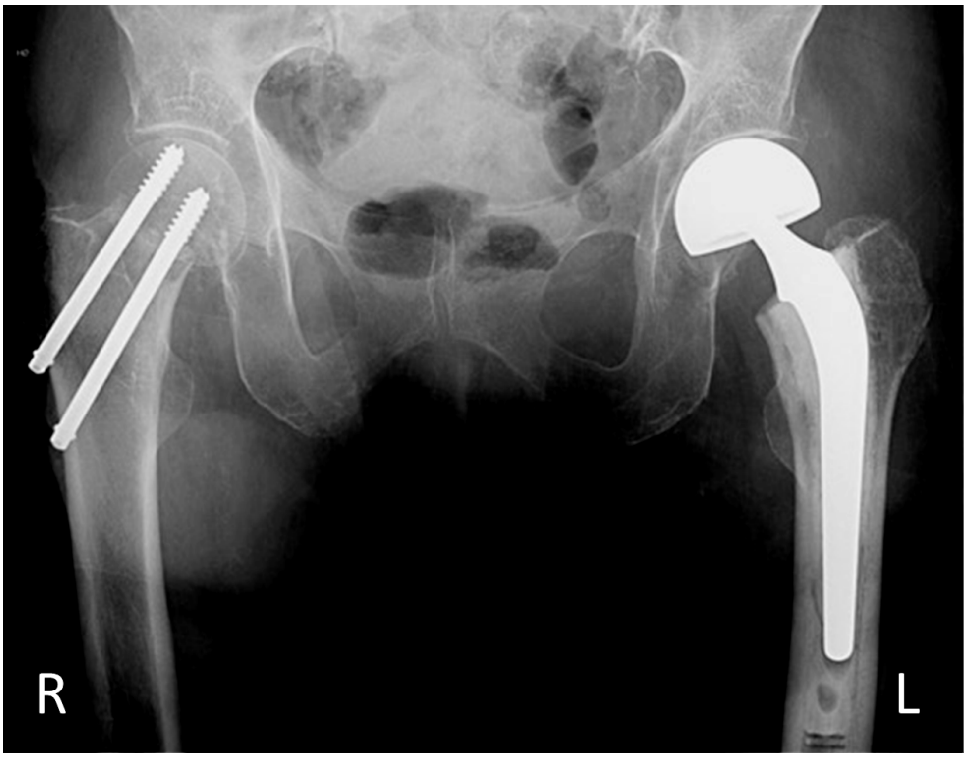

Figure 4: *X-ray of a bipolar hemiarthroplasty of the left hip and osteosynthesis of the right hip.*

1.1.3 Trends and epidemiology of hip arthroplasty

In Norway with 5.0 million inhabitants, 7,360 primary THAs were reported to the NAR in 2011 (The Norwegian Arthroplasty Register 2012). There has been an increase in the incidence of THA from 109 per 100,000 inhabitants in 1991-1995 to 140 per 100,000 in 2006-2008 (Espehaug et al. 2011). A similar increase in incidence has been observed in other Western countries (Pedersen et al. 2005, Kurtz et al. 2005, Singh 2011). An overall similarity in THA incidence is described for the Nordic countries although there are some epidemiological differences between the countries concerning demographics, type of implants, fixation, and survival of implants (Lohmander et al. 2006, Havelin et al. 2009).

In 2011 the number of primary HAs in Norway was 3,214 (The Norwegian Hip Fracture Register 2012). The fraction of patients treated with HA instead of osteosynthesis for their hip fracture is increasing (Jain et al. 2008, The Norwegian Hip Fracture Register 2012).

The dominant cause of primary THA is idiopathic osteoarthritis (OA) whereas HA is predominantly performed instead of osteosynthesis after hip fractures (Figures 1 and 4). Patient characteristics for Norwegian THA and HA patients are presented in Table 1. The HA patients are generally older and in poorer health than the THA patients. In addition the majority of the HA patients are suffering from a trauma (hip fracture).

	Hips reported to the NAR		**Hips reported to the NHFR**	
	Primary THA	**Revised due to infection**	**Primary HA**	**Revised due to infection**
Age				
Mean years (Range)	69 (11-100)	69 (16-92)	82 (27-104)	81 (54-98)
Sex				
Female	69 %	48 %	74 %	69 %
Male	31 %	52 %	26 %	32 %
ASA Class				
1	26 %	16 %	5 %	4 %
2	55 %	54 %	35 %	34 %
≥3	19 %	29 %	60 %	62 %
Diagnosis				
Osteoarthritis	73 %	72 %		
Inflammatory disease	3 %	4 %		
Hip fracture	1 %	1 %	86 %	82 %
Sequelae after hip fracture	10 %	9 %	14 %	18 %
Sequelae after childhood hip disease	9 %	7 %		
Femoral head necrosis	1 %	2 %		
Other diagnoses	4 %	5 %		

Table 1: *Patient characteristics of patients reported for THA to the NAR and HA to the NHFR (The Norwegian Arthroplasty Register 2012, The Norwegian Hip Fracture Register 2012)*.

1.2 Revision after hip arthroplasty

Revision after arthroplasty is defined as surgical removal or exchange of the prosthesis or prosthesis parts. Such operations are reported to the NAR and the NHFR. The most common causes of revision are a loose component, luxation, deep infection, fracture, osteolysis, or wear of liner. The annual revision rate reported to the NAR and the NHFR is approximately 0.5% after THA and 0.3% after HA (The Norwegian Arthroplasty Register 2012, The Norwegian Hip Fracture Register 2012).

1.3 Definitions of infection after primary hip arthroplasty

Infection may be defined as invasion and multiplication of microorganisms in body tissues, causing cellular injury and inflammatory response. Infection after primary arthroplasty is not unambiguous as a notion, and different publications use different definitions of infection. Some publications may use diagnostic codes as a measure of "infection", without clarifying the diagnostic criteria or extent of the infection (Kurtz et al. 2008, Wolf et al. 2012). These "infections" may include both superficial *surgical site infections* and true *prosthetic joint infections*, and may or may not be reoperated or revised. Time trends and risk patterns may vary for different definitions of infection after arthroplasty. The most commonly used definitions of infection after arthroplasty are the Centres of Disease Control and Prevention's (CDC) criteria for postoperative *surgical site infection*, The Mayo Clinic's criteria for *prosthetic joint infection* and the arthroplasty registries' definition *of revision due to infection* (Horan et al. 1992, Espehaug et al. 1997, Berbari et al. 1998, Mangram et al. 1999). In the three publications included in the present thesis we used the definitions of *surgical site infection* (Paper II) and *revision due to infection* in the NAR, NHFR and NARA (Papers I-III) (Horan et al. 1992, Espehaug et al. 1997).

1.3.1 Definition of prosthetic joint infection (PJI)

There is at present no international consensus about the criteria for a true *prosthetic joint infection*. A commonly used definition is from the Mayo Clinic (Berbari et al. 1998, Del Pozo and Patel 2009):

Presence of at least 1 of the following:

1) Acute periprosthetic inflammation on histopathological examination
2) Sinus tract communicating with the prosthesis
3) Gross purulence in the joint space
4) Isolation of significant amounts of the same microorganism from ≥2 cultures of joint aspirates

In the USA the Workgroup of the Musculoskeletal Infection Society have proposed the following criteria for a definite prosthetic joint infection (Parvizi et al. 2011):

1) There is a sinus tract communicating with the prosthesis; or

2) A pathogen is isolated by culture from at least two separate tissue or fluid samples obtained from the affected prosthetic joint; or

3) Four of the following six criteria exist:

   a) Elevated serum erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) concentration,
   b) Elevated synovial leukocyte count,
   c) Elevated synovial neutrophil percentage (PMN %),
   d) Presence of purulence in the affected joint,
   e) Isolation of a microorganism in one culture of periprosthetic tissue or fluid, or
   f) More than five neutrophils per high-power field in five high-power fields observed from histologic analysis of periprosthetic tissue at 9400 times magnification

Prosthetic joint infection may be present if fewer than four of these criteria are met.

1.3.2 Definition of postoperative surgical site infection (SSI)

Postoperative *surgical site infection* is the outcome measure used by postoperative infection surveillance systems like the Norwegian NOIS and the European HELICS. The aim is to monitor incidence and outbursts of postoperative infection after some common surgical procedures. One of these procedures is primary hip arthroplasty. The Norwegian NOIS surveys both primary HA and THA. *Surgical site infection* is

defined in three categories as follows (Horan et al. 1992, Mangram et al. 1999, HELICS 2004) (Appendix 6):

Superficial incisional surgical site infection

Infection occurs within 30 days (365 for arthroplasty) of primary surgery and involves only skin and subcutaneous tissue of the incision and at least one of the following:

1) Purulent drainage from the superficial incision
2) Organisms isolated from aseptically obtained samples
3) At least one sign and symptom of infection and the superficial incision is deliberately opened by the surgeon unless incision is culture-negative

Deep incisional surgical site infection

Infection occurs within 365 days of primary arthroplasty and appears to be related to the operation and infection involves deep soft tissue of the incision and at least one of the following:

1) Purulent drainage from the deep incision
2) Spontaneous dehiscence or deliberate surgical opening of the deep incision on a patient with at least one sign or symptom of local infection.
3) Clinical, surgical, radiological or histopathological finding of an abscess on direct examination in the deep incision

Organ/Space (bone/joint) surgical site infection

Infection occurs within 365 days of primary arthroplasty and appears to be related to the operation and infection involves any part of the anatomy other than the incision (bone, implant and joint in THA) and at least one of the following:

1) Purulent drainage from a stab drain into the periprosthetic space
2) Organisms isolated from aseptically obtained samples from fluid or tissue in the periprosthetic space

3) Clinical, surgical, radiological or histopathological finding of an abscess or other evidence of infection involving the periprosthetic space found on direct examination in the deep incision

All diagnoses have to be made by a surgeon or attending physician.

The definition of *surgical site infection* is wider than for true *prosthetic joint infection* and *revision due to infection* by including also superficial wound infections, but follow-up is limited by only including infections during the first postoperative year.

1.3.3 Definition of reoperation due to infection

Reoperation due to infection is any kind of surgical procedure performed to treat a postoperative infection after e.g. hip arthroplasty. Such procedures might include a debridement of a superficial wound, drainage of an abscess or a full debridement and "wash-out" procedure on a monoblock THA. *Revision due to infection* is also a reoperation. Reoperations without a *revision due to infection* are to be reported to the NOIS and the NHFR. These reoperations were not to be reported to the NAR until 2011 but since then should also be reported to the NAR (Appendices 4-6). The NARA dataset does not contain information on reoperations without revision.

1.3.4 Definition of revision due to infection

Revision due to infection is defined as surgical removal or exchange of the whole prosthesis or parts of the prosthesis due to infection. In the NHFR, NAR and NARA the infection as cause of the revision is determined by the operating surgeon immediately after surgery, based on the pre- and peroperative evaluation (Appendices 1-5). Unexpected isolation of organisms in peroperative samples found at a later stage will not be reported to the registries. In Norway, there has been an increase in the use of minor revisions for infected prostheses in recent years without a concordant decrease in major revisions (Engesæter et al. 2011).

1.4 Epidemiology and trends of infection after primary hip arthroplasty

When modern primary hip arthroplasty was introduced on a large scale in the 1960s periprosthetic infection rates were high at 7-9% (Charnley 1972). Through systematic improvements of ventilation and aseptic procedures in the operating room and stricter pre- and peroperative routines during the 1970s this was reduced to 3-5% (Charnley 1972, Lidgren et al. 2003). Introduction of prophylactic antibiotics systemically and in the cement reduced the revision rate due to infection in Norway to 0.5% in the 1990s (Engesæter et al. 2003).

Pedersen reported an incidence of revision due to infection of 0.7% in Denmark for the period 1995-2008, and an increased risk of *revision due to infection* for the period 2005-2008 compared to 1995-1997 (Pedersen et al. 2010b).

Kurtz reported a trend of increase in "total infection burden" in the USA from 0.7% to 1.3% between 1990 and 2004 based on the United States Nationwide Inpatient Sample (Kurtz et al. 2008). In contrast Wolf reported a decrease in incidence of the diagnosis of infection during the first 90 days postoperatively from 0.8 to 0.6% during 1991-2008, based on the United States Medicare Database (Wolf et al. 2012). Both Kurtz and Wolf defined infection by ICD-9 diagnostic codes.

Surgical site infection rates after THA are reported to be 0.9-4.6% (Ridgeway et al. 2005, HELICS 2006, Wilson et al. 2007, Manniën et al. 2008). Manniën reported a 60% decrease in incidence of *surgical site infections* in the Netherlands between 1996 and 2006 using the Dutch surveillance system for healthcare-acquired infections (PREZIES) and the CDC definitions of *surgical site infection* (Manniën et al. 2008). In other words, there is controversy regarding the time trend of infection after THA.

The rate of revision due to infection after HA in Sweden is reported to be 1.1% (The Swedish Hip Arthroplasty Register 2010). Incidence of *surgical site infection* after HA is reported to be 2.4-5.0% (Ridgeway et al. 2005, Wilson et al. 2008, Health Protection Agency 2011). There are to my knowledge no publications on time trends of infections after HA.

1.5 Microbiology in infected hip arthroplasty

The most common bacteria causing *prosthetic joint infections* are *Coagulase-Negative Staphylococci* (CoNS) and *Staphylococcus aureus* (Moran et al. 2007, Sharma et al. 2008, Stefánsdóttir et al. 2009a, Langvatn et al. 2010). In Scandinavia, in contrast to most of the world, the problem with methicillin-resistant *Staphylococcus aureus* (MRSA) infections after arthroplasty has so far been negligible (Stefánsdóttir et al. 2009a, Lutro et al. 2010). There is however an increasing resistance against methicillin and gentamicin among CoNS (Stefánsdóttir et al. 2009a, Lutro et al. 2010). One example is methicillin-resistant *Staphylococcus epidermidis* (MRSE). Also CoNS have emerged as an important agent of low grade implant infection, whereas they previously often were considered as contaminants (Raad et al. 1998, Costerton et al. 1999, von Eiff et al. 2006). Bacterial biofilm formation is a common feature of implant infections (Zimmerli et al. 2004, Neut et al. 2007). This biofilm consists of a glycocalyx protecting aggregated bacteria, making microorganisms difficult to identify and protected against antimicrobial agents. Biofilm-forming bacteria may cause low grade chronic infections without planktonic bacteria, and thereby mimic aseptic loosening (Zimmerli et al. 2004, Neut et al. 2007, Moojen et al. 2010). Antibiotic agents may have poor penetration in such biofilm (Costerton et al. 1999, Fux et al. 2005). Staphylococci form biofilm in the interphase between tissue and the prosthesis. This makes them difficult to treat with antibiotics alone. Other difficult-to-treat microorganisms causing *prosthetic joint infections* are streptococci and enterococci, *Propionibacterium acnes, Escherichia coli, Pseudomonas aeruginosa,* and fungi.

1.6 Aetiopathogenesis of prosthetic joint infection

Prosthetic joint infections are assumed to be caused by peroperative bacterial contamination, direct bacterial spread from a local infection (e.g. superficial *surgical site infection*) or haematogenous spread from an infection in other parts of the body

(e.g. respiratory, urinary, gastrointestinal, dental or skin infections) (Zimmerli et al. 2004).

Within minutes of implantation “the race for the surface” is on (Gristina 1987). This is a contest between tissue repair and bacterial adhesion in the tissue-implant interface (Neut et al. 2007). Plasma proteins and platelets cover the implant and facilitate adhesion of contaminant bacteria that may multiply and encase themselves in the slimy matrix called biofilm (Costerton et al. 1999). This biofilm formation may start within hours and protect the bacteria against host defence mechanisms and make bacterial adhesion irreversible. The colonization of the implant and periprosthetic tissue will, if uninterrupted by antibiotics and host defence mechanisms, lead to *prosthetic joint infection*. Virulent bacteria may cause acute symptoms of inflammation or even sepsis, whereas less virulent bacteria embedded in a biofilm may be asymptomatic for years before returning to the planktonic phase to cause a low-grade late infection resembling aseptic loosening (Zimmerli et al. 2004).

1.7 Diagnostics of prosthetic joint infection

The clinical presentation of *prosthetic joint infection* may vary from an acute fulminant septic condition to a low-grade infection with pain and loosening of the prosthesis as the only signs. The infections may be classified as *early* (debut of symptoms < 3 months after surgery and mainly due to peroperative contamination), *delayed* (3-24 months after surgery), or *late* (>24 months after surgery and probably due to haematological bacterial spread) (Garvin and Hanssen 1995, Zimmerli et al. 2004). The diagnosis is made by a combination of clinical symptoms, radiological findings, bacterial samples and histopathological examination of periprosthetic tissue and fluid. Preferably the microbial agent with its susceptibility pattern should be identified before the start of antibiotic treatment and revision surgery (Zimmerli et al. 2004, Moran et al. 2010). Laboratory markers include white blood cell count (WBC), neutrophil count, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Tissue samples should include at least three tissue biopsies for

bacteriological and histopathological examination. Synovial fluid aspirate may be analysed for leukocyte and granulocyte count, in addition to bacterial culturing. Polymerase chain reaction (PCR) and Gram staining may be used for bacterial identification (Zimmerli et al. 2004, Moojen et al. 2007, Ghanem et al. 2008, Moran et al. 2010, Bjerkan et al. 2012). Plain serial radiographs can be of some use in the case of low-grade infections (Tigges et al. 1994). Postoperative sonication of the removed implant and culturing and PCR testing of the sonicate fluid may be of help in identifying the bacterial agent (Dempsey et al. 2007, Bjerkan et al. 2009). The individual diagnostic tests may have insufficient specificity and sensitivity which must be taken into consideration when interpreting the results, and culture negative *prosthetic joint infections* are still frequent. The diagnostics therefore should include a combination anamnestic information, clinical evaluation, tissue and fluid samples, radiological evaluation, laboratorial tests, and bacterial sampling.

1.8 Risk factors for infection after hip arthroplasty

Risk factors for infection after hip arthroplasty have been presented in numerous publications, with a variety of definitions of infection, methodology and quality. Because infection after arthroplasty is a relatively rare event, a large number of THAs or considerable differences in risk estimates are needed to achieve sufficient power of conclusions. Thus, most studies on risk factors are based on data from surveillance systems, health registries and arthroplasty registries. The Cochrane Collaboration has no conclusive systematic reviews on infection after arthroplasty. There is one systematic review on risk factors of *surgical site infection* after THA (Urquhart et al. 2010). In the following chapters some risk factors of infection will be briefly presented. Different publications may conclude differently about some of the risk factors, and risk patterns may vary for different definitions of infection, and between HA and THA.

1.8.1 Risk factors of infection after THA

In the following, risk factors of infection after primary THA will be sorted according to the definition of arthroplasty infection, and into patient and surgery related risk factors in addition to postoperative risk factors of infection.

Risk factors of *prosthetic joint infection* after THA

Patient related risk factors

- Systemic malignancy
- Rheumatologic disease
- Obesity (body mass index > 40)
- Coagulopathy
- Preoperative anaemia
- Comorbidity (ASA score > 2)
- Immunosuppression
- Cardiovascular disease
- Excessive anticoagulation (INR > 1.5)
- Diabetes
- Prior surgery on the joint

Surgery related risk factors

- Allogeneic blood transfusion
- Duration of surgery
- NNIS risk index score > 0

Postoperative risk factors

- Prolonged wound drainage
- Prolonged hospital stay
- Postoperative superficial *surgical site infection*

(Berbari et al. 1998, Parvizi et al. 2007, Lai et al. 2007, Pulido et al. 2008, Bozic et al. 2012, Berbari et al. 2012)

Risk factors of *surgical site infection* after THA

Patient related risk factors

- Advanced age (> 75 years)
- Comorbidity (ASA score, Charlson index)
- Low income
- Arthroplasty performed after trauma
- Smoking
- Diabetes/Hyperglycaemia
- Obesity

Surgery related risk factors

- NNIS risk index score >0

Postoperative risk factors

- Prolonged wound drainage and haematoma

(Saleh et al. 2002, Ridgeway et al. 2005, Mraovic et al. 2011, Singh et al. 2011)

Risk factors of *revision due to infection* after THA

Patient related risk factors

- Male sex
- Comorbidity (Charlson comorbidity index > 1)
- THA due to avascular necrosis of the femoral head
- THA due to proximal femoral fracture
- Diabetes

Surgery related risk factors

- Cemented implants
- Cement without antibiotics
- Hybrid fixation
- Prolonged duration of surgery (> 120 minutes)

(Småbrekke et al. 2004, Engesæter et al. 2006, Pedersen et al. 2010a, Pedersen et al. 2010b)

1.8.2 Changes in risk factors of infection after THA

There are few publications on time trends of risk factors for infection after THA. Wolf, who found reduced incidence of 90 days postoperative infection in the elderly in the USA, also found increased incidence of the risk factors diabetes (7.3% to 15.2%), obesity (2.3% to 7.2%), congestive heart failure (3.0% to 4.4%), renal failure (0.5% to 3.7%), and also the number of comorbid conditions for each patient increased during the period 1991-2008, whereas the median length of stay decreased (8 days to 3 days) (Wolf et al. 2012).
In Norway the comorbidity of patients receiving THA, according to reported ASA class, increased during 2005-2010 (The Norwegian Arthroplasty Register 2012). The general incidence of specific comorbidities associated with increased risk of infection after THA, such as obesity and diabetes, is increasing in several countries (Pedersen et al. 2010a, Danaei et al. 2011, Haverkamp et al. 2011, Mraovic et al. 2011, Doak et al. 2012, Iorio et al. 2012, Jämsen et al. 2012, Wolf et al. 2012, Witsø 2012). Also the fraction of THA patients on prophylactic antithrombotic treatment due to cardiovascular disease may have increased (Wolf et al. 2012). There has also been an increase in the duration of thrombotic prophylaxis after THA in the last decade (The Norwegian Arthroplasty Register 2012).
In general it looks as if THA is performed on more patients with risk factors for infection in recent years than previously.

1.8.3 Risk factors of infection after HA

There are to our knowledge only a few studies on risk factors of infection after hemiarthroplasty of the hip and time trends of such risk factors. Despite methodological limitations, findings from two studies will be presented below.

Risk factors of *prosthetic joint infection* after HA

Patient related risk factors

- Female gender
- Previous surgery
- Obesity (body mass index > 30)
- Immunosuppressive medication

Surgery related risk factors
- Prolonged duration of surgery

Postoperative risk factors
- Prolonged wound drainage and haematoma
- Dislocation
- Skin, urinary and/or abdominal infection

(Cordero-Ampuero and de Dios 2010)

Risk factors of *surgical site infection* after HA
Patient related risk factors
- Advanced age (> 80 years)
- Comorbidity (ASA class ≥ 3)

(Ridgeway et al. 2005)

Risk factors of *revision due to infection* after HA
There are to our knowledge no studies of risk factors of *revision due to infection* after HA except Paper II in the present thesis.

1.9 Prevention of infection after hip arthroplasty

Prevention of infection after arthroplasty is most important, and has been in focus since Sir John Charnley started his studies to reduce the risk of peroperative air contamination (Charnley 1972). Such prevention of postoperative infection consists

of a wide range of pre-, per- and postoperative preventive measures in combination with antibiotic prophylaxis.

1.9.1 Prophylactic measures against postoperative infection.

Studies on prophylactic measures to counteract infection after arthroplasty are abundant. Systematic reviews have resulted in guidelines that involve risk assessment of the patient, preparation of the patient before surgery, antibiotic prophylaxis before and during surgery, reduction of peroperative contamination, surgical technique, postoperative routines, and organization of the ward, staff and hospital stay (National institute of health and clinical excellence (NICE) 2008, Swedish Council on Health Technology Assessment (SBU) 2010, WHO Patient Safety 2011, Merollini et al. 2012). Some recommendations apply to surgery in general rather than specifically to orthopaedic surgery or hip arthroplasty, and the level of evidence varies for the different prophylactic measures.

It is beyond the scope of this thesis to thoroughly discuss all prophylactic measures against postoperative infection concerning primary arthroplasty. The only measure that is considered sufficiently evidence-based is systemic pre- and peroperative antibiotic prophylaxis (Chapter 1.9.2) (Merollini et al. 2012).

Reduction in the incidence of prosthetic joint infection through air cleanliness has been in focus and has resulted in extensive use of ultraclean air ventilation systems in operating rooms, first by the use of a ultraclean “greenhouse” system with “tents” and surgical “spacesuits”, and later in the form of laminar air flow ventilation trough HEPA filters (Charnley 1972, Lidwell et al. 1982, Stocks et al. 2011). However, the positive effects of laminar air flow have recently been questioned (Gastmeier et al. 2012, Merollini et al. 2012).

At the time of inception of the NAR in 1987 total hip arthroplasty was highly specialised surgery performed in most hospitals with strict antiseptic and aseptic routines by few and dedicated surgeons. There are indications that the standards of prophylactic measures may have fallen. The demand for an economically effective health care system may have resulted in overcrowded, under-staffed, mixed patient wards with less compliance to prophylactic routines (Borg et al. 2008, Griffiths et al. 2009, Schwab et al. 2012).

Over the years THA has become a part of the basic training for all orthopaedic surgeons and is performed in almost all hospitals. Through THA becoming routine surgery, often performed on low-volume hospitals or by inexperienced surgeons and staff, the quality of prophylactic measures and surgery may have been reduced (Geubbels et al. 2005, Kurtz et al. 2008, Stefánsdóttir et al. 2009b, Ames et al. 2010, Harrison et al. 2012). As Stefánsdóttir stated: “This “industrialization” has probably made it increasingly difficult to constantly maintain important prophylactic measures” (Stefánsdóttir et al. 2009b).

1.9.2 Antibiotic prophylaxis against postoperative infection

The efficacy of antibiotic prophylaxis given systemically for THA is well documented, and it is used routinely by most surgeons (Engesæter et al. 2003, Albuhairan et al. 2008, Gillespie and Walenkamp 2010, Jämsen et al. 2010a). The discussion is about type, timing and duration of the intravenous antibiotic prophylaxis (Espehaug et al. 1997, Engesæter et al. 2003, van Kasteren et al. 2007, Albuhairan et al. 2008, Stefánsdóttir et al. 2009b).

The most commonly used antibiotic prophylaxis in arthroplasty in the Nordic countries today is first or second generation cephalosporins or β-lactam resistant penicillin, which targets the most common microorganisms of implant infections (The Danish Arthroplasty Register 2011, The Swedish Arthroplasty Register 2011, The Norwegian Arthroplasty Register 2012). Optimally the prophylaxis should be administered between 30-60 minutes before surgery and repeated peroperatively according to the half-life of the drug in a total of 1-4 doses (Engesæter et al. 2003, van Kasteren et al. 2007, Stefánsdóttir et al. 2009b, The Swedish Arthroplasty Register 2011).

If a cemented primary hip arthroplasty is performed, systemic antibiotic prophylaxis in combination with cement containing antibiotics seems to provide better survival (Engesæter et al. 2006, Parvizi et al. 2008, Pedersen et al. 2010b). The efficacy of bone cement containing antibiotics is documented (Engesæter et al. 2003, Parvizi et al. 2008, Gillespie and Walenkamp 2010). But the use of cement containing antibiotics in primary arthroplasty remains controversial and is not approved by FDA

in the USA (van de Belt et al. 2001, Block and Stubbs 2005, Jiranek et al. 2006, Parvizi et al. 2008, Campoccia et al. 2010).
Cements containing antibiotics have unfavourable aspects with regard to release dynamics of antibiotics, biofilm formation and effects on microorganisms (van de Belt et al. 2001, Neut et al. 2007, Campoccia et al. 2010). For instance, after high initial release of antibiotics from the cement, concentrations below the levels required to inhibit susceptible pathogens are present in the interface and the surroundings of the prosthesis (Fletcher et al. 2004). This may lead to false negative cultures in some patients with failing implants, and will provide a selective pressure for the emergence of resistance where infection is present in other patients (Hope et al. 1989, Fletcher et al. 2004, Campoccia et al. 2010). Both plain and antibiotic-loaded bone cement have shown increased colonization of *CoNS and Staphylococcus aureus,* compared to metal and polyethylene, due to surface properties (Oga et al. 1988, van de Belt H. et al. 2000, Campoccia et al. 2010). However, the better survival provided by cement containing antibiotics in primary THA has resulted in use of antibiotic-laded cement in almost all cemented arthroplasties in the Nordic countries in the last decade (The Danish Arthroplasty Register 2011, The Swedish Arthroplasty Register 2011, The Norwegian Arthroplasty Register 2012).

1.10 Treatment of infection after primary hip arthroplasty

Treatment of infections after arthroplasty may span from a small superficial debridement of the wound to extensive multidisciplinary, multistage, long-lasting treatment for an infected prosthetic hip joint. To choose the right management of a prosthetic joint infection may be challenging. The primary goal of the treatment is an infection-free, painless and functional hip. This is dependent on a stable prosthesis. Other important factors for the choice of management are the time since operation or the duration of symptoms of infection, patient risk factors (physical state, mobility, comorbidity, etc.), identification, virulence and antibiotic susceptibility of the microorganism, and the state of periprosthetic bone and soft tissue. The

combination of these factors will decide what treatment options may be considered (Zimmerli et al. 2004, Aslam and Darouiche 2012). Below the most common strategies are listed.

1.10.1 Treatment of superficial infections

Superficial *surgical site infection*s after arthroplasty are isolated soft tissue or wound infections superficial to the fascia lata. The treatment may be small reoperations like drainage of an abscess, removal of sutures with irrigation of the wound or a superficial debridement. These reoperations may be combined with short-term targeted antibiotic treatment.

1.10.2 Debridement and retention of the infected implant

If the duration of clinical symptoms is less than three weeks or it is less than three months since primary surgery, thorough debridement and irrigation, exchange of modular prosthesis parts but retention of the prosthesis, and postoperative targeted antibiotic treatment is one possible treatment (Zimmerli et al. 2004, Del Pozo and Patel 2009). Preconditions for this treatment are also a stable implant, mainly intact bone and soft tissue, and growth of microorganisms susceptible to antibiotics against surface-adhering microbes (Zimmerli et al. 2004). The success rate is reported to vary between 20 and 100% according to indication and inclusion criteria (Zimmerli et al. 2004, Azzam et al. 2010, Aslam and Darouiche 2012, Choi et al. 2012).This treatment has been increasingly used in recent years in Norway and survival of implants after this minor revision is reported to be 71-76% (Engesæter et al. 2011, Westberg et al. 2012).

1.10.3 One-stage exchange revision due to infection

If any of the conditions for retention of the prosthesis are not fulfilled, all foreign material (prosthesis and cement), unviable tissue and biofilm have to be removed in order to cure the infection. If the damage of periprosthetic soft tissue is minor and the infection is not caused by a difficult-to-treat microorganism, a one-stage revision is an option (Zimmerli et al. 2004, Aslam and Darouiche 2012). This procedure

involves extraction of all components of the prosthesis together with cement and thorough debridement of the periprosthetic tissue, before implanting a new prosthesis during the same session. The operation is then followed by targeted antibiotic treatment. The success rate of one-stage exchange revisions due to infection is reported to be 82-100% (Zimmerli et al. 2004, Lange et al. 2012, Klouche et al. 2012). In Norway the two-year survival rate of this one-stage revision is 88% (Engesæter et al. 2011).

1.10.4 Two-stage exchange revision

In cases with longer duration of symptoms, damaged periprosthetic tissue and difficult-to-treat microorganisms identified, a two-stage revision is the recommended option (Zimmerli et al. 2004, Aslam and Darouiche 2012). This procedure involves extraction of all components of the prosthesis together with cement and thorough debridement of the periprosthetic tissue in a first stage of the revision. A spacer eluting antibiotics or antibiotic beads may or may not be implanted during the first stage of the revision. After an interval of 2-12 weeks with targeted antibiotic treatment and remission a new prosthesis is implanted in a second operation. This treatment strategy has the best success rate with regard to eradication of the infection, but also imposes two major surgeries and a substantial burden on the patient (Zimmerli et al. 2004, Klouche et al. 2012, Lange et al. 2012). The success rate of two-stage exchange revisions due to infection is reported to be 82-96% (Zimmerli et al. 2004, Aslam and Darouiche 2012, Choi et al. 2012). In Norway the two-year survival of this two-stage revision is 92% (Engesæter et al. 2011).

1.10.5 Resection arthroplasty

If there is moderate to severe damage to periprosthetic bone and soft tissue, several eradication attempts have failed, or there are underlying problems like severe immunosuppression, intravenous drug abuse, short life expectancy or no expected functional improvement from an exchange arthroplasty, extraction of all components of the prosthesis together with cement and thorough debridement of the periprosthetic tissue without later implantation of a new implant may be considered

(Girdlestone procedure) (Zimmerli et al. 2004, Aslam and Darouiche 2012). This leaves the patient with severe disability but a fair chance of eradicating the infection. In the NAR such resection revisions constitute 13% of the *revisions due to infection* (Engesæter et al. 2006).

1.10.6 Long-term antimicrobial suppression

If the general health status of a patient is poor, life expectancy is short and the general surgical risk is high, one may opt for long-term antibiotic suppression without revision surgery for low-grade prosthetic joint infections. This may also be an alternative if the patient refuses further surgery. Such suppression treatment may only be given if the infecting microorganisms are susceptible to the antibiotic given and the adverse effects are tolerable. This is a palliative strategy where the goal is control of the clinical manifestations of infection rather than eradication. The result is normally poor, mainly due to sustained symptoms and adverse effects of antibiotics (Goulet et al. 1988, Garvin and Hanssen 1995). Such infections are not to be reported to the NAR and the NHFR, so we do not know to what extent long-term suppression is used in Norway.

1.10.7 Antibiotic treatment

Surgical treatment of *prosthetic joint infections* should always be combined with antibiotic treatment. The antibiotic treatment should be instituted and coordinated by a specialist in infectious diseases on the basis of thorough identification of the microbe by a microbiologist. Antibiotics can be delivered locally in the joint by impregnated spacers or beads and systemically by oral or intravenous administration. If possible, the treatment should be targeted, based on good and representative pre- or peroperative samples with identification of microbes and susceptibility pattern. Some infections are difficult to treat due to biofilm, resistance and growth pattern (Zimmerli et al. 2004, Neut et al. 2007). Preferably, the antibiotic agents should have good bioavailability and bactericidal activity against surface-adhering, slow-growing and biofilm-producing microorganisms (Zimmerli et al. 2004). Mostly the need is for long-term treatment (weeks or months) with a

combination of antibiotics (Trampuz and Zimmerli 2006). Empiric treatment should only be used after thorough sampling and for life-threatening septicaemias, clinically defined culture-negative infections, or if there are concerns about awaiting results of bacterial samples.

1.11 Surveillance of infection after hip arthroplasty

Surveillance of infection after hip arthroplasty is facilitated by two prospective systems, the infection surveillance systems and the arthroplasty registers (Mangram et al. 1999, Havelin et al. 2000, HELICS 2004, Havelin et al. 2009).

1.11.1 Arthroplasty registers

The purpose of the arthroplasty registers is to identify inferior implants and surgical techniques and supply hospitals with information on their long-term results compared to other hospitals, concerning patients, surgery, implants and outcome (Havelin et al. 2000). Revision due to infection is one outcome that is to be reported to the arthroplasty registers. The NAR and NHFR are examples of such registers, whereas the Nordic Arthroplasty Register Association (NARA) is an example of collaboration between national registers.

1.11.2 Infection surveillance systems

The aim of infection surveillance systems is to survey, describe and evaluate the incidence of *surgical site infection* after certain procedures (HELICS 2004). Furthermore, the intention is to assess effects of prophylactic interventions and discover cases of *surgical site infection*. The Norwegian Surveillance System for Healthcare Associated Infections (NOIS) is the Norwegian infection surveillance organization, whereas the Hospitals in Europe Link for Infection Control through Surveillance (HELICS) is a collaboration between the European national infection surveillance systems.

2 Aims of the project

The overall objective of this thesis was to utilize comprehensive health registers to identify risk factors, determine incidences, and assess changes in risk of infection after hip arthroplasty.
The specific aims of the three papers included in the thesis were:

Paper I
- To estimate the incidence of *revision due to infection* in Norway for the period 1987-2007.
- To investigate time trends of *revision due to infection* after primary THAs reported to the Norwegian Arthroplasty Register.
- To assess risk factors associated with *revision due to infection*.

Paper II
- To estimate the incidence of *surgical site infections* and *revision due to infection* after primary HA and THA in Norway during the period 2005-2009.
- To compare the registrations on infection after HA and THA in data from the Norwegian Arthroplasty Register, the Norwegian Hip Fracture Register and the Norwegian Surveillance System for Healthcare-Associated Infections.
- To assess risk factors for revision due to infection and surgical site infection after primary HA and THA.
- To investigate differences in risk patterns between of infection for HA and THA.
- To investigate differences in risk patterns between *surgical site infection* and *revision due to infection*.

Paper III
- To estimate the incidence of *revision due to infection* in four Nordic countries for the period 1995-2010.

- To investigate if increased risk of *revision due to infection* was a common feature in the Nordic countries of Denmark, Finland, Norway, and Sweden by utilizing the dataset of the Nordic Arthroplasty Register Association.
- To assess risk factors associated with *revision due to infection*.

3 Data sources

3.1 The Norwegian Arthroplasty Register (NAR)

Since its inception in 1987 the NAR has registered data on primary THAs and THA revisions. These data include the patients' identity and characteristics, the indication for primary THA and revision, the surgical procedure, and prostheses inserted or removed. The unique identification number of each Norwegian citizen is used to link the primary THA to a later revision (Havelin et al. 2000)(Appendices 1-4).
Revision due to deep infection was the primary infection event in the NAR in the present thesis. Isolated soft tissue revisions were not reported to the NAR before 2012 and are therefore not assessed.
The case report form is filled in by the surgeon immediately after surgery (Appendices 1-4). In Paper II, detailed information on the arthroplasty was sorted into the NOMESCO groups, cemented (NFB 40), uncemented (NFB 20) and hybrid THAs (NFB 30), to enable comparison with registrations in the NOIS and the NPR. The NAR did not register HAs until 2012.
All THAs were followed until their first revision due to deep infection or revision due to other causes, until the date of death or emigration of the patient, or until the end of follow-up. Paper I included 97,344 THAs from the period 1997-2007. Paper II included 31,086 primary THAs from the period 2005-2009.

3.2 The Norwegian Hip Fracture Register (NHFR)

The NHFR has a similar administrative basis and purpose as the NAR. Since January 1, 2005 all hip fractures treated surgically with HA or osteosynthesis and later revisions have been reported using a similar case report form as for registration in the NAR (Gjertsen et al. 2008) (Appendix 5). THAs due to hip fractures were reported directly to the NAR.

Procedures included in Paper II of the present thesis were HAs performed as a primary operation for a femoral neck fracture, and HAs inserted secondary to failure of the primary osteosynthesis of a femoral neck fracture.
The primary endpoint in the present thesis was, as for the NAR, *revision due to infection*.
In Paper II, for comparison of registrations in the NHFR with the NOIS and the NPR, the groups cemented (NFB 12) and uncemented HA (NFB 02) were defined based on detailed information on implant type and fixation reported. HAs inserted due to other causes than hip fractures or complications after hip fractures (e.g. osteoarthritis or malignancies) are not registered in the NHFR. All HAs were followed until their first revision due to deep infection or revision due to other causes, until the date of death or emigration of the patient, or until the end of follow-up.
Paper II included 10,972 primary HAs from the period 2005-2009.

3.3 The Norwegian Surveillance System for Healthcare Associated Infections (NOIS)

The NOIS is based on a modified version of the HELICS infection surveillance system manual, which is again based on the Centres for Disease Control and Prevention (CDC) infection surveillance system (Mangram et al. 1999, HELICS 2004, Appendix 6).
From 2005 it has been mandatory for all Norwegian hospitals to report arthroplasty or 4 other procedures (Caesarean section, coronary by-pass, appendectomy, and cholecystectomy) over a three-month period (September-November) each year. Data are collected either electronically from the patients' medical records or entered manually by infection control nurses into a standardized case report form. Among the information collected is hospital affiliation, patient characteristics, date of admission, surgery, discharge, first infection and last follow-up, type of arthroplasty, type of infection, source of diagnosis (patient or physician), and reoperations.

The verification of *surgical site infection* is by a general physician, or from the hospital's medical records if the patient had the *surgical site infection* diagnosed at a hospital.
The endpoint in the NOIS was *surgical site infection* and was defined according to the CDC guidelines (Horan et al. 1992, Mangram et al. 1999). Reoperations reported to the NOIS comprise all types of surgery due to infection including debridement and revision due to infection. If no infection was recorded, the patient was censored at death or last date of surveillance.
Registration of *surgical site infection* is done at discharge and by questionnaires to the patients and evaluation of the medical records at 30 and 365 days postoperatively. If patients reported a postoperative infection they were urged to attend a general physician or hospital for verification.
The procedures included in Paper II were primary THAs and HAs with the NOMESCO codes NFB 02, 12, 20, 30 and 40.
Contrary to the NHFR, the NOIS also included HAs due to other causes than femoral neck fractures. With this exception, the THAs in the NOIS should also have been reported to the NAR and the HAs should have been reported to the NHFR.
In Paper II 5,540 primary THAs and 1,416 primary HAs from the period 2005-2009 met the inclusion criteria.

3.4 The Norwegian Patient Register (NPR)

The NPR is a national administrative health register. It is compulsory by law to report medical treatment to the NPR, which is the basis for funding of Norwegian hospitals. Primary THAs and HAs with the NOMESCO codes NFB 02, 12, 20, 30 and 40, regardless of diagnosis, were included for the assessment of case reporting in Paper II. 12,115 primary HAs and 33,865 primary THAs were reported to the NPR during the period 2005-2009.

3.5 The dataset of the Nordic Arthroplasty Register Association (NARA)

The NARA dataset contains merged individual-based data from the Danish, Finnish. Norwegian and Swedish arthroplasty registers (Herberts et al. 1989, Havelin et al. 2000, Herberts and Malchau 2000, Lucht 2000, Puolakka et al. 2001, Malchau et al. 2005, Havelin et al. 2009). Within each register the selected data are categorized according to a common set of definitions, and revisions are linked to the primary procedures (Appendix 7). The data are then de-identified nationally before the anonymous data are merged into the NARA dataset. The data are treated in full confidentiality and in compliance with the rules of each country (Havelin et al. 2009). The NARA dataset contains information on primary THAs and first revisions from 1995-2009, and information on year of primary surgery and first revision, age, sex, diagnosis (OA, inflammatory hip disease, hip fracture, childhood hip disease, femoral head necrosis or other diagnoses), prosthesis (monoblock or modular) and type of fixation (uncemented, cemented, hybrid or inverse hybrid, with plain or antibiotic-loaded cement). The national datasets were harmonized according to definitions before being merged into the NARA dataset. 432,168 primary THAs met the inclusion criteria in Paper III, of which Denmark contributed 83,853, Finland 78,106, Norway 88,455 and Sweden 181,754.

3.6 Combination of registers

There was no true combination of the different registers in the three papers in this thesis. The NOIS and the NPR contain both THA and HA. These implants can therefore be compared within the registers. The NHFR and the NAR were harmonized and merged as a dataset in Paper II to enable comparison of HA and THA. However, the NPR just recently became person-identifiable, and a retrospective coupling was impossible. We therefore compared the registers by assessing similar primary arthroplasties from the same period of time in Paper II.

The NARA dataset is a merged, anonymized dataset that is combined yearly from limited datasets from the four Nordic arthroplasty registers; hence the NARA produces yearly datasets and is not in itself a merged register.

3.7 Coverage, completeness and validation of registrations

The data in the present thesis is only partly checked for coverage and completeness of reporting of arthroplasty. There is also limited validation of the infection endpoints (*surgical site infection* and *revision due to infection).*

The completeness of reporting to the NAR was 98% for primary THAs during the period 1999-2002, while the reporting of revisions was even higher (Espehaug et al. 2006). According to the annual report the coverage has been nearly 100% (The Norwegian Arthroplasty Register 2012). Completeness studies on the NAR have demonstrated 10-20% underreporting of Girdlestone procedures, which is a common procedure of revision surgery in cases of deep infection (Arthursson et al. 2005, Espehaug et al. 2006).

The Danish and Swedish arthroplasty registers (and thereby partly the NARA) had 95-99% coverage and completeness of primary THAs in 2010 (The Swedish Arthroplasty Register 2011, The Danish Arthroplasty Register 2011). An individual-based completeness study of the Danish Arthroplasty Register found 94% completeness for primary THAs and 81% for revisions during the years 1995-2000 (Pedersen et al. 2004).

There is limited data on coverage and completeness for the NHFR and the NOIS.

The coverage presented in Paper II for primary THA was 94% in the NOIS and 100% in the NAR, whereas the coverage of primary HAs was 93% for the NHFR and 90% in the NOIS. But the NOIS only contains registrations from three months of every year. The accumulated completeness in the NHFR was 99% compared to the

NPR for primary HAs (Paper II). The completeness of reported *revisions due to infection* and *surgical site infections* has not been assessed and validations of these specific events have not been performed.

3.8 Ethics and conflict of interest

None of the studies in the present thesis needed approval from the regional ethical committee since they had already been approved by the permissions and regulations of the individual registers. All co-authors declared no conflict of interest. All registers involved had governmental funding, and the data were treated in full confidentiality and within laws and regulations.

4 Methods

4.1 Statistics

The present thesis includes primary arthroplasty (HA and THA). The primary endpoints were first *revision due to infection* (Papers I-III) and *surgical site infection* (Paper II). Secondary endpoints were other causes of revision (Papers I and III). The cases were observed until the first revision, death, emigration or end of follow-up. Descriptive statistics were used for presentation of the characteristics of patient and procedure. Unadjusted cumulative risks were estimated by the Kaplan-Meier (KM) method (Kaplan and Meier 1958). Adjusted Cox regression analyses were performed to assess relative risk estimates and to estimate adjusted cumulative probabilities (risks) of the different endpoints (Cox 1972). The risk estimates were given with 95% confidence intervals (CI). The Cox analyses were performed with as long follow-up as available in addition to sub-analyses with homogenous follow-up for groups and time periods.

In Papers I and III changes in the revision rates due to deep infection as a function of the year of operation were assessed, in order to give a graphical display of the relationship based on a generalized additive model for survival data (Hastie and Tibshirani 1990).

The analyses were performed in concordance with the guidelines for statistical analysis of arthroplasty register data (Ranstam et al. 2011). The proportionality of the main risk factors was checked and verified by the log minus log test in Papers I and II, and assessed by smoothed Schoenfeld residuals in Paper III (Mantel and Haenzel 1959, Schoenfeld D. 1982, Therneau and Grambsch 2000, Ranstam et al. 2011). Potential overestimation of the incidence of revision due to infection through the effect of competing risks (death and revision due to other causes than infection) was assessed by the cumulative incidence function (Fine and Gray 1999, Gillam et al. 2010). The extent of bilateral THA was estimated and considered to have

negligible influence on the results (Lie et al. 2004, Ranstam and Robertsson 2010, Ranstam et al. 2011).
The level of significance was set at 0.05. The SPSS, S-Plus and R statistical software packages were used for analysis.

4.2 Statistical power

Statistical power may be explained as the probability of a detected difference between two groups being statistically significant, given that there is a difference. For a reasonable assessment the risk of a false positive conclusion should be less than 20%, hence the statistical power should be over 80%. In our context, the power of statistical test results will depend on the number of hip arthroplasties and *revisions due to infection* or *surgical site infections*, the sizes of the groups compared, the chosen level of significance (e.g. 0.05), the anticipated size of the difference in relative risks between the groups (effect size), and the loss to follow-up. In the case of gender and hip arthroplasty, to be able to conclude with a power of 80% that there is a 50% increased risk of revision due to infection after hip arthroplasty (approx. 1% incidence), with a level of significance of 0.05 between the two groups of patients, with 1/3 men and 2/3 women, and with 95% completeness of registration of the endpoint, one would need approximately 18,000 arthroplasties included in the analysis. At least twice that number is needed for a risk factor stratified into four groups.

5 Summary of Papers I-III

Paper I

Dale H, Hallan G, Espehaug B, Havelin L I, Engesæter L B. **Increasing risk of revision due to deep infection after hip arthroplasty**. Acta Orthop 2009; 80 (6): 639-45.

Background and purpose: Over the decades, improvements in surgery and perioperative routines have reduced the incidence of deep infections after total hip arthroplasty (THA). There is, however, some evidence to suggest that the incidence of infection is increasing again. We assessed the risk of *revision due to deep infection* for primary THAs reported to the Norwegian Arthroplasty Register (NAR) over the period 1987-2007.

Method: We included all primary cemented and uncemented THAs reported to the NAR from September 15, 1987 to January 1, 2008, and performed adjusted Cox regression analyses with the first *revision due to deep infection* as the endpoint. Changes in revision rate as a function of year of operation were investigated.

Results: Of the 97,344 primary THAs that met the inclusion criteria, 614 THAs had been *revised due to deep infection* (5-year survival rate 99.46%). Risk of revision due to deep infection increased throughout the period studied. Compared to the THAs implanted in 1987-1992, the risk of *revision due to infection* was 1.3 times higher (95% CI 1.0-1.7) for those implanted in 1993-1997, 1.5 times (95% CI 1.2-2.0) for 1998-2002, and 3.0 times (95% CI 2.2-4.0) for 2003-2007. The most pronounced increase in risk of being revised due to deep infection was for the subgroup of uncemented THAs from 2003-2007, which was 5 times greater (95% CI 2.6-11) than for uncemented THAs from 1987-1992.

Interpretation: The incidence of deep infection after THA increased during the period 1987-2007. Concomitant changes in confounding factors, however, complicate the interpretation of the results.

Paper II

Dale H, Skråmm I, Løwer H L, Eriksen H M, Espehaug B, Furnes O, Skjeldestad F E, Havelin L I, Engesæter L B. **Infection after primary hip arthroplasty**. Acta Orthop 2011; 82 (6): 646-54.

Background and purpose: The aim of this study was to assess incidence and risk factors for infection after hip arthroplasty in data from 3 national health registries. We investigated differences in risk pattern between *surgical site infection* (SSI) and *revision due to infection* after primary total hip arthroplasty (THA) and hemiarthroplasty (HA).

Materials and methods: This observational study was based on prospective data from 2005-2009 on primary THAs and HAs from the Norwegian Arthroplasty Register (NAR), the Norwegian Hip Fracture Register (NHFR), and the Norwegian Surveillance System for Healthcare Associated Infections (NOIS). The Norwegian Patient Register (NPR) was used for evaluation of case reporting. Cox regression analyses were performed on the data from the NAR and the NHFR on *revision due to infection*, and on the data from the NOIS on *SSI*.

Results: The one-year incidence of *SSI* in the NOIS was 3.0% after THAs (167/5,540) and 7.3% after HAs (103/1,416), while the one-year incidence of *revision due to infection* was 0.7% for THAs in the NAR (128/24,512) and 1.5% for HAs in the NHFR (128/8,262). Risk factors for *SSI* after THA were advanced age, ASA class higher than 2, and short duration of surgery. For THAs, the risk factors for *revision due to infection* were male sex, advanced age, ASA class higher than 1, emergency surgery, uncemented fixation, and a National Nosocomial Infection Surveillance (NNIS) risk index of 2 or more. For HA inserted after fracture, age less than 60 was the only risk factor of *revision due to infection*.

Interpretation: The incidences of *SSI* and *revision due to infection* after primary hip replacements in Norway are similar to those in other countries. There may be differences in risk pattern between *SSI* and *revision due to infection* after arthroplasty. The risk patterns for *revision due to infection* appear to differ between HA and THA.

Paper III

Dale H, Fenstad A M, Hallan G, Havelin L I, Furnes O, Overgaard S, Pedersen A B, Kärrholm J, Garellick G, Pulkkinen P, Eskelinen A, Mäkelä K, and Engesæter L B. **Increasing risk of prosthetic joint infection after total hip arthroplasty**. Acta Orthop 2012; 83 (5): 449-58 (In press)

Background and purpose: The risk of *revision due to infection* after primary total hip arthroplasty (THA) has been reported to be increasing in Norway. We investigated whether this increase was a common feature in the Nordic countries (Denmark, Finland, Norway and Sweden).

Materials and methods: The study was based on the dataset of the Nordic Arthroplasty Register Association (NARA). 432,168 primary THAs from 1995 to 2009 were included (Denmark 83,853, Finland 78,106, Norway 88,455 and Sweden 181,754). Adjusted survival analyses were performed using Cox regression models with *revision due to infection* as the endpoint. The effect of risk factors such as the year of surgery, age, sex, diagnosis, type of prosthesis and fixation were assessed.

Results: 2,778 (0.6%) of the primary THAs were revised due to infection. Compared to the period 1995-1999, the relative risk (with 95% CI) of *revision due to infection* was 1.1 (1.0-1.2) in 2000-2004 and 1.6 (1.4-1.7) in 2005-2009. Adjusted cumulative 5-year revision rates due to infection were 0.46% (0.42-0.50) in 1995-1999, 0.54% (0.50-0.58) in 2000-2004, and 0.71% (0.66-0.76) in 2005-2009. The entire increase in risk of *revision due to infection* was within 1 year of primary surgery, and most notably in the first 3 months. The risk of *revision due to infection* increased in all 4 countries. Risk factors for *revision due to infection* were male sex, hybrid fixation, cement without antibiotics and THA performed due to inflammatory disease, hip fracture or femoral head necrosis. None of these risk factors increased in incidence during the study period.

Interpretation: We found increased relative risk of revision and cumulative 5-year revision rates due to infection after primary THA during the period 1995-2009. No change in risk factors in the NARA dataset could explain this increase. We believe that there has been an actual increase in the incidence of prosthetic joint infections after THA.

6 Results and general discussion

6.1 Incidence and risk of infection after arthroplasty

The total incidence of *revision due to infection* was 0.6% after primary THAs registered in the NAR during 1987-2007 (Paper I), and 0.8% during the period 2005-2009 (Paper II). The adjusted cumulative five-year rate of *revision due to infection* was 0.54% (Paper I). In Paper III the incidence of *revision due to infection* after primary THA in the four Nordic countries during the period 1995-2010 was 0.6% whereas the overall cumulative five-year rate of *revision due to infection* was 0.62%. The one-year incidence of *surgical site infection* after primary THA during 2005-2009 was 3.0%, and nearly five times more frequent than one-year incidence of *revision due to infection* (0.7%) (Paper II).
For primary HAs during 2005-2009 the one-year incidence rates for *surgical site infection* and *revision due to infection* were 7.3% and 1.5% respectively (Paper II). Although there are difficulties in comparing incidences across countries due to methodology issues, we found the incidences of *revision due to infection* and *surgical site infection* after primary THA and HA in Norway to be similar to the other Nordic and Western countries (Ridgeway et al. 2005, HELICS 2006, Wilson et al. 2007, The Health Protection Agency 2007, Manniën et al. 2008, Havelin et al. 2009, Urquhart et al. 2010, The National Joint Replacement Registry 2011).

6.2 Increasing risk of revision due to infection after primary THA

Our main finding in Papers I and III was an increased risk of *revision due to infection* after primary THA in Denmark, Finland, Norway and Sweden in recent years. Also the cumulative rate of *revision due to infection* after THA increased and we concluded that there seems to be a true increase in incidence of *prosthetic joint infections*. Such an increase has also been suggested by two other publications

(Kurtz et al. 2008, Pedersen et al. 2010b). Pedersen's study from Denmark was based on the Danish Hip Arthroplasty Register from 1995-2008 and these data were also included in our Paper III. Kurtz reported a two-fold increase in overall incidence of deep infection after THA from 0.66% in 1990 to 1.23% in 2004 (Kurtz et al. 2008). This study on "total infection burden" was based on aggregated data from the American Inpatient Sample, without linkage between primary THA and revision after discharge and with both primary and revision arthroplasty included in the analyses (Agency for Healthcare Research and Quality 2010). For primary THAs only, they found a lower incidence of infection, probably due to shorter length of hospital stay. Another study based on adverse outcomes of total hip arthroplasty based on the US Medicare database found a reduction in the 90-day incidence of the diagnosis of infection after primary THA between 1991 and 2008 (Wolf et al. 2012). Both these studies from the USA have limitations which make it difficult to conclude about time trend of infection after primary THA.

The Dutch National Nosocomial Surveillance Network (PREZIES) reported a decrease in surgical site infections after primary THA between 1996 and 2006, as did the British mandatory surveillance of *surgical site infection* between 2004 and 2010 (Manniën et al. 2008, Health Protection Agency 2011). Capturing of *surgical site infections* is highly dependent on length of stay after primary THA or type and length of post-discharge surveillance (Huotari and Lyytikäinen 2006). For instance low-grade *prosthetic joint infections*, presented by pain and loosening of the implant at a later stage, will generally be missed in *surgical site infection* surveillance programmes. The reported decrease in the incidence of *surgical site infections* may therefore be due to shorter length of stay and lack of or incomplete post-discharge surveillance, and not to a reduction in the incidence of *prosthetic joint infections* in need of revision (Manniën et al. 2008, Health Protection Agency 2011).

If the increase in risk of *revision due to infection* reflects a true increase in *prosthetic joint infections*, what may be the changes that have caused the increase? These may include changes in patient-related factors (e.g. more comorbidity), changes in microbiology (e.g. increased bacterial virulence or more resistant strains) or

changes in surgery-related factors (e.g. duration of surgery or changed surgical technique). These possible causes will be discussed below (Chapter 6.5). The changes in risk of *revision due to infection* may also be influenced by confounding factors causing increased reporting (e.g. changes in diagnostics, new surgical methods for treating infections after arthroplasty, altered awareness of *prosthetic joint infection*). Such possible confounders will be discussed in Chapter 6.6.

6.3 Risk factors for infection after arthroplasty

6.3.1 Risk factors for infection after THA

Old *age* was not found to be a risk factor for *revision due to infection* after THA (Papers I and III). However, when adjusting for comorbidity (ASA class), old age is a risk factor for both *revision due to infection* and *surgical site infection* (Paper II). This may indicate that young patients are in poorer health at THA compared to the average population of the same age, whereas old patients (> 80 years) are healthier than average when selected for THA (Lie et al. 2000). A recent large Danish study, adjusted for co-morbidity, did not find age as a risk factor (Pedersen et al. 2010b). On the other hand, revision surgery on hip arthroplasty is extensive, and surgeons may perhaps sometimes choose a non-operative approach in old and frail patients. These cases of infections may therefore not be registered in our data.

Male sex was a risk factor of *revision due to infection* after THAs (Papers I, II and III). Some other studies have also shown this (Ong et al. 2009, Pedersen et al. 2010b), whereas other studies have not (Mahomed et al. 2003, Ridgeway et al. 2005). It appears from our study that males had a higher risk than females of *revision due to infection* (Paper II). For the risk of *surgical site infection* there was a smaller difference between the sexes (Paper II). The gender difference in revision due to infection may be due to different thresholds for referral or revision surgery, or to the fact that surgery on males represents a greater degree of surgical trauma and tissue damage (Franks and Clancy 1997, Ridgeway et al. 2005, Borkhoff et al. 2008, Pedersen et al. 2010b). There may also be differences in bacterial carriage

between men and women (Skråmm et al. 2007, Skråmm et al. 2011). Why the gender difference in relative risk is not so pronounced for *surgical site infections* remains unclear, but may either indicate that surgeons are more prone to revise these infections in males than in females, or that there is a true difference in risk pattern between these two definitions of infection.

The cause of the primary THA, the *diagnosis*, was found to be a risk factor for *revision due to infection* in Paper III. THA performed due to inflammatory disease, hip fracture or femoral head necrosis had increased risk of *revision due to infection*. The reason for this may be the association of these conditions with comorbidity and trauma. This was also found in other publications (Pedersen et al. 2010b, Bozic et al. 2012, Berbari et al. 2012). This trend was also seen for inflammatory disease in Paper I, but was not statistically significant. In Paper II THA due to hip fracture was associated with increased risk of *revision due to infection*, with a similar trend for *surgical site infection*, as also found by Ridgeway (Ridgeway et al. 2005).

Comorbidity (ASA class) has only been reported to the NAR since 2005. In Paper II elevated ASA class was associated with increased risk of *revision due to infection* (ASA > 1) and *surgical site infection* (ASA ≥ 3). Comorbidity is a well-documented risk factor of revision due to infection, *surgical site infection* and *prosthetic joint infection* (Mahomed et al. 2003, Ridgeway et al. 2005, Pulido et al. 2008, Pedersen et al. 2010b, Berbari et al. 2012).

Duration of surgery was found to be associated with infection after THA. In Paper I, duration of surgery longer than 100 minutes had increased risk for *revision due to infection*. A similar trend was found for *surgical site infection* and *revision due to infection* in Paper II. However THA of less than 60 minutes more than doubled the risk of *surgical site infection* (Paper II). Ridgeway also found this for revision THAs, and it may indicate that too rapid surgery may result in inferior soft tissue treatment and haemostasis and thereby increased risk of *surgical site infection* (Ridgeway et al. 2005). Long duration of surgery as a risk factor for infection is also found in other

publications (Småbrekke et al. 2004, Ridgeway et al. 2005, Ong et al. 2009, Pedersen et al. 2010b, Berbari et al. 2012).

Uncemented *fixation* compared to fixation with cement containing antibiotics was associated with increased risk of *revision due to infection* after THA in Papers I and II, but not in Paper III. The risk of *surgical site infection* was not influenced by type of fixation (Paper II). In Papers I and III we also found that plain bone cement was inferior to cement containing antibiotics. Previous studies from the NAR have shown similar risk for uncemented fixation and fixation with cement containing antibiotics (Engesæter et al. 2006). Sub-analyses in the work on the present thesis indicate that the protection by cement containing antibiotics is more pronounced in old and comorbid patients.
In Paper III the overall risk of *revision due to infection* was similar for cemented and uncemented THAs, in contrast to Papers I and II that showed higher risk for uncemented THAs in Norway. A publication from the Danish Arthroplasty Register found cemented THA to have a higher risk of *revision due to infection* than uncemented THA (Pedersen et al. 2010b). As in most other Western countries, Danish orthopaedic surgeons have a tradition of choosing uncemented implants for primary THA. Reasons for choosing THAs inserted with cement containing antibiotics within such a tradition may be comorbidity or higher surgical risk. Therefore there may be a selection bias towards sicker patients for cemented implants that could explain the finding of higher risk of revision due to infection, as found in Denmark.

The efficacy of *systemic antibiotic prophylaxis* is well documented and accepted (Engesæter et al. 2003, Albuhairan et al. 2008). In Paper I we assessed systemic antibiotic prophylaxis and found a trend of lower risk of *revision due to infection*. However, nearly all patients received antibiotic prophylaxis systemically, making further investigations difficult (Paper I). We found that improvements in antibiotic prophylaxis in primary THAs in Norway during 1987-2007 reduced the risk of *revision due to infection* (Dale et al. 2008).

Ventilation in the operating room has had a strong focus in preventing infections in the history of arthroplasty (Charnley 1972, Evans 2011). Although Evans' review recommends vertical laminar air flow (LAF), some recent studies indicate no improvement regarding incidence of infection after THA for vertical LAF compared to conventional turbulent ventilation (Pedersen et al. 2010b, Hooper et al. 2011, Gastmeier et al. 2012). In Paper I we found higher risk for revision due to infection when the primary THA was performed in a LAF operation room compared to conventional ventilation. Danish health authorities no longer recommend LAF in operation theatres (The Danish National Board of Health 2011). Large scale randomized studies and further investigation of register data seem to be needed on this topic.

The *NNIS risk index* is a combined surgery-related assessment tool developed to identify high risk patients and to evaluate risk of *surgical site infection* (Mangram et al. 1999). The NNIS index comprises ASA class of more than 2, duration of surgery longer than the 75th percentile for the procedure, and contamination of the wound. A high NNIS risk index has been found to be associated with increased risk of *surgical site infection* and *prosthetic joint infection* (Berbari et al. 1998, Ridgeway et al. 2005, Muilwijk et al. 2006). For *surgical site infection* after HA and THA this could not be reproduced, but the risk for *revision due to infection* after THA increased for an NNIS risk index of two or more in Paper II. Considering our findings on ASA class, duration of surgery and the fact that arthroplasty is a clean procedure, the NNIS does not appear to be optimal for identifying patients at risk of infection after arthroplasty (Paper II).

6.3.2 Risk factors for infection after HA

In Paper II, patients with femoral neck fractures, younger than 60 years had increased risk of *revision due to infection*. No risk factors were identified for *surgical site infection* after HA. In Norway the common policy is to use HA in young patients only if they have a high risk of complications or a short life expectancy.

There was also a trend of increased risk of *revision due to infection* and *surgical site infection* at advanced age (>90 years) in Paper II, as has been found in another study (Ridgeway et al. 2005).
For short duration of surgery (< 60 minutes) we found a trend of increased risk of infection after HA. As mentioned for THAs, rapid surgery may result in inferior surgery and haemostasis and thereby increased risk of infection. This may lead to prolonged wound drainage and haematoma, which are found to be risk factors for *prosthetic joint infection* after HA (Berbari et al. 1998, Cordero-Ampuero and de Dios 2010). A surprising finding in Paper II was that comorbidity (> ASA class) did not result in increased risk of infection after HA. This may be due to the small number of primary HAs in the study. However, it may also be that ASA class is too crude a measurement for the state of health of the old HA patient who may be frail, obese or malnourished, may have diabetes with hyperglycaemia and may be suffering from a major trauma.

6.3.3 Differences in risk patterns for infection

A Spanish case-control study on late infection (more than three months) after arthroplasty found differences in risk patterns between HA and THA with regard to postoperative infection (Cordero-Ampuero and de Dios 2010). In HA the more frequent risk factors associated with late *prosthetic joint infection*, compared to THA, were female sex, previous surgery, obesity (BMI > 30), immunosuppression, inadequate antibiotic prophylaxis, and haematoma (Cordero-Ampuero and de Dios 2010). Risk factors more frequently associated with associated late infection after THA were THA due to posttraumatic osteoarthritis, previous or subsequent surgery, chronic liver disease, and alcohol or intravenous drug abuse (Cordero-Ampuero and de Dios 2010).
In Paper II we also found indications of differences in risk patterns between HA and THA. Age below 60 was a risk factor for *revision due to infection* after HA but not THA. Risk factors associated with *revision due to infection* after THA but not HA were comorbidity (ASA class > 1), THA performed as emergency surgery, and NNIS risk index of two or more.
For *surgical site infections* comorbidity (ASA class ≥ 3) was a risk factor for THA but not HA. ASA class estimations may not capture the effect of the physiological

inflammatory responses to an acute trauma, tissue damage or haematoma, or medical frailty of the old which would be more frequent among the HA patients who have suffered a femoral neck fracture. This may be one reason why ASA class was not found to be a risk factor for *revision due to infection (Ridgeway et al. 2005, Makary et al. 2010)*. Surgeons may also be reluctant to revise an infected HA if the patient is in poor health, has a short life expectancy, and has acquired an infection susceptible to long-term antibiotic suppression.

Surgical site infections appeared to be nearly five times more frequent than *revisions due to infections* after arthroplasty (Paper II). We also found indications of differences in risk patterns between surgical *site infection* and *revision due to infection* in Paper II. After THA, age over 90 was associated with increased risk of *surgical site infection* but not for *revision due to infection*. After HA, age below 60 had a higher risk of *revision due to infection* but no increased risk of *surgical site infection*. Also less than 60 minutes duration of THA surgery was associated with increased risk of *surgical site infection*, but not *revision due to infection.* These findings indicate that different definitions of infection and different arthroplasty procedures may have distinct risk patterns.

6.3.4 Changes in incidence of risk factors

None of the risk factors we assessed in Papers I and III could fully explain the increase in the risk of *revision due to infection* during the period studied. The incidence of unfavourable risk factors did not increase through the study period except for the use of laminar air flow in Norway (Paper I). The increase in risk with laminar air flow and the increase in operating rooms having such ventilation seem too small to explain our finding of increased *risk of revision due to infection*. In addition these confounders were adjusted for in the analyses.

6.4 True increase in incidence of infection after primary THA?

Since none of the risk factors we assessed in Papers I and III could fully explain the finding of increased risk of *revision due to infection*, an increased incidence of *prosthetic joint infection* would have to be caused by factors not registered in the NAR or NARA datasets. These may include changes in patient-related factors (e.g. more comorbidity), changes in microbiology (e.g. increased bacterial virulence or more resistant strains) or changes in surgery-related factors (e.g. duration of surgery or altered surgical technique).

The datasets in Papers I and III contain limited information on comorbidity, which is a well-documented risk factor for infection after THA (Mahomed et al. 2003, Ridgeway et al. 2005, Huotari et al. 2007, Pulido et al. 2008, Pedersen et al. 2010b, Berbari et al. 2012). If THA was performed on more patients with poor health in the later part of our study period, an increased incidence of *prosthetic joint infections* could result. In Norway the comorbidity of patients receiving THA, according to reported ASA class, increased during 2005-2010 (The Norwegian Arthroplasty Register 2012).

The general incidence of specific comorbidities associated with increased risk of infection after THA, such as obesity and diabetes, is increasing in several countries (Pedersen et al. 2010a, Danaei et al. 2011, Haverkamp et al. 2011, Mraovic et al. 2011, Doak et al. 2012, Iorio et al. 2012, Jämsen et al. 2012, Wolf et al. 2012, Witsø 2012). Also the fraction of THA patients on prophylactic antithrombotic treatment due to cardiovascular disease may have increased. Increased or “excessive” antithrombotic treatment in relation to hip surgery may lead to prolonged wound drainage and subsequently *surgical site infection* and *revision due to infection* (Parvizi et al. 2007, Cordero-Ampuero and de Dios 2010, Berbari et al. 2012). Given that the THA patients reported to the NAR and NARA are representative of the general population, an increased incidence of *prosthetic joint infections* requiring revision could result.

It may also be that more peroperative anticoagulation and extended thrombotic prophylaxis after hip arthroplasty in recent years has led to more haematomas and

prolonged wound drainage prone to postoperative infection (Saleh et al. 2002, Patel et al. 2007, Cordero-Ampuero and de Dios 2010, Berbari et al. 2012).
Surgery-related risk factors such as duration of surgery and timing and type of systemic antibiotic prophylaxis are not included in the NARA dataset. However, there are indications that both short and long duration of surgery are risk factors of infection in Papers I and II and in other publications (Ridgeway et al. 2005, Pulido et al. 2008, Pedersen et al. 2010b, Berbari et al. 2012). In Paper I there is a trend toward shorter duration of surgery. If the proportion of very rapid THAs has increased, this could lead to a greater risk of infection.
Less compliance to guidelines for optimal systemic antibiotic prophylaxis could also have contributed to increased incidence of *prosthetic joint infections*, as could increase in the bacterial virulence or resistance to the antibiotic prophylaxis (Kerttula et al. 2007, Stefánsdóttir et al. 2009a, Stefánsdóttir et al. 2009b, Lutro et al. 2010).
Finally, also changes in operation room ventilation, as found in Paper I, or changed adherence to guidelines of prophylactic routines may have influenced the trend of increased risk of *revision due to infection*, as could reduction in the volume of THA and the experience of the individual surgeons performing THA (Geubbels et al. 2005, National institute of health and clinical excellence (NICE) 2008, Kurtz et al. 2008, Merollini et al. 2012).

6.5 No increase in incidence of infection after primary THA?

Other factors not recorded in the arthroplasty registers, such as improved awareness and reporting, may have contributed to an increase in *revision due to infection* without reflecting a corresponding increase in the true incidence of *prosthetic joint infection*. Other unknown confounders could be changes in revision policy and in the threshold of revision (e.g. new surgical methods) or changes in diagnostics (e.g. improved microbiological detection methods and changed definitions).

Since 2000, in Norway, there has been an increase in the reporting of minor revision procedures, such as soft tissue debridement with exchange of removable parts (head and liner) of modular implants and retention of the femoral stem and the acetabular cup (Engesæter et al. 2011). These minor revisions may have a lower threshold for performance. However, since the incidence of major *revisions due to infection* in Norway also increased during 1995-2009, we do not believe that increased use of modular implants and the changes in revision policy alone can explain the increased risk of revision due to infection (Engesæter et al. 2011).
There have been improvements in the diagnostics of *prosthetic joint infections*. Some bacteria like coagulase-negative staphylococci have been increasingly acknowledged for their pathogenicity (von Eiff et al. 2006). In addition, improvements in preoperative bacterial sampling and identification may also have increased the number of infections being identified preoperatively, leading to more correct reporting of low-grade infections (Tunney et al. 1998, Ince et al. 2004, Trampuz and Widmer 2006, Moojen et al. 2007, Moojen et al. 2010). .
If knowledge and awareness have changed throughout the study period, there may have been a corresponding change in reporting of infection as the cause of the revision. Unexpectedly positive peroperative bacterial samples will be identified postoperatively and will not be reported to the registers. Some *prosthetic joint infections* may therefore erroneously have been registered as aseptic loosening, but possibly to a lesser extent in the later parts of the study period due to improvements in diagnostics.
The definition of *surgical site infection* is wider than for prosthetic joint infection and revision due to infection, the risk pattern is different and the follow-up is limited compared to arthroplasty registers (HELICS 2004). It may be that the treatment strategy of early postoperative soft tissue infections, or even prolonged wound drainage, has become more aggressive in recent years, resulting in an increased revision rate of superficial *surgical site infections* (Berbari et al. 1998, Cordero-Ampuero and de Dios 2010, Witsø 2012, Berbari et al. 2012).
In Paper II it appeared that only one fifth of the *surgical site infections* reported to the Norwegian Surveillance System for Healthcare-Associated Infections after primary THAs were also reported to the Norwegian Arthroplasty Register for

revisions due to infection in the period 2005-2009. In light of the above, both *revision due to infection* and *surgical site infection* will be surrogate endpoints of true *prosthetic joint infections* and the time trends may be different.

6.6 Methodological considerations and limitations

Large populations and long follow-up are needed to study a rare complication like revision due to infection. It would hardly be possible to study time trends of such an event in other ways than through large observational studies on data from extensive health registers. Even risk factors of infection after arthroplasty would need a substantial number of cases and sufficient length of follow-up to be adequately addressed. However register studies have limitations on data and methodology. In all Papers (I-III) methodological limitations were addressed. The analyses in Paper III were performed in concordance with the recently presented guidelines for statistical analyses of arthroplasty register data (Ranstam et al. 2011).

6.6.1 Completeness and quality of the registers

As mentioned in Chapter 3.6, the data in the four Nordic arthroplasty registers are prospective and show high completeness (Soderman et al. 2000, Pedersen et al. 2004, Espehaug et al. 2006). However the NHFR and NOIS have only partly been subject to studies on completeness and coverage. Reporting to the Swedish and Danish Arthroplasty Registers is mandatory, and these registers also have the advantage of yearly evaluation of coverage and completeness of both primary arthroplasty and revisions. The Finnish Arthroplasty Register, the NAR, the NHFR and the NOIS would benefit from updated completeness data by individual-based coupling to the respective national patient registers. Such individual-based coupling of registers has not been possible until recently in Norway. However all registers in Papers I, II and III are national and have high aggregated completeness (>90%). There are few studies on the validity of the reports and registrations of primary arthroplasty (Soderman et al. 2000, Arthursson et al. 2005). Some registers (the NOIS and the Swedish Arthroplasty Register) have electronic reporting, whereas

others use reports in paper form that are subsequently loaded into the database (the NHFR and the NAR). The reports to the NHFR and the NAR are filled in by the operating surgeons and checked and loaded into the register by secretaries. In the case of other registers the report is filled in by nurses or secretaries with variable involvement in the treatment of the patient, which may affect the quality of the reporting. However, considering all the data available on coverage and completeness, we considered the data of the registers to be of good quality.

6.6.2 Outcome measures

The reported outcome measures in Papers I, II and III, *revisions* and *surgical site infections* are also only partly validated. *Surgical site infections* may have been underreported to the NOIS just as revision due to infection has been to the NAR and other registers (Arthursson et al. 2005, Espehaug et al. 2006, Huotari et al. 2007, Jämsen et al. 2009, Jämsen et al. 2010b). There is also a possibility of overestimation of *surgical site infection* in surveillance systems as superficial infections may be difficult to distinguish from aseptic wound complications, and it has been found to be great inter-observer variability in the evaluation of superficial *surgical site infection* (Allami et al. 2005, Walenkamp 2009). There is thus a need for systematic validation of outcome measures and reporting. This can be achieved through individual coupling with administrative databases, as in Sweden and Denmark, or by random sampling of patients' medical records.
Differences in follow-up between THAs from different time periods will result in an underestimation of cumulative risk of *revision due to infection* in periods with short follow-up. *Surgical site infection* is an early event (<30 days) (Paper II). The majority of *revisions due to infection* are reported in the first two years postoperatively but can occur throughout the lifespan of a patient or implant (Papers I, II and III). *Revisions due to aseptic loosening* are mostly later events (Papers I and III). The 5-year cumulative risks in the last periods of time trend studies, as in Papers I and III, are therefore probably underestimated. This potential underestimation may be more pronounced for outcome measures occurring late postoperatively. We checked for underestimation due to inequities in follow-up in all three papers, by performing sub-analyses with similar follow-up for all time periods and risk factors.

6.6.3 Confounding

The number of variables in health registers is limited. Therefore, register studies, even if adjusted for several well-known confounders, will be subject to unmeasured confounding (e.g. cementing technique, awareness, diagnostics etc.). For our studies possible confounders are discussed in Chapter 6.6. Confounders may also change over time, making the confounding time-dependent, which may have an influence in time trend studies. In Papers I and III we have addressed this by assessing the risk factors for each time period separately or adjusting the analyses for year of primary surgery. When similar results were found for each time period we concluded that time-dependent confounding was minor. The causes of increasing risk *of revision due to infection* as found in Papers I and III can only be discussed and causality cannot be concluded by the methods used in the present thesis.

6.6.4 Bias

The high completeness in our studies indicates minor *selection bias*. However, as may be the case for low-grade THA infections resembling aseptic loosening, erroneous reporting may occur. This would represent a *reporting bias*, and the extent of such bias in our data is not known. The selection of primary THAs in the NOIS is based on calendar month of primary arthroplasty only. The selected cases are therefore thought to be representative.

6.6.5 Competing risk

In Papers II and III potential overestimation of incidence of *revision due to infection* through the effect of competing risks (death and revision due to other causes than infection) was assessed by the cumulative incidence function (Fine and Gray 1999, Gillam et al. 2010). The THAs revised due to other causes than infection and the THA patients that died during the follow-up imposed a negligible effect on the Cox analyses.

6.6.6 Proportional hazard

In Papers I and II the proportional hazards assumptions of the Cox analyses were inspected and verified by the log minus log plot (Mantel and Haenzel 1959). In Paper III we assessed the proportionality of the main risk factors by smoothed Schoenfeld residuals (Schoenfeld D. 1982, Therneau and Grambsch 2000). This resulted in assessment of the risk factors before and after 1 year, since the adjusted revision rates of the 3 time periods were not fully proportional.

6.6.7 Bilateral hip prostheses

Bilateral arthroplasties are not independent observations but were included in the analyses of all three papers. For example, in Paper III, the extent of bilateral THA was estimated at 18% and the incidence of revision due to infection was 0.6% both in the first and second hip. Only 0.05% of the bilateral THAs were identified with *revisions due to infection* in both hips. We therefore considered bilateral THA to have negligible influence on the results, which is in accordance with findings by other authors (Lie et al. 2004, Ranstam and Robertsson 2010, Ranstam et al. 2011)

6.6.8 Statistical power

As mentioned in Chapter 3.6, a rare event like infection after arthroplasty needs large numbers to enable a detailed study of risk factors with sufficient certainty of the conclusions. In Papers I and III we considered the number of primary THAs and events to be large enough to achieve sufficient power, whereas Paper II was considered to have insufficient power for some of the analyses due to low numbers and loss to follow-up. In the case of the NOIS it is important to set up the register to accumulate sufficient data to fulfil the aims of the register. It may therefore have been insufficient to have registrations on arthroplasties from only three months a year; however, the NOIS is at present about to start all-year registrations.

6.6.9 Internal and external validity

Because of the documented good quality of the NAR data, we consider the findings in Paper I to have high internal validity (Arthursson et al. 2005, Espehaug et al.

2006). The fact that the main finding of increased risk of revision due to infection is reproduced in Paper III also indicates external validity. Due to low numbers we consider some of the risk assessments in Paper II to have limited internal and external validity.

7 Interpretations and conclusions

Paper I

- The incidence of *revision due to infection* after primary THA in Norway was 0.6% during 1987-2007.
- The relative risk of *revision due to infection* increased throughout the study period for cemented and uncemented THAs.
- Risk factors associated with increased risk for revision due to infection were male sex, more than 100 minutes duration of surgery, laminar air flow in the operation room, uncemented THAs, and the use of plain bone cement.
- Only laminar air flow in the operation room increased in incidence throughout the study period.

We believe that the incidence of *prosthetic joint infection* after primary THA has increased in Norway during the study period, but concomitant changes in confounding factors complicate the interpretation of the results.

Paper II

- The incidence of *revision due to infection* in Norway was 0.8% after primary THA and 1.5% after primary HA during 2005-2009.
- The incidence of *surgical site infection* in Norway was 3.0% after primary THA and 7.3% after primary HA during 2005-2009.
- Risk factors for *surgical site infection* after THA were age over 80, ASA class higher than two, and duration of surgery of less than 60 minutes.
-Risk factors for *revision due to infection* after THA were male sex, age between 70 and 90, ASA class higher than 1, emergency surgery, uncemented fixation, and NNIS risk index of two or more.
- Risk factor for *revision due to infection* after HA after hip fracture was age below 60 years.
- We found differences in risk patterns between HA and THA and between *surgical site infection* and *revision due to infection*.

The incidences of *surgical site infection* and *revision due to infection* after primary hip arthroplasty are similar to those in other countries. Probably only a fraction of the reported superficial *surgical site infections* are revised due to infection.

Paper III

- The incidence of revision due to infection was 0.6% in the Nordic countries during 1996-2009.
- The relative risk of revision due to infection increased throughout the study period.
- Risk factors for *revision due to infection* were male sex, hybrid fixation, cement without antibiotics and THA performed due to inflammatory disease, hip fracture or femoral head necrosis.
- None of these risk factors increased in incidence during the study period.

The increase in *revision due to infection* is a common feature for the Nordic countries, and we believe it reflects a true increase in incidence of *prosthetic joint infection*. This study could not provide an answer as to why there may be such an increased risk for infection.

8 Future research

Important topics for future research will be:

- Validation of data on exposures and outcomes in the health registries through true individual-based combinations.
- Studies on risk factors, course, treatment and outcome of *prosthetic joint infections* in such combinations of registries.
- To identify modifiable risk factors and effective prophylactic measures against *prosthetic joint infection*.
- To identify the best treatment of *prosthetic joint infections* through a combination of studies of course, treatment and outcome of infection in merged health registries, including patient-reported outcomes.

Because of the NPR, NAR, NHFR and NOIS, Norway has a unique potential for such research, to the benefit of patients, if regulatory authorities support utilization.

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Appendices

Appendix 1 Operation form for the Norwegian Arthroplasty Register (1987-1991) (Norwegian)
Appendix 2 Operation form for the Norwegian Arthroplasty Register (1992-1999) (Norwegian)
Appendix 3 Operation form for the Norwegian Arthroplasty Register (2000-2004) (Norwegian)
Appendix 4 Operation form for the Norwegian Arthroplasty Register (2005-2011) (Norwegian)
Appendix 5 Operation form for the Norwegian Hip Fracture Register (2005-2011) (Norwegian)
Appendix 6 NOIS-5 manual (Norwegian)
Appendix 7 Description of the NARA data files (English)

NASJONALT REGISTER FOR TOTALPROTESER I HOFTELEDD

991

Ortopedisk avdeling
Haukeland sykehus,
5021 BERGEN

F. nr. (11 sifre) :

Navn:

Sykehus:

(Bruk blokkbokstaver)

ANAMNESE:

1. SMERTER (ett kryss):
- ☐1 Sterke spontane i hvile og om natten.
- ☐2 Sterke som hindrer all gangaktivitet.
- ☐3 Moderate, tillater begrenset gange.
- ☐4 Etter noe aktivitet, forsvinner i hvile.
- ☐5 Lette eller periodevise. Startsmerter.
- ☐6 Ingen smerter.

2. GANGEVNE (ett kryss):
- ☐1 Få meter med 2 krykker/stokker/sengeliggende.
- ☐2 Sterkt begrenset med eller uten stokker.
- ☐3 Begrenset med stokk (under en time). Kan stå lenge.
- ☐4 Kan gå lange avstander med en stokk.
- ☐5 Ingen stokk, men halter.
- ☐6 Normal gangevne.

3. FUNKSJONSGRUPPE (ett kryss):
- ☐1 Aktuelle hofte syk ellers frisk.
- ☐2 Begge hofter syke ellers frisk.
- ☐3 Annet som reduserer gangevnen.

4. TIDLIGERE OPERASJON(ER) I AKTUELLE HOFTE:
- ☐0 Nei (evt. flere kryss)
- ☐1 Osteosyntese pga. fraktur i prox.femurende.
- ☐2 Hemiprotese pga. fraktur
- ☐3 Osteotomi.
- ☐4 Artrodese.
- ☐5 Totalprotese(r) Type(r): . . . . . Årstall siste protese: ☐☐☐☐
- ☐6 Annet: . . . . .

5. VARIGHET AV SYMPT. I AKT. HOFTE: ☐☐☐ år (under 1 år = 0).

OPERASJONSOPPLYSNINGER:

6. OPERASJONSDATO: dag ☐☐ mnd ☐☐ år ☐☐

7. AKTUELLE OPERASJON ER (ett kryss).
- ☐1 Primær totalproteseoperasjon.
- ☐2 Reoperasjon.

8. AKTUELLE SIDE (ett kryss).
- ☐1 Høyre
- ☐2 Venstre
- ☐3 Høyre - venstre allerede protese.
- ☐4 Venstre - høyre allerede protese.

9. AKTUELLE HOFTEOPERASJON ER (ett kryss).
a) Primæroperasjon pga.:
- ☐1 Idiopatisk coxartrose
- ☐2 Rheumatoid artritt.
- ☐3 Seq.fr. colli fem.
- ☐4 Seq.dysplasi.
- ☐5 Seq.dysplasi med luksasjon.
- Seq.Perthes/epifys.
- ☐7 Bechterew.
- ☐8 Annet: . . . . .

b) Reoperasjon pga. (evt. flere kryss):
- ☐1 Løsning av acetabulardel.
- ☐2 Løsning av femurdel.
- ☐3 Luksasjon.
- ☐4 Dyp infeksjon.
- ☐5 Fraktur av femur.
- ☐6 Smerter.
- ☐7 Annet: . . . . .

10. **HVIS** reoperasjon (ett kryss):
- ☐1 Reop. - bytte av femurdelen.
- ☐2 Reop. - bytte av acetabulardelen.
- ☐3 Reop. - bytte av hele protesen.
- ☐4 Reop. - annet: (f.eks. Girdlestone) . . . . .

11. TILGANG (ett kryss):
- ☐1 Fremre (Smith-Pettersen).
- ☐2 Anterolateral.
- ☐3 Lateral.
- ☐4 Posterolateral
- ☐5 Annen: . . . . .

12. TROCHANTEROSTEOTOMI:
- ☐0 Nei
- ☐1 Ja

13. BENTRANSPLANTASJON:
- ☐0 Nei
- ☐1 I acetabulum.
- ☐2 I femur.
- ☐3 I acetabulum og femur.

PROTESE. NAVN/TYPE **(Spesifiser nøyaktig):**

14. **Acetabulum:**
Navn/Type: . . . . .
Evt. Kat. nr: . . . . .
- ☐1 Sement med antibiotika. Navn: . . . . .
- ☐2 Sement uten antibiotika. Navn: . . . . .
- ☐3 Ikke sementert.

15. **Femur:**
Navn/Type: . . . . .
Evt. Kat. nr. . . . . .
- ☐1 Sement med antibiotika. Navn: . . . . .
- ☐2 Sement uten antibiotika. Navn: . . . . .
- ☐3 Ikke sementert.

16. **Caput:**
- ☐1 Fastsittende caput.
- ☐2 Separat caput. Navn/Type: . . . . .
Evt. Kat. nr. . . . . Diam.: . . . . .

17. SYSTEMISK ANTIBIOTIKAPROFYLAKSE:
- ☐0 Nei
- ☐1 Ja. Hvilken: . . . . .
Dose: . . . . .
Varighet: . . . . .

18. OPERASJONSSTUE:
- ☐1 "Green house"
- ☐2 Operasjonsstue med laminær luftstrøm.
- ☐3 Vanlig operasjonsstue.

19. OPERASJONSTID (hud til hud): ☐☐☐ min.

20. PEROPERATIVE KOMPLIKASJONER:
- ☐0 Nei.
- ☐1 Ja. Hvilken: . . . . .

Lege : . . . . .
(Legen som har fylt ut skjemaet)

RETTLEDNING

Registreringen gjelder innsetting, skifting eller fjerning av totalproteser i hofteledd. Ett skjema fylles ut for hver operasjon. Pasientens fødselsnummer, i alt 11 sifre, og sykehus må være påført. Aktuelle ruter markeres med kryss.

Pkt. 4: Kryss av for de operasjoner som er utført tidligere. Eventuelle totalproteser angis med type og årstall for innsettingen. Skulle samme protese inneha såvel sementert som usementert alternativ, skal det aktuelle anføres.

Pkt. 9: Kryss av **enten** i 9a **eller** i 9b. I 9b må en krysse av for **alle** årsakene til reoperasjon.

Pkt. 10: Fjerning av protesedeler (f.eks. Girdlestone opr.) føres opp under »annet»

Pkt. 13: Benpropp som sementstopper regnes ikke som bentransplanat.

Pkt. 14: Her anføres komersielle navn, materiale, størrelse og design, f.eks. Ceraver, Titan, 50mm, skru. Eller f.eks. Charnley, large, OGEE, LPW. Alternativt kan en føre opp protesenavn og katalognr. Vikositetsgraden på sementen må anføres, f.eks. CMW III.

Pkt. 15: Utfylles tilsvarende, f.eks. Charnley, flanged 40 og eventuelt anføres spesialutførelse som long neck, magnum, long stem, krage, etc.
Alternativt kan en føre opp bare protesenavn og katalognr.
Ang. sement. Se punkt 14.

Pkt. 16: Ved separat caput (evt også separat collum) må navn, materiale, diameter, halslengde og lateralisering anføres. F.eks. Ceraver, keramikk, 32mm, standard neck.
Alternativt anføres bare protesenavn og katalognr.

Kopi beholdes til pasientjournalen, originalen sendes til Haukeland sykehus.

Kontaktpersoner vedrørende registreringsskjema er
Dr. Leif Ivar Havelin, Ortopedisk-traumatologisk avd., Haukeland sykehus, 5021 Bergen, telefon 05/298060.

Sekretærer: for Hofteregisteret: Adriana Opazo og Kari Tollefsen, Kirurgisk Institutt, Haukeland Sykehus, telefon 05/972763.

App. II

NASJONALT REGISTER FOR LEDDPROTESER
Ortopedisk avdeling
Haukeland Sykehus
5021 BERGEN
Tlf.: 55 97 27 63

1. F. nr. (11 sifre):.....
2. Navn:.....
3. Sykehus: .....

Skriv tydelig!

HOFTEPROTESER

ALLE TOTALPROTESER I HOFTELEDD REGISTRERES (ikke hemiproteser)
Innsetting, skifting eller fjerning av protese eller protesedeler.

4. TIDLIGERE OPERASJON I AKTUELLE HOFTE:
(evt. flere kryss)
☐0 Nei
☐1 Osteosyntese for fraktur i prox.femurende
☐2 Hemiprotese pga fraktur
☐3 Osteotomi
☐4 Artrodese
☐5 Totalprotese(r)
☐6 Annen operasjon .....

5. Hvis protese tidligere, TYPE(R): .....
Årstall siste protese: ☐☐

6. OPERASJONSDATO: dag ☐☐ mnd ☐☐ år ☐☐

7. AKTUELLE OPERASJONER ER (ett kryss):
☐1 Primæropr. (Også hvis hemiprotese tidl.)
☐2 Reoperasjon (totalprotese tidligere).

8. AKTUELLE SIDE (ett kryss):
(Bilateral opr.= 2 skjema)
☐1 Hø
☐2 Ve
☐3 Hø - Venstre allerede protese
☐4 Ve - Høgre allerede protese

9. AKTUELLE OPERASJONER ER:
(kryss av enten i 9a eller 9b.)

a. Primæroperasjon pga. (ett kryss):
☐1 Idiopatisk coxartrose
☐2 Rheumatoid artritt
☐3 Seqvele etter frakt.colli fem.
☐4 Seqv.dysplasi
☐5 Seqv.dysplasi med total luksasjon
☐6 Seqv.Perthes/Epifysiolyse
☐7 Mb.Bechterew
☐8 Annet: .....
(f.eks. caputnekrose, tidl.artrodese, akutt fraktur o.l.)

b. Reoperasjon pga. (evt. flere kryss)
☐1 Løs acetabular komponent
☐2 Løs femur komponent
☐3 Luksasjon
☐4 Dyp infeksjon
☐5 Fraktur (ved protesen)
☐6 Smerter
☐7 Annet: .....
(f.eks. Girdlestone etter tidl. infisert protese, protesefraktur, utslitt plastforing osv.)

10. REOPERASJONSTYPE (ett kryss):
☐1 Bytte av femur komponent
☐2 Bytte av acetabularkomponent
☐3 Bytte av hele protesen
☐4 Andre operasjoner:
☐ Fjernet protese (f.eks Girdlestone).
Angi hvilke deler som ble fjernet. .....
.....
☐ Bytte av bare plastforing. .....
☐ Bytte av bare caput
☐ Annet: .....
.....

11. TILGANG
☐1 Fremre (Smith-Pettersen)
☐2 Anterolateral
☐3 Lateral
☐4 Posterolateral
☐5 Annen: .....

12. TROCHANTEROSTEOTOMI
☐0 Nei
☐1 Ja

13. BENTRANSPLANTASJON
☐0 Nei
☐1 I acetabulum
☐2 I femur
☐3 I acetabulum og femur

PROTESE: NAVN/TYPE/DESIGN/"COATING"
Spesifiser nøyaktig eller bruk klistrelapp på baksida.

14. Acetabulum
Navn/Type: .....
Evt. katalognummer: .....
☐ Med hydroksyapatitt ☐ Uten HA

☐1 Sement med antibiotika Navn: .....
☐2 Sement uten antibiotika Navn: .....
☐3 Usementert

15. Femur
Navn/Type: .....
Evt. katalognummer: .....
☐ Med hydroksyapatitt ☐ Uten HA

☐1 Sement med antibiotika Navn: .....
☐2 Sement uten antibiotika Navn: .....
☐3 Usementert

16. Caput
☐1 Fastsittende caput
☐2 Separat caput: Navn/Type: .....
Evt Katalognummer: .....
Diameter: ☐☐ millimeter

17. SYSTEMISK ANTIBIOTIKAPROFYLAKSE
☐0 Nei
☐1 Ja, hvilken: .....
Dose: .....
Varighet (antall døgn): ☐☐

18. OPERASJONSSTUE
☐1 "Green house"
☐2 Operasjonsstue med laminær luftstrøm
☐3 Vanlig operasjonsstue

19. OPERASJONSTID (HUD TIL HUD): ☐☐☐ MINUTTER

20. PEROPERATIV KOMPLIKASJON
☐0 Nei
☐1 Ja, hvilken: .....
.....

Lege: .....
Legen som har fylt ut skjemaet (Navnet registreres ikke)

Haukeland Sykehus Trykkeri - 13.9.93-1A

RETTLEDNING

Registreringen gjelder innsetting, skifting eller fjerning av totalproteser i hofteledd. Ett skjema fylles ut for hver operasjon. Pasientens fødselsnummer, (11 sifre), og sykehus må være påført. Aktuelle ruter markeres med kryss.

Kommentarer til de enkelte punktene:

Pkt. 4: Kryss av for de operasjoner som er utført tidligere. Eventuelle totalproteser angis med type og årstall for innsettingen. Skulle samme protese inneha såvel sementert som usementert alternativ, skal det anføres hva som ble brukt.

Pkt. 9: Kryss av **enten** i 9a **eller** 9b. I 9b må en krysse av for alle årsakene til reoperasjon.

Pkt. 10: Fjerning av protesedeler (f.eks. Girdlestone opr) må føres opp.

Pkt. 13: Benpropp som sementstopper regnes ikke som bentransplantat.

Pkt. 14: Her anføres komersielle navn, materiale, størrelse og design, f.eks. Ceraver, Titan, 50mm, skru. Eller f.eks. Charnley, large, OGEE, LPW. Vær nøye med å anføre om protesen har belegg av f.eks. hydroxyapatitt. Alternativt kan en føre opp protesenavn og katalognr., eller benytte klistrelapp som følger med de fleste protesene. Denne kan limes på baksiden av skjemaet.
Navnet på sementen må anføres, f.eks. CMW III.

Pkt. 15: Utfylles tilsvarende, f.eks. Charnley, flanged 40 og eventuelt anføres spesialutførelse som long neck, magnum, long stem, krage etc.
Alternativt kan en føre opp bare protesenavn og katalognr., eller bruke klistrelapp (på baksiden av skjema). Ang. sement. Se pkt. 14.

Pkt. 16: Ved separat caput (evt. også separat collum) må navn, materiale, diameter, halslengde og lateralisering anføres. F.eks. Ceraver, keramikk, 32mm, standard neck.
Alternativt anføres bare protesenavn og katalognr., eller en benytter klistrelapp fra produsenten.

Pkt. 20: Dersom det foreligger komplikasjon i form av stor blødning, må mengden angis.

Kopi beholdes til pasientjournalen, originalen sendes til Haukeland Sykehus.

Kontaktpersoner vedrørende registreringsskjema er:

Overlege Leif Ivar Havelin, Ortopedisk avd., Haukeland Sykehus, 5021 Bergen, tlf.: 55 97 29 18

Sekretærer for Hofteregisteret: Adriana Opazo og Kari Tollefsen,
Ortopedisk/Traumatologisk avd., Haukeland Sykehus, tlf.: 55 97 27 63

Haukeland Sykehus Trykkeri - 13.9.93-1B

App. III

NASJONALT REGISTER FOR LEDDPROTESER
Ortopedisk avdeling
Haukeland Sykehus
5021 BERGEN
Tlf.: 55 97 27 63

1. F. nr. (11 sifre):.....
2. Navn:.....
3. Sykehus: .....

Skriv tydelig!

HOFTEPROTESER

ALLE TOTALPROTESER I HOFTELEDD REGISTRERES (ikke hemiproteser)
Innsetting, skifting eller fjerning av protese eller protesedeler.

4. TIDLIGERE OPERASJON I AKTUELLE HOFTE:
(evt. flere kryss)
☐0 Nei
☐1 Osteosyntese for fraktur i prox.femurende
☐2 Hemiprotese pga fraktur
☐3 Osteotomi
☐4 Artrodese
☐5 Totalprotese(r)
☐6 Annen operasjon .....

5. Hvis protese tidligere, TYPE(R): .....
Årstall siste protese: ☐☐

6. OPERASJONSDATO: dag ☐☐ mnd ☐☐ år ☐☐

7. AKTUELLE OPERASJONER ER (ett kryss):
☐1 Primæropr. (Også hvis hemiprotese tidl.)
☐2 Reoperasjon (totalprotese tidligere).

8. AKTUELLE SIDE (ett kryss):
(Bilateral opr.= 2 skjema)
☐1 Hø
☐2 Ve
☐3 Hø - Venstre allerede protese
☐4 Ve - Høgre allerede protese

9. AKTUELLE OPERASJONER ER:
(kryss av enten i 9a eller 9b.)

a. Primæroperasjon pga. (ett kryss):
☐1 Idiopatisk coxartrose
☐2 Rheumatoid artritt
☐3 Seqvele etter frakt.colli fem.
☐4 Seqv.dysplasi
☐5 Seqv.dysplasi med total luksasjon
☐6 Seqv.Perthes/Epifysiolyse
☐7 Mb.Bechterew
☐8 Annet: .....
(f.eks. caputnekrose, tidl.artrodese, akutt fraktur o.l.)

b. Reoperasjon pga. (evt. flere kryss)
☐1 Løs acetabular komponent
☐2 Løs femur komponent
☐3 Luksasjon
☐4 Dyp infeksjon
☐5 Fraktur (ved protesen)
☐6 Smerter
☐7 Annet: .....
(f.eks. Girdlestone etter tidl. infisert protese, protesefraktur, utslitt plastforing osv.)

10. REOPERASJONSTYPE (ett kryss):
☐1 Bytte av femur komponent
☐2 Bytte av acetabularkomponent
☐3 Bytte av hele protesen
☐4 Andre operasjoner:
☐ Fjernet protese (f.eks Girdlestone).
Angi hvilke deler som ble fjernet. .....
.....
☐ Bytte av bare plastforing. .....
☐ Bytte av bare caput
☐ Annet: .....
.....

11. TILGANG
☐1 Fremre (Smith-Pettersen)
☐2 Anterolateral
☐3 Lateral
☐4 Posterolateral
☐5 Annen: .....

12. TROCHANTEROSTEOTOMI
☐0 Nei
☐1 Ja

13. BENTRANSPLANTASJON
☐0 Nei
☐1 I acetabulum
☐2 I femur
☐3 I acetabulum og femur

PROTESE: NAVN/TYPE/DESIGN/"COATING"
Spesifiser nøyaktig eller bruk klistrelapp på baksida.

14. Acetabulum
Navn/Type: .....
Evt. katalognummer: .....
☐ Med hydroksyapatitt ☐ Uten HA

☐1 Sement med antibiotika Navn: .....
☐2 Sement uten antibiotika Navn: .....
☐3 Usementert

15. Femur
Navn/Type: .....
Evt. katalognummer: .....
☐ Med hydroksyapatitt ☐ Uten HA

☐1 Sement med antibiotika Navn: .....
☐2 Sement uten antibiotika Navn: .....
☐3 Usementert

16. Caput
☐1 Fastsittende caput
☐2 Separat caput: Navn/Type: .....
Evt Katalognummer: .....
Diameter: ☐☐ millimeter

17. SYSTEMISK ANTIBIOTIKAPROFYLAKSE
☐0 Nei
☐1 Ja, hvilken: .....
Dose: .....
Varighet (antall døgn): ☐☐

18. OPERASJONSSTUE
☐1 "Green house"
☐2 Operasjonsstue med laminær luftstrøm
☐3 Vanlig operasjonsstue

19. OPERASJONSTID (HUD TIL HUD): ☐☐☐ MINUTTER

20. PEROPERATIV KOMPLIKASJON
☐0 Nei
☐1 Ja, hvilken: .....
.....

Lege: .....
Legen som har fylt ut skjemaet (Navnet registreres ikke)

Haukeland Sykehus Trykkeri - 13.9.93-1A

RETTLEDNING

Registreringen gjelder innsetting, skifting og fjerning av totalproteser i hofteledd.
Ett skjema fylles ut for hver operasjon.
Pasientens fødselsnummer (11sifre) og sykehus må være påført.
Aktuelle ruter markeres med kryss.
Pasientene skal på eget skjema gi samtykke til registrering i Hofteregisteret.

Kommentarer til de enkelte punktene:

Pkt. 4: Kryss av for de operasjoner som er uført tidligere. Eventuelle totalproteser angis med type og årstall for innsettingen. Skulle samme protese inneha såvel sementert som usementert alternativ, skal det anføres hva som ble brukt.

Pkt. 9: Kryss av enten i 9a eller 9b. I 9b må en krysse av for alle årsakene til reoperasjon, eller forklare dette med tekst på linjen.

Pkt. 10: Fjerning av protesedeler (f.eks.Girdlestone opr.) må føres opp.

Pkt. 13: Benpropp som sementstopper regnes ikke som bentransplantat.

Pkt. 14: Her anføres kommersielle navn, materiale, størrelse og design, f.eks. Ceraver, Titan, 50 mm, skru. Eller f.eks. Charnley, large, OGEE, LPW.
Vær nøye med å anføre om protesen har belegg av f.eks. hydroksylapatitt.
Alternativt kan en føre opp protesenavn og katalognr., eller benytte klistrelapp som føler med de fleste protesene.
Denne kan limes på skjemaet. Navnet på sementen må anføres, f.eks. CMW III.

Pkt. 15: Utfylles tilsvarende, f.eks. Charnley, flanged 40 og eventuelt anføres spesial-utførelse som long neck, magnum, long stem, krage etc. Alternativt kan en føre opp bare protesenavn og katalognr., eller bruke klistrelapp på baksiden av skjemaet (vennligst ikke plasser klistrelapper på markeringskryss, som brukes ved scanning av skjema). Ang. sement. Se. pkt. 14.

Pkt. 16: Ved separat caput (evt. også separat collum) må navn, materiale, diameter, halslengde og lateralisering anføres. F.eks. Ceraver, keramikk, 32 mm, standard neck. Alternativt anføres bare protesenavn og katalognr., eller en benytter klistrelapper fra produsenten.

Pkt. 20: Dersom det foreligger komplikasjon i form av stor blødning, må mengden angis.

Kopi beholdes til pasientjournalen, originalen sendes Haukeland Universitetssykehus.

Kontaktpersoner vedrørende registreringsskjemaer:
Klinikkoverlege Leif Ivar Havelin, tlf.: 55 97 56 87 og overlege Ove Furnes, tlf.: 55 97 56 76
Ortopedisk klinikk, Haukeland Universitetssykehus.
Sekretærer i Nasjonalt Register for Leddproteser, Ortopedisk klinikk, Helse Bergen:
Ingunn Vindenes, tlf.: 55 97 37 43 og Inger Skar, tlf.: 55 97 37 42 eller Sentralbordet,
Haukeland Universitetssykehus: 55 97 50 00. Fax: 55 97 37 49.
Internet: http://www.haukeland.no/nrl/

Hustrykkeriet HUS - 27.01.04

App. IV

Nasjonalt Register for Leddproteser
Ortopedisk klinikk, Helse Bergen HF
Haukeland universitetssjukehus
Møllendalsbakken 11
5021 BERGEN
tlf 55973742/55973743

F.nr. (11 sifre).....

Navn:.....

(Skriv tydelig ev. pasient klistrelapp – **spesifiser sykehus**.)

Sykehus:.....

HOFTEPROTESER

ALLE TOTALPROTESER I HOFTELEDD REGISTRERES (ved hemiproteser etter hoftebrudd sendes hoftebruddskjema til Hoftebruddregisteret). Innsetting, skifting eller fjerning av protese eller protesedeler.

TIDLIGERE OPERASJON I AKTUELLE HOFTE (ev. flere kryss)
- ☐0 Nei
- ☐1 Osteosyntese for fraktur i prox. femurende
- ☐2 Hemiprotese pga. fraktur
- ☐3 Osteotomi
- ☐4 Artrodese
- ☐5 Totalprotese(r)
- ☐6 Annen operasjon .....

OPERASJONSDATO (dd.mm.åå) |__|__| |__|__| |__|__|

AKTUELLE OPERASJON (ett kryss)
- ☐1 Primæroperasjon (også hvis hemiprotese tidligere)
- ☐2 Reoperasjon (totalprotese tidligere)

AKTUELLE SIDE (ett kryss) (Bilateral opr.= 2 skjema)
☐1 Høyre ☐2 Venstre

AKTUELLE OPERASJON (KRYSS AV ENTEN I A ELLER B)

A . Primæroperasjon pga. (ev. flere kryss)
- ☐1 Idiopatisk coxartrose
- ☐2 Rheumatoid artritt
- ☐3 Sekvele etter frakt. colli. fem.
- ☐4 Sekv. dysplasi
- ☐5 Sekv. dysplasi med total luksasjon
- ☐6 Sekv. Perthes/Epifysiolyse
- ☐7 Mb. Bechterew
- ☐8 Akutt fraktura colli femoris
- ☐ Annet .....
  (f.eks caputnekrose, tidl. artrodese o.l)

B . Reoperasjon pga. (ev. flere kryss)
- ☐1 Løs acetabularkomponent
- ☐2 Løs femurkomponent
- ☐3 Luksasjon
- ☐4 Dyp infeksjon
- ☐5 Fraktur (ved protesen)
- ☐6 Smerter
- ☐7 Osteolyse i acetab. uten løsning
- ☐8 Osteolyse i femur uten løsning
- ☐ Annet .....
  (f.eks Girdlestone etter tidl. infisert protese)

REOPERASJONSTYPE (ev. flere kryss)
- ☐1 Bytte av femurkomponent
- ☐2 Bytte av acetabularkomponent
- ☐3 Bytte av hele protesen
- ☐4 Fjernet protese (f.eks Girdlestone)
  Angi hvilke deler som ble fjernet .....
- ☐5 Bytte av plastforing
- ☐6 Bytte av caput
- ☐ Andre operasjoner .....

TILGANG (ett kryss)
- ☐1 Fremre (Smith-Petersen)
- ☐2 Anterolateral
- ☐3 Lateral
- ☐4 Posterolateral
- ☐5 Annen .....

LEIE ☐0 Sideleie ☐1 Rygg

TROCHANTEROSTEOTOMI ☐0 Nei ☐1 Ja

BENTRANSPLANTASJON (ev. flere kryss)
Acetabulum ☐0 Nei ☐1 Ja ☐2 Benpakking
Femur ☐0 Nei ☐1 Ja ☐2 Benpakking a.m. Ling/Gie

BENTAP VED REVISJON (Paprosky's klassifikasjon se baksiden)

Acetabulum			Femur	
☐1 Type I	☐4 Type II C		☐1 Type I	☐4 Type III B
☐2 Type II A	☐5 Type III A		☐2 Type II	☐5 Type IV
☐3 Type II B	☐6 Type III B		☐3 Type III A	

PROTESE NAVN / DESIGN / "COATING"
(spesifiser nøyaktig eller bruk klistrelapp på baksiden)

Acetabulum
Navn/Type .....
ev. katalognummer .....
☐ Med hydroksylapatitt ☐ Uten hydroksylapatitt
☐1 Sement med antibiotika – Navn .....
☐2 Sement uten antibiotika – Navn .....
☐3 Usementert

Femur
Navn/Type .....
ev. katalognummer .....
☐ Med hydroksylapatitt ☐ Uten hydroksylapatitt
☐1 Sement med antibiotika – Navn .....
☐2 Sement uten antibiotika – Navn .....
☐3 Usementert

Caput
☐1 Fastsittende caput
☐2 Separat caput - Navn/Type .....
ev. katalognummer .....
Diameter .....

MINI INVASIV KIRURGI (MIS) ☐0 Nei ☐1 Ja

COMPUTERNAVIGERING (CAOS) ☐0 Nei ☐1 Ja
Type navigering .....

TROMBOSEPROFYLAKSE
☐0 Nei ☐1 Ja, hvilken type.....

Dosering opr.dag.....Første dose gitt preopr ☐0 Nei ☐1 Ja

Senere dosering.....Antatt varighet.....døgn

Ev. i kombinasjon med .....

Dosering..... Antatt varighet.....døgn

Strømpe ☐0 Nei ☐1 Legg ☐2 Legg + Lår Antatt varighet .....døgn
Mekanisk pumpe ☐0 Nei ☐1 Fot ☐2 Legg Antatt varighet.....døgn

SYSTEMISK ANTIBIOTIKAPROFYLAKSE
☐0 Nei ☐1 Ja, hvilken (A).....

Dose (A)..... Totalt antall doser ..... Varighet .....timer

Ev. i kombinasjon med (B).....

Dose (B).....Totalt antall doser..... Varighet .....timer

OPERASJONSSTUE
- ☐1 "Green house"
- ☐2 Operasjonsstue med laminær luftstrøm
- ☐3 Vanlig operasjonsstue

OPERASJONSTID (hud til hud) .....min

PEROPERATIV KOMPLIKASJON
- ☐0 Nei
- ☐1 Ja,hvilke(n) .....

ASA KLASSE (se baksiden for definisjon)
- ☐1 Frisk
- ☐2 Asymptomatisk tilstand som gir økt risiko
- ☐3 Symptomatisk sykdom
- ☐4 Livstruende sykdom
- ☐5 Moribund

Lege .....
Legen som har fylt ut skjemaet (navnet registreres ikke i databasen).

Bergen Grafisk as - 10.08

RETTLEDNING TIL HOFTEPROTESER

Registreringen gjelder innsetting, skifting og fjerning av totalproteser i hofteledd. Ett skjema fylles ut for hver operasjon.
Pasientens fødselsnummer (11sifre) og sykehus må være påført. Aktuelle ruter markeres med kryss.
Pasientene skal på eget skjema gi samtykke til registrering i Leddregisteret, samtykkeskjema skal lagres i pasientjournalen.

Kommentarer til de enkelte punktene

AKTUELLE OPERASJON

Kryss av enten i A eller B.I B må en krysse av for alle årsakene til reoperasjon, eller forklare dette med tekst på linjen.

REOPERASJONSTYPE

Fjerning av protesedeler (f.eks. Girdlestone opr.) må føres opp.

BENTRANSPLANTASJON

Benpropp som sementstopper regnes ikke som bentransplantat.

PROTESE. Acetabulum.

Her anføres kommersielle navn, materiale, størrelse og design, f.eks. Ceraver, Titan, 50 mm, skru. Eller f.eks. Charnley, large, OGEE, LPW.
Vær nøye med å anføre om protesen har belegg av f.eks. hydroksylapatitt. **Alternativt kan en benytte klistrelapp** som følger med de fleste protesene eller føre opp protesenavn og katalognr., .
Klistrelappen bør helst limes på baksiden av skjemaet (vennligst ikke plasser klistrelapper på markeringskryss, som brukes ved scanning av skjema).
Navnet på sementen må anføres, f.eks. Simplex Erythromycin/colistin.

PROTESE. Femur

Utfylles tilsvarende, f.eks. Charnley, flanged 40 og eventuelt anføres spesialutførelse som long neck, magnum, long stem, krage etc. **Alternativt kan en benytte klistrelapp** som følger med de fleste protesene eller føre opp protesenavn og katalognr (på baksiden av skjema). Sementnavn må anføres.

PROTESE. Caput

Ved separat caput (evt. også separat collum) må navn, materiale, diameter, halslengde og lateralisering anføres. F.eks. Ceraver, keramikk, 32 mm, standard neck.
Alternativt anføres bare protesenavn og katalognr., eller en benytter **klistrelapp** fra produsenten.

KOMPLIKASJONER

Dersom det foreligger komplikasjon i form av stor blødning, må mengden angis.
Vi ønsker også meldt pasienter som dør på operasjonsbordet eller rett etter operasjon.

ASA-KLASSE American Society of Anesthesiologists klassifikasjon

ASA-klasse 1: Friske pasienter som ikke røker

ASA-klasse 2: Pasienter som har asymptomatisk tilstand som behandles medikamentelt, som for eksempel hypertensjon eller med kost (diabetes mellitus type 2) og ellers friske pasienter som røker

ASA-klasse 3: Pasienter med tilstand som kan gi symptomer, men som holdes under kontroll medikamentelt for eksempel moderat angina pectoris og mild astma

ASA-klasse 4: Pasienter med tilstand som ikke er under kontroll, for eksempel hjertesvikt og astma

ASA-klasse 5: Moribund/døende pasient. Skal normalt ikke forekomme i vår pasientgruppe som er opererte pasienter

COMPUTERNAVIGERING (CAOS = Computer Aided Orthopaedic Surgery.**)**

Vi ber om å få angitt type computernavigeringsutstyr som CT-veiledet, rtg. gjennomlysningveiledet eller andre teknikker som bruk av hofteleddets sentrum.

MINIINVASIV KIRURGI (MIS = Minimally Invasive Surgery**)**

Her menes at kirurgen har brukt kort snitt pluss at det er brukt spesialinstrument laget for MIS

SYSTEMISK ANTIBIOTIKAPROFYLAKSE

Her føres det på hvilket antibiotikum som er blitt benyttet i forbindelse med operasjonen. Det anføres hvor stor dose, hvor mange doser og profylaksens varighet. Hvis en f.eks. kun har gitt 2g Keflin 4 ganger operasjonsdagen med 4 timers mellomrom dvs. 12 timer mellom første og siste dose, så angis det i skjema: Hvilken (A) Keflin Dose(A) 2g Totalt antall doser 4 Varighet 12 timer.

BEINTAP VED REVISJON

Femur (Paprosky`s klassifikasjon)

Type I: Minimalt tap av metafysært ben og intakt diafyse.
Type II: Stort tap av metafysært ben, men intakt diafyse.
Type IIIA: Betydelig tap av metafysært ben uten mulighet for proximal mekanisk støtte. Over 4 cm intakt corticalis i isthmusområdet.
Type IIIB: Betydelig tap av metafysært ben uten mulighet for proximal mekanisk støtte. Under 4 cm intakt corticalis i isthmusområdet.
Type IV: Betydelig tap av metafysært ben uten mulighet for proximal mekanisk støtte. Bred isthmus med liten mulighet for cortical støtte.

Acetabulum (Paprosky`s klassifikasjon)

Type I: Hemisfærisk acetabulum uten kantdefekter. Intakt bakre og fremre kolonne.
Defekter i forankringshull som ikke ødelegger den subchondrale benplate.
Type IIA: Hemisfærisk acetabulum uten store kantdefekter, intakt bakre og fremre kolonne, men med lite metafysært ben igjen.
Type IIB: Hemisfærisk acetabulum uten store kantdefekter, intakt bakre og fremre kolonne, men med lite metafysært ben igjen og noe manglende støtte superiort.
Type IIC: Hemisfærisk acetabulum uten store kantdefekter, intakt bakre og fremre kollonne, men med defekt i medial vegg.
Type IIIA: Betydelig komponentvandring, osteolyse og bentap. Bentap fra kl. 10 til 2.
Type IIIB: Betydelig komponentvandring, osteolyse og bentap. Bentap fra kl. 9 til 5.

Kopi beholdes til pasientjournalen, originalen sendes Haukeland universitetssjukehus.

Kontaktpersoner vedrørende registreringsskjema er
Overlege Leif Ivar Havelin, tlf.: 55 97 56 87 og klinikkoverlege Ove Furnes, tlf.: 55 97 56 80
Ortopedisk klinikk, Haukeland universitetssjukehus. Besøksadresse: Møllendalsbakken 11.
Sekretærer i Nasjonalt Register for Leddproteser, Ortopedisk klinikk, Helse Bergen:
Ingunn Vindenes, tlf.: 55 97 37 43 og Ruth Wasmuth, tlf.: 55 97 37 42 eller Sentralbordet, Haukeland universitetssjukehus: 55 97 50 00. Fax: 55 97 37 49.
Epost Ingunn Vindenes: ingunn.elin.vindenes@helse-bergen.no
Internet: http://www.haukeland.no/nrl/

App. V

NASJONALT HOFTEBRUDDREGISTER
Nasjonalt Register for Leddproteser
Helse Bergen HF, Ortopedisk klinikk
Haukeland universitetssjukehus
Møllendalsbakken 11
5021 BERGEN
Tlf: 55976452

F.nr. (11 sifre).....

Navn:.....

(Skriv tydelig ev. pasient klistrelapp – **spesifiser sykehus**.)

Sykehus:.....

HOFTEBRUDD

PRIMÆRE OPERASJONER PÅ BRUDD I PROKSIMALE FEMURENDE og ALLE REOPERASJONER, inkludert lukket reponering av hemiproteser. Ved primæroperasjon med totalprotese og ved reoperasjon til totalprotese brukes kun hofteproteseskjema. Alle produktklistrelapper settes i merket felt på baksiden av skjemaet.

AKTUELLE OPERASJON
☐1 Primæroperasjon ☐ 2 Reoperasjon

SIDE (ett kryss) (Bilateral opr.= 2 skjema)
☐1 Høyre ☐2 Venstre

OPR TIDSPUNKT (dd.mm.åå) |__|__| |__|__| |__|__| kl |__|__|

BRUDD TIDSPUNKT (dd.mm.åå) |__|__| |__|__| |__|__| kl |__|__|

Dersom det er usikkerhet om brudd tidspunkt, fyll ut neste punkt.

TID FRA BRUDD TIL OPERASJON I TIMER
☐1 0-6 ☐2 >6-12 ☐3 >12-24 ☐4 >24-48 ☐5 >48

DEMENS
☐0 Nei ☐1 Ja (Se test på baksiden) ☐2 Usikker

ASA-KLASSE (se bakside av skjema for definisjon)
☐1 Frisk
☐2 Asymptomatisk tilstand som gir økt risiko
☐3 Symptomatisk sykdom
☐4 Livstruende sykdom
☐5 Moribund

TYPE PRIMÆRBRUDD (ÅRSAK TIL PRIMÆROPERASJON) (Kun ett kryss)
Se baksiden for klassifikasjon
☐1 Lårhalsbrudd udislokert (Garden 1 og 2)
☐2 Lårhalsbrudd dislokert (Garden 3 og 4)
☐3 Lateralt lårhalsbrudd
☐4 Pertrokantært tofragment (AO klassifikasjon A1)
☐5 Pertrokantært flerfragment (AO klassifikasjon A2)
☐9 Intertrokantært (AO klassifikasjon A3)
☐6 Subtrokantært
☐7 Annet .....

TYPE PRIMÆROPERASJON (Kun ett kryss)
(Fylles ut bare ved primæroperasjon - eget skjema for totalproteser)
(Spesifiser nøyaktig produkt eller fest evt produktklistrelapp på baksiden)
☐1 To skruer eller pinner
☐2 Tre skruer eller pinner
☐3 Bipolar hemiprotese
☐4 Unipolar hemiprotese
☐5 Glideskrue og plate
☐6 Glideskrue og plate med trochantær støtteplate
☐7 Vinkelplate
☐8 Kort margnagle uten distal sperre
☐9 Kort margnagle med distal sperre
☐10 Lang margnagle uten distal sperre
☐11 Lang margnagle med distal sperre
☐12 Annet, spesifiser.....

Navn / størrelse ev. katalognummer.....

ÅRSAK TIL REOPERASJON (Flere enn ett kryss kan brukes)
☐1 Osteosyntesesvikt/havari
☐2 Ikke tilhelet brudd (non-union/pseudartrose)
☐3 Caputnekrose (segmentalt kollaps)
☐4 Lokal smerte pga prominerende osteosyntesemateriale
☐5 Brudd tilhelet med feilstilling
☐6 Sårinfeksjon – overfladisk
☐7 Sårinfeksjon – dyp
☐8 Hematom
☐9 Luksasjon av hemiprotese
☐10 Osteosyntesematerialet skåret gjennom caput
☐11 Nytt brudd rundt implantat
☐12 Løsning av hemiprotese
☐13 Annet, spesifiser.....

TYPE REOPERASJON (Flere enn ett kryss kan brukes)
(Spesifiser nøyaktig produkt eller fest evt produktklistrelapp på baksiden)
☐1 Fjerning av implantat (Brukes når dette er eneste prosedyre)
☐2 Girdlestone
(= fjerning av osteosyntesemateriale/hemiprot. og caputresten)
☐3 Bipolar hemiprotese
☐4 Unipolar hemiprotese
☐5 Re-osteosyntese
☐6 Drenasje av hematom eller infeksjon
☐7 Lukket reposisjon av luksert hemiprotese
☐8 Åpen reposisjon av luksert hemiprotese
☐9 Annet, spesifiser.....

Navn / størrelse ev. katalognummer.....

FIKSASJON AV HEMIPROTESE
(For totalprotese sendes eget skjema til hofteproteseregisteret)
☐1 Usementert
☐1 med HA ☐2 uten HA
☐2 Sement med antibiotika Navn.....

☐3 Sement uten antibiotika Navn.....

PATOLOGISK BRUDD (Annen patologi enn osteoporose)
☐0 Nei
☐1 Ja, type.....

TILGANG TIL HOFTELEDDET VED HEMIPROTESE (Kun ett kryss)
☐1 Anterolateral
☐2 Lateral
☐3 Posterolateral
☐4 Annet, spesifiser.....

ANESTESITYPE
☐1 Narkose ☐2 Spinal ☐3 Annet, spesifiser.....

PEROPERATIVE KOMPLIKASJONER
☐0 Nei
☐1 Ja, hvilke(n).....

OPERASJONSTID (hud til hud).....minutter.

SYSTEMISK ANTIBIOTIKAPROFYLAKSE
☐0 Nei ☐1 Ja, Hvilken (A).....

Dose (A).....Totalt antall doser.....Varighet .....timer

Ev. i kombinasjon med (B).....

Dose (B).....Totalt antall doser.....Varighet .....timer

TROMBOSEPROFYLAKSE
☐0 Nei ☐1 Ja, hvilken type.....

Dosering opr.dag.....Første dose gitt preopr ☐0 Nei ☐1 Ja

Senere dosering.....Antatt varighet.....døgn

Ev. i kombinasjon med .....

Dosering.....Antatt varighet.....døgn

Strømpe ☐0 Nei ☐1 Legg ☐2 Legg + Lår Antatt varighet .....døgn

Mekanisk pumpe ☐0 Nei ☐1 Fot ☐2 Legg Antatt varighet.....døgn

Lege.....
Legen som har fylt ut skjemaet (navnet registreres ikke i databasen).

RETTLEDNING

Registreringen gjelder alle operasjoner for hoftebrudd (lårhals, pertrokantære og subtrokantære) og alle reoperasjoner, også reposisjoner, på pasienter som er primæroperert og reoperert for hoftebrudd. **Ved primæroperasjon med totalprotese og ved reoperasjon til totalprotese sendes bare skjema til hofteproteseregisteret.**

Ett skjema fylles ut for hver operasjon. Originalen sendes Haukeland universitetssjukehus og kopien lagres i pasientens journal. Pasientens fødselsnummer (11 sifre) og sykehuset må være påført. Aktuelle ruter markeres med kryss. Pasienten skal på eget skjema gi samtykke til registrering i Nasjonalt hoftebruddregister og samtykkeerklæringen lagres i pasientens journal på sykehuset.

Kommentarer til enkelte punkt:

OPERASJONS- OG BRUDDTIDSPUNKT
Operasjonstidspunkt (dato og klokkeslett) må føres opp på alle primæroperasjoner. Det er også sterkt ønskelig at dato og klokkeslett for *bruddtidspunkt* føres opp. Dette bl.a for å se om tid til operasjon har effekt på prognose. (Hvis en ikke kjenner klokkeslettet for bruddtidspunkt lar en feltet stå åpent. En må da prøve å angi omtrentlig tidsrom fra brudd til operasjon på neste punkt).

Ved reoperasjon er ikke klokkeslett nødvendig.

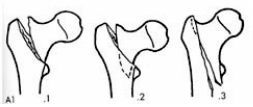
DEMENS
Demens kan eventuelt testes ved å be pasienten tegne klokken når den er 10 over 11. En dement pasient vil ha problemer med denne oppgaven.

ASA-KLASSE (ASA=American Society of Anesthesiologists)
ASA-klasse 1: Friske pasienter som røyker mindre enn 5 sigaretter daglig.
ASA-klasse 2: Pasienter med en asymptomatisk tilstand som behandles medikamentelt (f.eks hypertensjon)
eller med kost (f.eks diabetes mellitus type 2) og ellers friske pasienter som røyker 5 sigaretter eller mer daglig.
ASA-klasse 3: Pasienter med en tilstand som kan gi symptomer, men som holdes under kontroll medikamentelt
(f.eks moderat angina pectoris og mild astma).
ASA-klasse 4: Pasienter med en tilstand som ikke er under kontroll (f.eks hjertesvikt og astma).
ASA-klasse 5: Moribund/døende pasient

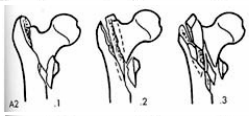
GARDENS KLASSIFISERING AV LÅRHALSBRUDD
Garden 1: Ikke komplett brudd av lårhalsen (såkalt innkilt)
Garden 2: Komplett lårhalsbrudd uten dislokasjon
Garden 3: Komplett lårhalsbrudd med delvis dislokasjon. Fragmentene er fortsatt i kontakt, men det er feilstilling av lårhalsens trabekler.
Caputfragmentet ligger uanatomisk i acetabulum.
Garden 4: Komplett lårhalsbrudd med full dislokasjon. Caputfragmentet er fritt og ligger korrekt i acetabulum slik at trabeklene er normalt orientert.

AO KLASSIFIKASJON AV TROKANTÆRE BRUDD

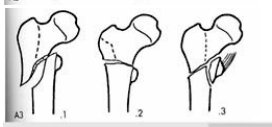
A1: Pertrokantært tofragment brudd



A2: Pertrokantært flerfragment brudd



A3: Intertrokantært brudd



Subtrokantære brudd: Hovedbruddlinje mellom nedre kant av trokanter minor og til 5 cm distalt for denne.

IMPLANTAT
Implantattype må angis entydig. Produktklistrelapp er ønskelig for å angi katalognummer for osteosyntesematerialet eller protesen som er brukt.

PEROPERATIVE KOMPLIKASJONER
Vi ønsker også å få meldt dødsfall på operasjonsbordet og peroperativ transfusjonstrengende blødning.

ANTIBIOTIKAPROFYLAKSE
Her føres det på hvilket antibiotikum som er blitt benyttet i forbindelse med operasjonen. Det anføres hvor stor dose, hvor mange doser og profylaksens varighet. Hvis en f.eks. har gitt 2g Keflin 4 ganger operasjonsdagen med 4 timers mellomrom dvs. 12 timer mellom første og siste dose, så angis det i skjema: Hvilken (A) *Keflin* Dose(A) *2g* Totalt antall doser *4* Varighet *12* timer.

Kontaktpersoner vedrørende registreringsskjema er:
Kst. Overlege Jan-Erik Gjertsen, Ortopedisk klinikk, Haukeland universitetssjukehus. Tlf. 55 97 56 72 (email: jan-erik.gjertsen@helse-bergen.no)
Professor Lasse Engesæter, Ortopedisk klinikk, Haukeland universitetssjukehus. Tlf. 55 97 56 84
Prosjektkoordinator Nasjonalt Hoftebrudddregister: Lise B. Kvamsdal. Tlf. 55 97 64 52 (email: lise.kvamsdal@helse-bergen.no)
Internett: http://www.haukeland.no/nrl/

PRODUKTKLISTRELAPPER:

App. VI

folkehelseinstituttet

Norsk overvåkingssystem for infeksjoner i sykehustjenesten (NOIS)

Mal for overvåkingsperioden f.o.m 1. sep t.o.m 30. nov 2009

NOIS-5

POSTOPERATIVE SÅRINFEKSJONER

Innhold

1 Endringer siden NOIS-4

NOIS-5 er en videreføring av NOIS-4. Det er gjort noen endringer og presiseringer i malen for NOIS-5, og de viktigste er:

1. Inngrep som skal overvåkes er blitt endret; utvalgte kolonkirurgiske inngrep er inkludert i overvåkingen og overvåking av appendektomi utgår.
2. Følgende nye variabler er inkludert som nasjonale (obligatoriske): ICD-10 koder og EuroSCORE
3. Blandete inngrep skal også overvåkes (se nedenfor)
4. Alle NOMESCO-koder registrert i forbindelse med overvåkingsinngrepet skal registreres og vil bli benyttet for å avgjøre om et inngrep er blandet.
5. Alle aortakoronare bypass-inngrep og kolecystektomier skal inkluderes i overvåkingen, også de blandete. Blandete inngrep vil bli behandlet spesielt i de statistiske analysene
6. Det vil fra januar 2010 være mulig å levere NOIS-data fra kontinuerlig (helårs) overvåking (jf Nasjonal strategi for å forebygge infeksjoner i helsetjenesten og antibiotikaresistens (2008-2012)). Avtaler om tidspunkt for levering av data må gjøres med Nasjonalt folkehelseinstitutt.

Følgende problemstillinger er under diskusjon i referansegruppen for NOIS og endringene vil sannsynligvis bli implementert fra NOIS-6. Vi ber sykehus om å gjøre de nødvendige grep for å kunne imøtekomme disse forandringene i sine systemer:

1. Nytten av ettårs oppfølging av hofteinngrep evalueres. Det er mulig at ettårs oppfølgingen blir frivillig.
2. Følgende variabler vil sannsynligvis bli nasjonale: Høyde og vekt (for å regne ut kroppsmasseindeks), og diabetes. Nytten av histologisvar diskuteres.
3. Variablen ”Antibiotikaprofylakse” vil redefineres.

2 Begrunnelse og bakgrunn

Postoperative sårinfeksjoner er en av de tre hyppigste helsetjenesteervervete infeksjoner og medfører økt sykelighet og dødelighet. Overvåking er et sentralt smitteverntiltak.

Med Forskrift om innsamling og behandling av helseopplysninger i Norsk overvåkingssystem for infeksjoner i sykehustjenesten (NOIS-registerforskriften) er det skapt hjemmel for innsamling av data fra sykehusenes overvåking av helsetjenesteervervete infeksjoner til et nasjonalt register. Protokollen er en nasjonal mal for prospektiv overvåking av postoperative sårinfeksjoner. Malen bygger på og er forenlig med den endelige protokollen fra det europeiske samarbeidsprosjektet for overvåking av infeksjoner ervervet i sykehus; Improving Patient Safety in Europe (IPSE).

Overvåkingssystemet innebærer at visse pasientgrupper følges opp under og etter oppholdet for å se om de utvikler en helsetjenesteervervet infeksjon. I henhold til NOIS-registerforskriften fastsetter Helsedirektoratet hva som skal inngå i overvåkingen.

Etter at overvåkingsperioden er avsluttet, sendes data fra alle deltakende sykehus til Folkehelseinstituttet for utarbeiding av statistikk. Data vil i første omgang inngå i en nasjonal database. Avidentifiserte data kan overføres til den europeiske databasen for å bidra til europeiske referanseverdier.

2.1 Formål

Formålet med NOIS er å forebygge infeksjoner gjennom en fortløpende og systematisk innsamling, analyse, tolkning og rapportering av opplysninger om forekomst av infeksjoner i virksomhetene og legge grunnlaget for å:

1. Beskrive forekomsten av infeksjoner i den enkelte virksomhet og nasjonalt, over tid og etter kjennetegn ved pasientene, aktuell behandling og virksomhetene
2. Gi råd til helsepersonell, virksomheter og forvaltning om smitteverntiltak
3. Evaluere virkninger av smitteverntiltak i virksomhetene
4. Oppdage og bidra til oppklaring av utbrudd av smittsomme sykdommer i virksomhetene
5. Bidra med nasjonale data til en europeisk database
6. Drive og fremme forskning om årsaker til, utbredelse og kostnader av infeksjoner i sykehus og dagkirurgiske klinikker, både på lokalt og nasjonalt nivå

Merk punkt 2, 3, og 4 som fokuserer spesielt på lokal, systematisk datapresentasjon for kirurger og kliniske avdelinger.

2.2 Deltaking

Alle sykehus som utfører en av de operasjoner som skal overvåkes (gitt ved utvalgte NOMESCO-koder) skal delta. I spesielle tilfeller kan det søkes om fritak.

2.3 Overvåkingsperiode

Helsedirektoratet har med hjemmel i NOIS-registerforskriften § 2-3 bestemt at overvåkingsperioden for NOIS-5 skal være fra og med 01.09.2009 til og med 30.11.2009 (oppfølgingstiden kommer i tillegg). Minimumskravet er overvåkingsdata fra tre hele kalendermåneder. Det enkelte sykehus anbefales imidlertid å ha kontinuerlig overvåking. Fra januar 2010 er det mulig å levere NOIS-data fra kontinuerlig (helårs) overvåking (jf Nasjonal strategi for å forebygge infeksjoner i helsetjenesten og antibiotikaresistens (2008-2012)). Avtaler om tidspunkt for levering av data må gjøres med Nasjonalt folkehelseinsitutt.

2.4 Inngrep som skal overvåkes

Hvilke NOMESCO-koder (jf også NCSP2008 ”NOMESCO Classification of Surgical Procedures” på www.kith.no) som skal overvåkes er fastsatt av Sosial- og helse-direktoratet. Sykehus som deltar i overvåkingen kan velge å følge opp en eller flere av operasjonene beskrevet i listen nedenfor. Alle sykehus som utfører prosedyren aortokoronar bypass skal overvåke dette inngrepet. Hvis sykehuset ikke utfører dette inngrepet, skal sykehuset velge neste inngrep på listen (basert på prioritet).

Tabell 1 – Operasjonskoder for overvåking

PRIORITET	*NOMESCO-KODE*	*INNGREP*
1	FNA, FNB, FNC, FNE	Aortokoronar bypass
2	MCA 10	Keisersnitt, nedre uterinsegment
3	NFB	Innsetting av proteser i hofteledd
4	JKA 20 JKA 21	Kolecystektomi
5.	JFB 20 - JFB 47 JFC 10 - JFC51	Kolonkirurgi: reseksjon av tarm og tarmanastomoser

Der kun hovedkoden i NOMESCO-systemet er gitt, skal alle underkoder til disse inngå i overvåkingen. For keisersnitt, kolecystektomi, og kolonkirurgi er det kun MCA 10, JKA 20 og 21, og JFB 20-47 og JFC 10-51 som overvåkes og ikke andre underkoder. Alle NOMESCO-koder registrert i forbindelse med overvåkingsinngrepet skal registreres og vil bli benyttet for å avgjøre om et inngrep er blandet. Blandete inngrep vil bli behandlet spesielt i de statistiske analysene.

2.5 Pasienter som skal overvåkes

Alle pasienter som gjennomgår det eller de inngrep som overvåkes ved sykehuset, skal inkluderes.

3 Definisjoner av nøkkelbegrep i overvåking av postoperative sårinfeksjoner

3.1 Diagnostisering og koding av postoperativ sårinfeksjon

Postoperative sårinfeksjoner diagnostiseres av leger i henhold til epidemiologiske kriterier utarbeidet av Centers for Disease Control and Prevention (CDC). (Vedlegg 3). Det er viktig at leger som er involvert i diagnosesetting kjenner de epidemiologiske kriterier og at disse kan avvike fra kliniske, diagnostiske kriterier. Leger skal diagnostisere postoperative sårinfeksjoner oppstått på sykehuset. Infeksjoner diagnostiseres i sykehuset ved direkte og jevnlig observasjon av kliniske tegn i og rundt operasjonssåret.

Pasienter oppfordres til, men kan ikke pålegges, å kontakte lege ved tegn på overflatiske postoperative sårinfeksjoner oppstått etter utskrivelse. Pasienters egenerklæring om puss (verk) fra såret godtas derfor som overflatisk postoperativ sårinfeksjon. For å sikre best mulig datakvalitet registreres overflatiske postoperative sårinfeksjoner diagnostisert etter utskrivelse av pasienten eller av legen hver for seg. Alle dype postoperative sårinfeksjoner og postoperative infeksjoner i indre organ eller hulrom skal bekreftes av lege

Det skal registreres om pasienten har:

- ingen infeksjon (IN)
- overflatisk postoperativ sårinfeksjon (diagnostisert av pasienten etter utskrivelse) (PS)
- overflatisk postoperativ sårinfeksjon (diagnostisert av lege) (SI)
- dyp postoperativ sårinfeksjon (må diagnostiseres av lege) (DI)
- postoperativ sårinfeksjon i organ eller hulrom (må diagnostiseres av lege) (OS)

I tillegg kan det kodes for infeksjonstype ”ikke aktuell” (IA). Denne koden brukes for eksempel dersom:

- pasienten fortsatt er inneliggende ved 30 dagers oppfølging (da vil pasienten ha IA som infeksjonsstatus ved utskrivelse)
- pasienten allerede har fått den mest alvorlige infeksjonen (OS) før utskrivelse (da er det ikke nødvendig å følge pasienten opp etter utskrivelse, og infeksjonstype ved 30 dager (1 år) vil være IA)
- Hvis pasienten dør før oppfølgingsperioden er fullført, vil infeksjonstype ved 30 dager (1 år) være IA.

Ukjent (UK) benyttes dersom man ikke vet pasientens infeksjonsstatus ved utskrivelse (noe som burde være sjeldent) eller det ikke har vært mulig å få informasjon om pasientens infeksjonsstatus ved 30 dagers oppfølging.

Ved aortokoronar bypass skal både infeksjoner i thoraxområdet og dets underliggende organer eller hulrom, og infeksjon i høstestedet registreres.

3.2 Nøkkelbegrep

3.2.1 Renhetsgrad

Kirurgen definerer renhetsgrad etter følgende kriterier:

1. **Rene sår** inkluderer ikke-infiserte operasjonssår uten tegn til betennelsesreaksjon, og hvor verken luftveier, gastrointestinal-, urogenitaltractus eller nese-svelgkaviteten er berørt. I tillegg er de lukket primært, og om nødvendig drenert med lukket drenasje. Operasjonssår etter inngrep pga. ikke-penetrerende (stumpe) traumer bør plasseres i denne kategorien.
2. **Rene-kontaminerte sår** inkluderer operasjonssår hvor luftveier, gastrointestinal- eller urogenitaltraktus er berørt under kontrollerte betingelser og uten uvanlig forurensing. Spesielt operasjoner i galleveier, appendix, vagina og svelg kan plasseres i denne kategori, dersom det ikke er tegn til infeksjon og det ikke har oppstått større svikt i teknikken.
3. **Kontaminerte sår** inkluderer åpne, friske, traumatiske sår; operasjoner med stor svikt i den aseptiske teknikk eller med mye søl fra mage-tarmtraktus og sår hvor det viser seg at man finner akutt ikke-purulent betennelsesreaksjon.
4. **Urene og infiserte sår** inkluderer gamle traumatiske sår med rester av devitalisert vev og alle sår med klinisk manifest infeksjon, eller perforerte innvoller. Denne definisjonen peker på at mikroorganismene som forårsaker den postoperative sårinfeksjonen, var til stede i operasjonsområdet før operasjonen.

Norsk oversettelse er hentet fra: *Nosokomiale infeksjoner. Retningslinjer for forebygging og kontroll av postoperative sårinfeksjoner. Tidsskr Nor Lægeforen 1985;105:41-46*, men korrigert i henhold til IPSEs protokoll.

3.2.2 Pasientens fysiske status (ASA-score)

Anestesilegen definerer ASA-score (American Society of Anesthesiology) på grunnlag av følgende kriterier:

1. **"Frisk pasient"**
   Ingen organisk, fysiologisk, biokjemisk eller psykiatrisk forstyrrelse. Aktuelle lidelse er lokalisert og gir ikke generelle systemforstyrrelser. Røker mindre enn 5 sigaretter per dag. Alder under 80 år.
   Eksempel: Frisk 50 åring, ikke-røyker, til variceoperasjon.
2. **Moderat organisk lidelse eller forstyrrelse som ikke forårsaker funksjonelle begrensninger,**
   men som kan medføre spesielle forholdsregler eller anestesitekniske tiltak. Lidelsen(e) kan enten være forårsaket av den aktuelle sykdom pasienten skal opereres for, eller annen patologisk prosess. Alder over 80 år og nyfødte under 3 mnd. Røyker mer enn 5 sigaretter per dag.
   Eksempel: Lett organisk hjertesykdom. Ukomplisert diabetes (type 1 og 2). Benign ukomplisert hypertensjon. Frisk 20-åring med kjeveleddsperre.
3. **Alvorlig organisk sykdom eller forstyrrelse som gir definerte funksjonelle begrensninger.**
   Eksempler: Diabetes med organkomplikasjoner. Invalidiserende hjertesykdom.

Moderat til alvorlig lungesykdom. Angina pectoris. Gjennomgått hjerteinfarkt (over seks måneder siden).

4. **Livstruende organisk sykdom**
   som ikke behøver å være relatert til den aktuelle kirurgiske lidelse eller - som ikke alltid bedres ved det kirurgiske inngrep.
   Eksempler: Malign hypertensjon. Nylig (mindre enn seks måneder) gjennomgått hjerteinfarkt. Sterkt fremskreden lever, nyre, lunge eller endokrin dysfunksjon. Manifest hjertesvikt. Ustabil angina pectoris. Subaraknoidalblødning, våken - somnolent pasient.
5. **Moribund pasient**
   som ikke forventes å overleve 24 timer uten kirurgi.
   Eksempler: Pasient med aortaaneurisme i sjokk. Dypt komatøs pasient med intrakraniell blødning.

Vedlegg til *Standard for anestesi i Norge 1995-96 etter American Society of Anaesthesiologists*.

3.2.3 Operasjonsvarighet

Defineres ut fra differansen mellom tidspunkt for operasjonsstart og operasjonsstopp (knivtid).

3.2.4 Pre- og perioperativ antibiotikaprofylakse

Pre- og perioperativ systemisk administrasjon er definert som antibiotika gitt ved første snitt i hud eller innen to timer før operasjonen, med det formål å hindre infeksjon i operasjonsområdet. Ved keisersnitt gis antibiotikaprofylakse etter kutting av navlestreng. Antibiotika som ikke gis etter denne definisjonen skal ikke regnes som antibiotikaprofylakse.

3.2.5 Elektiv operasjon

Operasjonen er elektiv dersom den var planlagt minst 24 timer før selve inngrepet.

3.2.6 Reoperasjon

Med reoperasjon forstås at det er mindre enn 30 dager (ett år ved innsetting av fremmedlegeme) mellom et tidligere inngrep og overvåkingsinngrepet i samme operasjonsområde. Dersom pasienten gjennomgår to inngrep med *mer* enn 30 dagers mellomrom (ett år ved innsetting av fremmedlegeme), regnes dette som to *uavhengige* inngrep. Fremmedlegeme forstås i denne sammenhengen som hofteprotese. For flere av de ulike inngrepene vil det komme fram i NOMESCO-koden om det aktuelle inngrepet er en reoperasjon. Det er likevel valgt å spesifisere dette som egen variabel.

Reoperasjon er et begrep som brukes ved tre forskjellige variabler i NOIS: 25, 26 og 41. Variabel 25 og 26 forholder seg til status *før* det inngrepet vi overvåker, mens variabel 41 (og 40 reinnlagt på grunn av infeksjon) viser til status *etter* inngrepet vi overvåker. Se også kapittel 6 Beskrivelse av variablene.

Variabel 25 og 26 – er overvåkingsinngrepet en reoperasjon?

Disse variablene skal reflektere risiko ved inngrepet som overvåkes. Vi ønsker å se om tidligere inngrep (siste 30 dager, ett år ved innsetting av fremmedlegeme) i samme område er assosiert med høyere risiko for sårinfeksjon.

Variabel 25: Overvåkningsinngrepet er en reoperasjon på grunn av infeksjon. Denne variabelen kartlegger om pasienten har vært operert i samme område de siste 30 dager (ett år ved innsetting av fremmedlegeme) *før* det inngrepet vi overvåker, og har den tidligere operasjonen ført til sårinfeksjon? Med andre ord, er overvåkingsinngrepet en reoperasjon på grunn av infeksjon?

Variabel 26: Overvåkingsinngrepet er en reoperasjon av annen årsak enn infeksjon. Denne variabelen kartlegger om pasienten har vært operert i samme område de siste 30 dager *før* det inngrepet vi overvåker, og har den tidligere operasjonen ført til andre komplikasjoner enn infeksjon? Er overvåkingsinngrepet en reoperasjon av annen årsak enn infeksjon?

Variabel 41 (40) – har overvåkingsinngrepet ført til en infeksjon som gjorde at pasienten måtte reopereres (eller reinnlegges)?

Hvis overvåkingsinngrepet fører til en infeksjon som gjør at pasienten på nytt må opereres eller reinnlegges, registreres det i disse variablene. Om en reoperasjon eller reinnleggelse er forbundet med den aktuelle postoperative sårinfeksjon avgjøres av en lege.

4 Overvåkingsprosedyre

Prosedyren har til hensikt å sikre mest mulig lik framgangsmåte, slik at det oppnås data som er sammenliknbare mellom sykehus (også internasjonalt).

4.1 Organisering

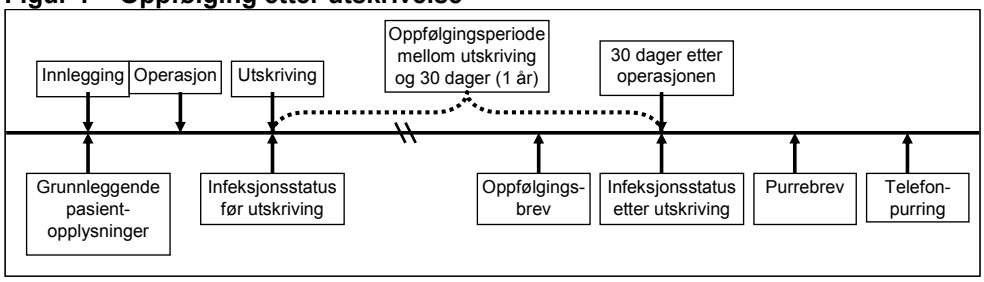
Ledelsen ved det enkelte helseforetak eller sykehus er ansvarlig for overvåkingen.

Ansvaret for å diagnostisere postoperative sårinfeksjoner i sykehus ligger hos den enkelte kirurg (jf 3.1), mens smittevernpersonell bør være ansvarlig for kvalitets-kontroll. Det anbefales at det oppnevnes en lege med ansvar for opplæring og rådgiving for å sikre at identifisering av infeksjoner skjer i henhold til definisjonene (jf Vedlegg 3).

4.2 Oppfølging av pasienter

Sykehuset må etablere en rutine for å overvåke postoperative sårinfeksjoner som oppstår etter utskrivelse. Det skal være et system for å fange opp reinnleggelser så vel som reoperasjoner. Sykehuset hvor pasienten er operert er ansvarlig for registrering av data og oppfølging etter utskrivelse. Dette gjelder også i tilfeller hvor pasienten overføres til annen institusjon (se også pkt 5.1.3 Identifisering av postoperative sårinfeksjoner under sykehusoppholdet og 5.1.4 Identifisering av postoperative sårinfeksjoner etter utskrivelse).

Figur 1 – Oppfølging etter utskrivelse



Målsettingen er å registrere de alvorligste infeksjonene, merk derfor spesielt punktene nedenfor:

- Pasienter som utvikler en overflatisk eller dyp infeksjon før oppfølgingstiden er omme, skal likevel følges opp i 30 dager (ett år), for å se om de utvikler en mer alvorlig infeksjon før oppfølgingstidens slutt.
- Hvis en pasient dør eller utvikler den alvorligste infeksjonstypen (infeksjon i organ eller hulrom) før oppfølgingstiden er omme, vil dødsdato eller infeksjonsdato regnes som siste oppfølgingsdato og oppfølgingen vil bli regnet som fullstendig.
- Hvis en pasient ved registreringstidspunktet har hatt flere typer postoperative sårinfeksjoner, registreres den alvorligste infeksjonstypen.
- Merk at det er infeksjoner som har oppstått *innen* 30 dager (ett år) som skal registreres. Hvis registreringen skjer etter disse tidspunktene må det

sannsynliggjøres at det er infeksjonsstatus innen 30 dager (ett år) postoperativt som registreres. Infeksjoner som oppstår *etter* at 30 dager (ett år ved implantatkirurgi) har forløpt, skal ikke tas med.

- Hvis sårinfeksjonen var overflatisk i løpet av perioden før utskrivelse og utviklet seg til dyp i løpet av neste oppfølgingsperiode (innen 30 dager etter operasjonen), registreres dette som overflatisk infeksjon ved utskrivelse og dyp ved 30 dager. Ved utregning av samlet insidens vil dette bare telle som én infeksjon.
- Hvis en infeksjon utvikler seg fra overflatisk til dyp innen samme registreringstidsrom (for eksempel etter utskrivelse men innen 30 dager), registreres kun den alvorligste typen (dyp).

4.2.1 Oppfølging av pasienter etter utskrivelse fra sykehuset

For alle inngrep følges pasienten opp i 30 dager etter inngrepet. Det registreres hvorvidt pasienten har hatt infeksjon i perioden

- etter inngrepet, men innen utskriving og
- etter utskriving, men innen 30 dager etter operasjonen

For inngrep hvor fremmedlegeme settes inn (ved innsetting av hofteproteser), følges pasienten opp i ett år etter inngrepet. Da registreres det i tillegg hvorvidt pasienten har hatt infeksjon i perioden

- etter 30 dager men innen ett år etter operasjonen

Oppfølgingsbrev sendes pasienten, med mindre pasienten fortsatt er innlagt, kontrolleres poliklinisk ved oppfølgingstidspunktet eller er død. Brevet skal følge malen (Vedlegg 1). Brevet bør være på ett ark (tosidig). Brevet sendes hjem til pasienten ca 3 1/2 uke (25 dager) etter operasjonen. I brevet presiseres det at endelig utfylling av infeksjonsstatus og retur av skjema ikke skal skje før 30 dager (ett år) postoperativt. Brev som er besvart etter denne tid kan inkluderes, så lenge vurderingen av operasjonsområdet er basert på status ved 30 dager (ett år).

Purring skjer ved utsendelse av et nytt brev ca 5 uker etter operasjonen. Hvis oppfølging ikke oppnås ved hjelp av purrebrevet, må pasientene stilles de samme spørsmålene over telefon.

Man bør ha rutiner for å unngå å sende brev til personer som dør i oppfølgingstiden.

Oppfølgingsbrevet er oversatt til flere språk. Disse kan lastes ned fra Folkehelseinstituttets hjemmesider (www.fhi.no).

Vurdering av innkomne pasientbrev

For at infeksjonen skal regnes som pasientdiagnostisert (PS), må pasienten ha svart ”Ja” på det første spørsmålet på pasientbrevet: *Har det kommet gulgrønn sårvæske (puss) fra operasjonssåret?* De andre spørsmålene er laget for å gjøre pasienten oppmerksom på en eventuell infeksjon, og oppfordre pasienten til å oppsøke lege hvis dette oppstår.

4.2.2 Siste oppfølgingsdato

Siste oppfølgingsdato er den siste datoen hvor det ble foretatt en evaluering av infeksjonsstatus. Dette er den dato som sist fremkommer av:

- utskrivingsdato
- dato pasienten/legen svarte på brev/telefon
- dato for poliklinisk kontroll
- dato for død (se nedenfor)
- datoen pasienten utviklet organ/hulrom infeksjon

Den reelle dato for siste kontakt skal registreres selv om denne er mer enn 30 dager (ett år) etter inngrepet. Det viktige er at *vurderingen av infeksjonsstatus* er innen 30 dager etter operasjonen.

Data fra pasienter som følges opp i mindre enn 30 dager (ett år), inkluderes i den nasjonale datasamlingen, men data merkes som ufullstendige. Disse pasientene vil bli fanget opp i systemet ved at siste oppfølgingsdag er før 30 dager (ett år ved implantatkirurgi), uten at de har utviklet den alvorligste infeksjonstypen (infeksjon i organ/hulrom eller død).

5 Kvalitetskrav og validering av data

5.1 Metoder for å sikre datakvaliteten

Den utpekte koordinatoren ved sykehuset er faglig ansvarlig for innsamling og kvalitetssikring av data, samt overføring av data til Folkehelseinstituttet (jf 5.3 Rapportering til Folkehelseinstituttet).

Ved oversendelse av data vedlegges et overføringsbrev hvor det bekreftes at metoden for registrering og kvalitetssikring av data er fulgt (jf Vedlegg 2 Overføringsbrev).

5.1.1 80 % oppfølging

Det stilles kvalitetskrav til datasett i den nasjonale databasen. I tillegg til at metoden for datasamling beskrevet i denne malen benyttes, vil det kreves at minst 80 % av de opererte innen en type inngrep er fulgt opp i 30 dager (ett år) etter operasjonen. Dette gjøres for å unngå seleksjonsskjevhet. Sykehus som ikke tilfredsstiller disse kravene, for eksempel de som har lavere oppfølgingsandel enn 80 % på et enkelt inngrep, skal sende inn sine data, men disse vil bli behandlet spesielt. De vil ikke inngå i alle resultater, med mindre analyser tilsier at seleksjonsskjevhet ikke er fremtredende.

5.1.2 Identifisering av opererte

For å sikre at alle operative inngrep inngår i insidensovervåkingen skal den endelige oversikten over gjennomførte operasjoner brukes som utgangspunkt for å identifisere opererte pasienter.

5.1.3 Identifisering av postoperative sårinfeksjoner under sykehusoppholdet

Postoperative sårinfeksjoner registrert før utskrivelsen skal:

- diagnostiseres av lege ved direkte observasjon av operasjonsområdet og
- klassifiseres i henhold til CDC-kriteriene (Vedlegg 3).

I tillegg bør smittevernpersonell sjekke at det er samsvar mellom registrerte data og minst én av de følgende datakildene:

- pasientens journal
- medikamentkurve
- laboratoriesvar
- røntgenbeskrivelser

Det kan også være aktuelt å konsultere behandlende lege ved eventuelle uklarheter.

5.1.4 Identifisering av postoperative sårinfeksjoner etter utskrivelse

Alle dype postoperative sårinfeksjoner og postoperative infeksjoner i organ eller hulrom skal bekreftes av lege.

5.1.5 Logiske kontroller av data

Følgende **skal** sjekkes før og etter overføring av data internt i sykehuset og fra sykehuset til Folkehelseinstituttet:

- at data er fullstendig og korrekt utfylt (alle felter merket med N er fylt ut jf kap 6).
- at data er konsistente (for eksempel at keisersnitt bare er utført på kvinner).
- at ekstreme verdier er riktige (for eksempel at uventet lang eller kort operasjonstid er korrekt) og
- at riktig dataformat benyttes

Det anbefales at sykehusets datasystem har funksjoner som sjekker for logiske brister, ukjente og ekstreme verdier, feilstaving og lignende. En oversikt over hvilke logiske kontroller som bør utføres på dataene før overføring finnes på Folkehelseinstituttets Internettsider.

5.2 Overvåkingsdatabase

Det enkelte sykehuset/foretaket er ansvarlig for etablering og drift av database til bruk for innsamling av data internt på institusjonen. Disse dataene omfattes av journalforskriften. Foretaksledelsen har ansvar for at data blir levert til Nasjonalt folkehelseinstitutt.

5.3 Rapportering til Folkehelseinstituttet

Rapportering til Folkehelseinstituttet på individnivå er nødvendig for å kunne nå målene med overvåkingssystemet, både nasjonalt og i europeisk sammenheng. Ved endt overvåkingsperiode skal sykehuset sende overvåkingsdata på individnivå samlet til Folkehelseinstituttet.

Tidsfrist for innlevering av data vil kunngjøres av FHI via e-post og instituttets internettsider.

Data kan sendes som diskett eller CD-ROM, eller det kan sendes på e-post i en kryptert fil (WinZip) til NOIS@fhi.no. Standardisert format brukes (jf kap 6 Beskrivelse av variablene). Det enkelte sykehus er ansvarlig for validering av data og at data sendes på et format som er forenlig med databasen ved Folkehelseinstituttet. Oversendelsesformat (CSV, XML, XLS) og flere detaljer og oppdaterte opplysninger finnes på Folkehelseinstituttets Internettsider www.fhi.no.

5.4 Konfidensialitet

5.4.1 Avidentifisering

Det er ikke mulig å identifisere enkeltpasienter i Folkehelseinstituttets database. Overvåkingsdata sendes avidentifisert, det vil si kodet, slik at ansvarlige i sykehuset kan spore data tilbake til enkeltpasienter ved hjelp av et løpenummer.

5.4.2 Dataoppbevaring (nasjonalt) og juridiske forhold

Folkehelseinstituttet har ansvar for å oppbevare nasjonale data på en sikker måte.

NOIS-registerforskriften gir Folkehelseinstituttet rett til å samle inn og oppbevare data nasjonalt.

Flere regioner har valgt felles dataløsninger for alle helseforetakene i regionen. Dersom data skal sammenstilles regionalt, kan dette utløse krav om konsesjon fra Datatilsynet. Det er imidlertid anledning til å gjøre anonyme uttrekk uten konsesjonsbehandling forutsatt at en følger personvernlovgivningen.

5.5 Publisering av data

Data vil bli brukt til å generere årlige rapporter om forekomst av postoperative sårinfeksjoner som vil bli lagt ut på Internett. Data fra NOIS vil etter nærmere bestemmelser i forskriften også kunne utgis til bruk i forskning med publisering av vitenskapelige artikler. Det enkelte helseforetak kan fritt publisere sine egne resultater.

5.5.1 Presentasjon av data fra Folkehelseinstituttet

Hver institusjon som sender inn data vil få en oversikt over sin infeksjonsforekomst sammenliknet med et nasjonalt gjennomsnitt. Det tas sikte på at tilbakemelding skjer så raskt som mulig etter hver overvåkingsperiode. Nasjonale data vil også presenteres på Folkehelseinstituttets hjemmesider.

6 Beskrivelse av variablene

De variabler som er merket med N, må inngå i de data som overføres til Folkehelseinstituttet. En pasientregistrering med ukjente verdier skal oversendes til Folkehelseinstituttet, men den vil bli behandlet spesielt i analysen. Vi oppfordrer alle til å unngå å oppgi "ukjent", eller å la felter være tomme.
Variablene er klassifisert som på nasjonalt nivå eller på sykehusnivå:

N = Nasjonal
S = Sykehus (lokal)

6.1 Pasientdata

Type	Var nr	Variabler	Kapittel	Variabeltype	Format	Ukjent verdi	Kommentar
N	0	Helseforetak		Tall	### ### ###	Ikke mulig	Helseforetakets organisasjonsnummer (fra Enhetsregistereret i Brønnøysund, oversikt finnes på www.fhi.no og www.brreg.no)
N	1	Sykehus		Tall	### ### ###	Ikke mulig	Sykehusets gamle enhetsnummer (samme nummeret som i NOIS 1 og 2, oversikt finnes på www.fhi.no)
		Pasientdata					
S	2	Fødselsdato			dd.mm.åååå		For identifikasjon av pasient internt i sykehuset brukes fødselsnummer. For data som overføres til Folkehelseinstituttet, brukes pasientidentitet (se under).
N	3	Pasientidentitet		Tall (løpenummer)	#####	Ikke mulig	Avidentifisert løpenummer. Dette unike nummeret gjør det mulig å tilbakespore pasientopplysninger i sykehusene for kvalitetssikring, mens pasientens identitet forblir ukjent utenfor institusjonen.
N	4	Kjønn		Bokstav	M/K/U	U=ukjent	Opplysninger om kjønn framkommer av tredje siffer i personnummeret, oddetall = mann, partall = kvinne.
N	5	Alder		Tall	###	999	Antall fylte år på operasjonsdagen. Spedbarn er 0 år før ettårsdagen.

6.2 Operasjonsvariabler

Operasjon forstås her som ett operativt inngrep som faller inn under de utvalgte NOMESCO-koder.

Type	Var nr	Variabler	Kapittel	Variabeltype	Format	Ukjent verdi	Kommentar
		Operasjonsvariabler					
N	6	Innleggelsesdato		Dato	dd.mm.åååå	Blank	Datoen pasienten ble innlagt på sykehuset hvor operasjonen gjennomføres.
N	7	Operasjonskoder	2.4	NOMESCO-koder	AAA##	Ikke mulig	Her registreres NOMESCO-koden som inkluderer pasienten i overvåkingen, og alle de andre NOMESCO-kodene registrert under dette inngrepet. MERK at det er viktig å inkludere de to sifrene som følger etter bokstavkoden.
N	8	Endoskopisk		Ja/Nei/ukjent	Y/N/U	U= ukjent	Dersom hele inngrepet foretas endoskopisk eller lapraskopisk.
N	9	Operasjonsdato		Dato	dd.mm.åååå	Ikke mulig	Dato pasienten ble operert. Hvis operasjonen passerer midnatt, oppgi dato for operasjonsstart.
S	10	Operasjonsstart	3.2.3	Klokkeslett	tt/mm		Klokkeslettet for første snitt i hud. Denne variabelen må registreres lokalt for å utregne operasjonsvarighet (jf variabel 16).
S	11	Operasjonsstopp	3.2.3	Klokkeslett	tt/mm		Klokkeslettet for avslutning av lukking av hud. Denne variabelen må registreres lokalt for å utregne operasjonsvarighet (jf variabel 16)
N	12	Utskrivningsdato		Dato	dd.mm.åååå	Blank	Datoen pasienten utskrives fra helseforetaket hvor operasjonen ble utført.
N	13	Siste oppfølgingsdato	4.2.2	Dato	dd.mm.åååå	Blank	Dato hvor infeksjonsstatus sist ble evaluert
S	14	Operatør		Tallkode	###		Kode for operatør(er).

6.3 Risikovariabler

Med risikovariabler menes faktorer som antas å øke risikoen for postoperativ infeksjon.

Type	Var nr	Variabler	Kapittel	Variabeltype	Format	Ukjent verdi	
		Risikovariabler					
N	15	Sårkontaminasjon	3.2.1	Tall (1–4)	#	9=ukjent	
N	16	Operasjonsvarighet	3.2.3	Minutter	###	999= ukjent	Fra første snitt i hud til avslutning av lukking (knivtid)
N	17	ASA klassifikasjon	3.2.2	Tall (1–5)	#	9=ukjent	
S	18	Risikopoeng	Vedlegg 4	Tall (-1–3)	#	9=ukjent	Beregnes nasjonalt, sykehus kan benytte egen utregning
N	19	Perioperativ antibiotikaprofylakse	3.2.4	Ja/Nei/Ukjent	Y/N/U	U= ukjent	
S	20a-c	Antibiotikatype		ATC-kode	A##A A##		Hvilke(t) antibiotika er gitt profylaktisk (inntil tre typer)
N	21	Elektiv operasjon	3.2.5	Ja/Nei/Ukjent	Y/N/U	U= ukjent	Planlagt minst 24 timer før selve inngrepet
S	22	Narkose		Ja/Nei	Y/N		Ble det gitt narkose under inngrepet
N	23	ICD-10 kode		ICD-10 kode	Tall og bokstaver, maks 5 tegn	U= ukjent	Her inkluderes alle ICD-10 koder som er blitt registrert under aktuelt opphold. Oppdatert kodeverk finnes på www.kith.no under publikasjoner.
N	24	EuroSCORE	Vedlegg 6	Tall	##	99	Se definisjon i Vedlegg 6
N	25	Overvåkingsinngrepet er en reoperasjon på grunn av infeksjon	3.2.6	Ja/Nei/Ukjent	Y/N/U	U= ukjent	Hvis aktuelt inngrep utføres for å diagnostisere eller behandle infeksjon etter tidligere inngrep (NB! forklaring i avsnitt 3.2.6)
N	26	Overvåkingsinngrepet er en reoperasjon av annen årsak enn infeksjon	3.2.6	Blødning (B), mekaniske (M), annet (A), ukjent (U), ikke aktuelt (I)	B/M/A/U/I	U= ukjent	Årsak til reoperasjon når årsak ikke er infeksjon. Eventuell annen årsak til reoperasjon kan være blødning, mekaniske misforhold eller annet (jf variabel 25).

Type	Var nr	Variabler	Kapittel	Variabeltype	Format	Ukjent verdi	
S	27	Antall prosedyrer siste 30 dager		Tall	##		Antall kirurgiske prosedyrer foretatt siste 30 dager før aktuelt inngrep (antall NOMESCO-koder, alle typer inngrep).

6.4 Utfallsvariabler

Type	Var nr	Variabler	Kapittel	Variabeltype	Format	Ukjent verdi	
		Utfallsvariabler					
S	28	Infeksjon (utskrivelse)		Ja/Nei	Y/N	Ikke mulig	Utgått som nasjonal variabel
N	29	Infeksjonsdato (utskrivelse)	4.2	Dato	dd.mm.åååå	Blank	Benytt den dato som første fremkommer av dato for første kliniske tegn eller dato for mikrobiologisk prøvetaking til den aktuelle postoperative sårinfeksjon.
N	30	Infeksjonstype (utskrivelse)	3.1	IN/SI/DI/OS/IA/UK*	AA	Ikke mulig	Infeksjonstyper diagnostiseres i henhold til CDC-kriterier
S	31	Infeksjon (30 dager)		Ja/Nei/	Y/N	Ikke mulig	Utgått som nasjonal variabel
N	32	Infeksjonsdato (30 dager)	4.2	Dato	dd.mm.åååå	Blank	Jf variabel 29
N	33	Infeksjonstype (30 dager)	3.1	IN/PS/SI/DI/OS/IA/ UK*	AA	Ikke mulig	Infeksjonstyper diagnostiseres i henhold til CDC-kriterier
S	34	Infeksjon (1 år)		Ja/Nei	Y/N	Ikke mulig	Utgått som nasjonal variabel
N	35	Infeksjonsdato (1 år)	4.2	Dato	dd.mm.åååå	Blank	Jf variabel 29
N	36	Infeksjonstype (1 år)	3.1	IN/PS/SI/DI/OS/IA/ UK*	AA	Blank hvis ikke hofte inngrep, UK hvis hofteinngrep	Infeksjonstyper diagnostiseres i henhold til CDC-kriterier
S	37-39	Mikrobiologisk funn 1		WHO-care-kode	AAAAAA		Angir hvilke funn som ble gjort ved prøvetaking fra operasjonssåret. Inntil tre mikrober kan oppgis. (jf www.fhi.no/she)

* IN= ingen infeksjon, PS= overflatisk postoperativ sårinfeksjon (diagnostisert av pasienten), SI= overflatisk postoperativ sårinfeksjon (diagnostisert av lege), DI= Dyp postoperativ sårinfeksjon, OS= postoperativ sårinfeksjon i organ eller hulrom, IA=ikke aktuell, UK= ukjent *(se forklaring s 4)*

Type	Var nr	Variabler	Kapittel	Variabeltype	Format	Ukjent verdi	
N	40	Reinnlagt pga infeksjon	3.2.6	Ja/Nei	Y/N/U	U=ukjent	Ja hvis det vurderes at pasienten ble reinnlagt i sykehus som følge av sin postoperative sårinfeksjon.
N	41	Reoperert pga infeksjon	3.2.6	Ja/Nei	Y/N/U	U=ukjent	Ja hvis det vurderes at pasienten ble reoperert som følge av sin postoperative sårinfeksjon.
S	42	Antibiotika		Ja/Nei	Y/N		Kryss av hvis det vurderes at pasienten fikk systemisk antibiotika som følge av sin postoperative sårinfeksjon. Om antibiotika er gitt for den aktuelle postoperative sårinfeksjon avgjøres av en lege.
N	43	Dato hvis død		Dato	dd.mm.åååå		Hvis pasienten dør under oppfølgingstiden (30 dager (ett år) postoperativt), oppgis dato for dødsfall.
S	44	Død assosiert med infeksjon		Ja/Nei	Y/N/U	U= ukjent	Kryss av hvis det vurderes at pasienten døde som følge av sin postoperative sårinfeksjon. Om pasientens død er forbundet med den aktuelle postoperative sårinfeksjon avgjøres av en lege.
N	45	Infeksjonsdato høstested	3.2.6	Dato	dd.mm.åååå	Blank= ikke aktuell	Gjelder kun ved aortokoronar bypass. Samme definisjoner benyttes som ved andre infeksjoner (jf variabel 29)
N	46	Infeksjonstype høstested	3.2.6	IN/PS/SI/DI/OS/IA/ UK*	AA	UK= ukjent	Gjelder kun ved aortokoronar bypass. Samme definisjoner og koder benyttes som ved andre infeksjoner (jf variabel 30)

* IN= ingen infeksjon, PS= overflatisk postoperativ sårinfeksjon (diagnostisert av pasienten), SI= overflatisk postoperativ sårinfeksjon (diagnostisert av lege), DI= Dyp postoperativ sårinfeksjon, OS= postoperativ sårinfeksjon i organ eller hulrom, IA=ikke aktuell, UK= ukjent *(se forklaring s 4)*

6.5 Frivillige variabler (pilot)

Type	Var nr	Variabler	Kapittel	Variabeltype	Format	Ukjent verdi	Kommentar
S	48	Høyde		Tall	###	blank	Høyde i cm
S	49	Vekt		Tall	###	blank	Vekt i kilo. Ved keisersnitt: siste vekt målt i graviditeten
S	51	Diabetes		N, D1, D2, UK	xx	UK=ukjent	Nei, Diabetes1 (D1), Diabetes2 (D2), ukjent.

Vedlegg 1 Brev til pasient

Tilpasses lokalt. Brev som sendes ved ettårs oppfølging må modifiseres (bytt ut 30 dager med ett år). Ved aortokoronare bypassoperasjoner må det også føres opp spørsmål om infeksjon er i thoraxområdet eller i høstestedet. Dette forslaget til oppfølgingsbrev er basert på et brev som er utviklet av Helse Vest. På FHIs hjemmesider finnes pasientbrev oversatt til andre språk.

========= ==========

Fornavn Etternavn
Gateadresse
Postnr Poststed

Deres ref.: Vår ref.: Dato:

Har du hatt infeksjon i operasjonssåret?

[Region/sykehus] undersøker rutinemessig hvor mange pasienter som får infeksjon i operasjonssåret etter utskrivelse/behandling ved våre sykehus. I den forbindelse henvender vi oss til deg, da du ble operert [operasjonsdato] på [Navn på sykehus]. Vi er svært takknemlig hvis du svarer på følgende spørsmål når det har gått 30 dager etter operasjonen. Skjemaet returneres i den vedlagte konvolutten, også om du ikke har hatt tegn til infeksjon.

Har det kommet gulgrønn sårvæske (puss) fra operasjonssåret?	☐ Ja	☐ Nei
Har det vært unormal rødme rundt operasjonssåret (mer enn ½ cm på hver side)?	☐ Ja	☐ Nei
Har lege åpnet såret på grunn av infeksjon?	☐ Ja	☐ Nei
Har du fått antibiotika på grunn av betennelse i såret?	☐ Ja	☐ Nei
Har du hatt feber (mer enn 38,5 grader) på grunn av betennelse i operasjonssåret?	☐ Ja	☐ Nei
Dato for når du evt. oppdaget infeksjonstegn:	_____	

Dato/underskrift _____ -- _____

Har du svart "ja" på ett av spørsmålene, tyder det på at du har hatt en infeksjon i såret. Vi ber deg da om å ta kontakt med din lege og medbringe dette brevet. Legen skal fylle ut spørsmålene på side 2 før du sender brevet tilbake til oss i den vedlagte konvolutten. Opplysningene blir behandlet konfidensielt.

Har du spørsmål om denne henvendelsen kan du kontakte [tittel] [kontaktperson] på telefon [telefonnummer1] / [telefonnummer2].

Vennlig hilsen

[Hygienesykepleier/seksjon for sykehushygiene]
Avdelingsleder

VEND

Side 2 ***Utfylles av lege***

Pasienten har/har hatt en overflatisk postoperativ sårinfeksjon		☐ Ja	☐ Nei
Pasienten har/har hatt en dyp postoperativ sårinfeksjon		☐ Ja	☐ Nei
Pasienten har/har hatt en postoperativ sårinfeksjon i underliggende organ/hulrom		☐ Ja	☐ Nei
Infeksjon ble oppdaget (dato)			
Bakteriologisk prøve:		☐ Ikke tatt	☐ Ingen vekst
Vekst av:		Dato for prøvetaking:	

Evt. klinisk vurdering:

Underskrift, dato og stempel

Kriterier for postoperative infeksjoner- utarbeidet av Centers for Disease Control and Prevention (CDC)

Overflatisk postoperativ sårinfeksjon:
Infeksjon som oppstår på insisjonsstedet innen 30 dager etter operasjonen og som bare involverer hud og subkutant vev og der minst ett av følgende symptomer eller funn finnes:

- Purulent sekresjon fra såret.
- Isolering av patogen mikroorganisme i prøve tatt fra såret med aseptisk teknikk.
- Når kirurg åpner såret på grunn av minst ett av de følgende symptomer eller tegn på infeksjon:
  - smerte eller ømhet
  - lokalisert hevelse, rødme eller varme
  og dyrkning av innholdet viser oppvekst av mikroorganismer
- Lege har stilt diagnosen overflatisk sårinfeksjon.

Overflatisk postoperativ sårinfeksjon. Diagnose av pasienten:
Hvis pasienten i egenerklæringen krysser av ja på at det var puss (verk) fra såret, regnes dette som en overflatisk postoperativ sårinfeksjon.

Dyp postoperativ sårinfeksjon
Infeksjon som oppstår innen 30 dager etter operasjoner uten innsetting av fremmedlegemer, eller inntil ett år etter operasjoner der det blir satt inn et fremmedlegeme, når infeksjonen synes å ha sammenheng med inngrepet og involverer dypt bløtvev omkring insisjonen (fascie og muskellag).

En dyp sårinfeksjon må tilfredsstille minst ett av følgende kriterier:

- Purulent sekresjon fra såret, uten at det er påvist infeksjon i dypereliggende organer eller kroppshulrom.
- Spontan ruptur som involverer sårets dypere lag (fascie eller muskulatur), eller nødvendig kirurgisk åpning av såret
  og dyrkning av innholdet viser oppvekst av mikroorganismer
  og pasienten har minst ett av følgende symptomer eller funn:
  - feber (>38ºC)
  - lokalisert smerte eller ømhet
- Klinisk undersøkelse, reoperasjon, ultralydundersøkelse, radiologisk eller histopatologisk undersøkelse viser en abscess eller andre tegn på infeksjon som involverer sårets dypere lag (fascie eller muskulatur).
- Lege har stilt diagnosen dyp sårinfeksjon.

Postoperativ infeksjon i indre organ eller hulrom
Postoperative infeksjoner utenom hud, fascie og muskulatur defineres som infeksjon i indre organ eller hulrom dersom organet eller hulrommet har vært åpnet eller manipulert under operasjonen. Infeksjonen regnes som postoperativ når den oppstår innen 30 dager etter operasjoner uten innsetting av fremmedlegemer, eller inntil ett år etter operasjoner der det blir satt inn et fremmedlegeme, når infeksjonen synes å ha sammenheng med inngrepet.

En infeksjon i organ eller hulrom må tilfredsstille minst ett av følgende kriterier:

- Purulent drenasje fra dren lagt inn gjennom et separat innstikksted.
- Isolasjon av mikroorganisme i en prøve tatt med aseptisk teknikk fra det aktuelle organ eller hulrom.
- Klinisk undersøkelse, reoperasjon, ultralyd, radiologisk eller histopatologisk undersøkelse viser en abscess eller andre tegn på infeksjon som involverer organet.
- Lege har stilt diagnosen infeksjon i indre organ eller hulrom.

Den norske oversettelsen er i all hovedsak hentet fra: Definisjon og klassifikasjon av sykehusinfeksjoner. IK-2556. Oslo: Statens helsetilsyn, 1996.

Vedlegg 2 Overføringsbrev til Folkehelseinstituttet

Vedlagt denne forsendelsen er en cd/ diskett eller data er sendt elektronisk med overvåkingsdata fra ……..... (sykehus)

Filen inneholder data om …….. (antall) operasjoner.

Det var ..…….. (antall) personer som gjennomgikk NOMESCO kode ……

Av disse ble ……..(antall) fulgt opp i 30 dager (ett år ved implantatkirurgi).

Det var ……..…….. (antall) personer som gjennomgikk NOMESCO kode ……

Av disse ble ……..(antall) fulgt opp i 30 dager (ett år ved implantatkirurgi).

Det var ……..…….. (antall) personer som gjennomgikk NOMESCO kode ……

Av disse ble ……..(antall) fulgt opp i 30 dager (ett år ved implantatkirurgi).

Det var ……..…….. (antall) personer som gjennomgikk NOMESCO kode ……

Av disse ble ……..(antall) fulgt opp i 30 dager (ett år ved implantatkirurgi).

Vi bekrefter at data er innsamlet i henhold til metoden beskrevet i den nasjonale malen. De kvalitetskrav beskrevet i malen er fulgt.

Hilsen

……..…

Telefonnummer:……..……

E-post adresse:……..

Vedlegg 3 Kriterier for postoperative sårinfeksjoner - utarbeidet av Centers for Disease Control and Prevention (CDC)

Dersom en pasient har en overflatisk postoperativ sårinfeksjon, godtas egenrapportering fra pasienten etter utskrivelse (ulik kode gis til infeksjon diagnostisert av pasienter og lege).

Dersom pasienten har en dyp postoperativ sårinfeksjon eller en postoperativ infeksjon i indre organ eller hulrom, kreves det at diagnosen stilles av en lege.

Overflatisk postoperativ sårinfeksjon:
Infeksjon som oppstår på insisjonsstedet innen 30 dager etter operasjonen og som bare involverer hud og subkutant vev og der minst ett av følgende symptomer eller funn finnes:

- Purulent sekresjon fra såret.
- Isolering av patogen mikroorganisme i prøve tatt fra såret med aseptisk teknikk.
- Når kirurg åpner såret på grunn av minst ett av de følgende symptomer eller tegn på infeksjon:
  - smerte eller ømhet
  - lokalisert hevelse, rødme eller varme
  og dyrkning av innholdet viser oppvekst av mikroorganismer
- Lege har stilt diagnosen overflatisk sårinfeksjon.

Registrering:
Følgende klassifiserer ikke som overflatisk sårinfeksjon:

- Suturabscess (minimal inflammasjon og sekresjon fra det punktet der suturen går gjennom huden).
- Sårinfeksjon som involverer fascie eller muskulatur.
- Lokalisert overflatisk infeksjon i stikk-kanal etter diagnostiske eller terapeutiske prosedyrer (f.eks. benmargpunksjon, pleuratapping, leddpunksjon).
- Infisert brannsår.

Overflatisk postoperativ sårinfeksjon. Diagnose av pasienten:
Hvis pasienten i egenerklæringen krysser av ja på at det var puss (verk) fra såret, regnes dette som en overflatisk postoperativ sårinfeksjon.

Dyp postoperativ sårinfeksjon
Infeksjon som oppstår innen 30 dager etter operasjoner uten innsetting av fremmedlegemer, eller inntil ett år etter operasjoner der det blir satt inn et fremmedlegeme, når infeksjonen synes å ha sammenheng med inngrepet og involverer dypt bløtvev omkring insisjonen (fascie og muskellag).

En dyp sårinfeksjon må tilfredsstille minst ett av følgende kriterier:

- Purulent sekresjon fra såret, uten at det er påvist infeksjon i dypereliggende organer eller kroppshulrom.
- Spontan ruptur som involverer sårets dypere lag (fascie eller muskulatur), eller nødvendig kirurgisk åpning av såret
  og dyrkning av innholdet viser oppvekst av mikroorganismer
  og pasienten har minst ett av følgende symptomer eller funn:

- feber (>38ºC)
- lokalisert smerte eller ømhet

- Klinisk undersøkelse, reoperasjon, ultralydundersøkelse, radiologisk eller histopatologisk undersøkelse viser en abscess eller andre tegn på infeksjon som involverer sårets dypere lag (fascie eller muskulatur).
- Lege har stilt diagnosen dyp sårinfeksjon.

Registrering:
- Infeksjoner som involverer både overflatisk og dypt vev skal registreres som dyp sårinfeksjon.
- Lokalisert dyp infeksjon i stikk-kanal etter diagnostiske eller terapeutiske prosedyrer (f.eks. benmargspunksjon, pleuratapping, leddpunksjon), regnes som infeksjon i bløtvev, ikke som dyp postoperativ sårinfeksjon.

Postoperativ infeksjon i indre organ eller hulrom
Postoperative infeksjoner utenom hud, fascie og muskulatur defineres som infeksjon i indre organ eller hulrom dersom organet eller hulrommet har vært åpnet eller manipulert under operasjonen. Infeksjonen regnes som postoperativ når den oppstår innen 30 dager etter operasjoner uten innsetting av fremmedlegemer, eller inntil ett år etter operasjoner der det blir satt inn et fremmedlegeme, når infeksjonen synes å ha sammenheng med inngrepet.

En infeksjon i organ eller hulrom må tilfredsstille minst ett av følgende kriterier:
- Purulent drenasje fra dren lagt inn gjennom et separat innstikksted.
- Isolasjon av mikroorganisme i en prøve tatt med aseptisk teknikk fra det aktuelle organ eller hulrom.
- Klinisk undersøkelse, reoperasjon, ultralyd, radiologisk eller histopatologisk undersøkelse viser en abscess eller andre tegn på infeksjon som involverer organet.
- Lege har stilt diagnosen infeksjon i indre organ eller hulrom.

Registrering:
Postoperativ infeksjon i organ/hulrom registreres for 24 ulike lokalisasjoner, som er listet opp nedenfor. Definisjonen for hver enkelt av disse er den samme som gjelder for den tilsvarende ikke-postoperative infeksjon (definisjonene finnes på www.fhi.no) . Et eksempel er appendectomi med påfølgende subdiafragmatisk abscess, som skal registreres som en organ/hulrom infeksjon.

Den norske oversettelsen er i all hovedsak hentet fra: Definisjon og klassifikasjon av sykehusinfeksjoner. IK-2556. Oslo: Statens helsetilsyn, 1996.

Eksempler på organ-hulrom infeksjoner fra CDC.

Andre infeksjoner i urinveiene	Øyeinfeksjon utenom konjunctiva
Andre infeksjoner i nedre luftveier	Øreinfeksjon
Osteomyelitt	Munnhuleinfeksjon
Ledd- eller bursainfeksjon	Sinusitt
Infeksjon i intervertebralskive	Øvre luftveisinfeksjon
Intrakranial infeksjon	Infeksjon i magetarmkanalen
Meningitt eller ventrikulitt	Andre intraabdominale infeksjoner
Spinalabscess uten meningitt	Endometritt
Infeksjon i arterie eller vene	Perivaginal infeksjon
Endokarditt	Andre inf. i kvinnelige genitalia
Myokarditt eller perikarditt	Infeksjon i mannlige genitalia
Mediastinitt	Brystabscess eller mastitt

Vedlegg 4 Utregning av risikopoeng

Risikopoeng for alle overvåkede inngrep vil beregnes automatisk i Folkehelseinstituttets datasystem. Dette behøver derfor ikke institusjonene å beregne selv for innsendelse. Vi anbefaler likevel at institusjonene beregner risikopoeng til eget bruk, da det er svært nyttig å kunne risikostratifisere egne inngrep. Metoden som brukes for utregning er beskrevet her.

Risikoindeksen er utarbeidet som et system for å stratifisere pasienter i henhold til utvalgte faktorer som antas å øke risikoen for postoperativ sårinfeksjon. Risikostratifisering medvirker til forbedring i sammenlikningsgrunnlaget av insidens mellom ulike sykehus og land. Metoden som benyttes er en risikoindeks fra USA (NNIS).

Variablene ASA-klassifikasjon, operasjonsvarighet, renhetsgrad av sårene og om prosedyren var gjennomført endoskopisk (gitt ved NOMESCO-koden), inngår i risikoindeksen. Antallet risikopoeng regnes ut etter følgende tabell:

75-persentilen normert for varighet av den gjennomførte operasjonen benyttes for å beregne risikopoeng.

75-persentiler for varighet av overvåkingsinngrepene

Type inngrep	*NOMESCO gruppe*	*75-persentil (minutter)*
Aortokoronar bypass	FNA	240
	FNB	240
	FNC	240
	FNE	240
Appendektomi	JEA	60
Kolecystektomi	JKA 20 og 21	120
Keisersnitt	MCA 10	60
Hofteprotese primær	NFB	120

Risikoindeksen og risikopoeng for variablene

STRATIFISERINGSVARIABEL	*RISIKOINDEKS*	*RISIKOPOENG*
ASA score	> 2	1
Operasjonstid	> 75 persentilen	1
Renhetsgrad av operasjonssår	Renhetsgrad > 2	1
Endoskopisk prosedyre*		-1

* Det gis ett minuspoeng ved kolecystektomi og colonoperasjoner foretatt med endoskopi. Ved appendektomi og ventrikkeloperasjoner gis det ett minuspoeng bare hvis pasienten i utgangspunktet er i risikoklasse 0.

Antall risikopoeng summeres. Dermed kan fem risikonivåer defineres: -1, 0, 1, 2 eller 3.

Vedlegg 5 Kortversjon av mal

- Ledelsen ved det enkelte helseforetak eller sykehus er ansvarlig for overvåkingen.
- Alle utførte operasjoner i angitt tidsperiode og innenfor de NOMESCO- som sykehuset eller helseforetaket har valgt å overvåke, skal inkluderes.
- Alle pasienter som gjennomgår en operasjon med gjeldende NOMESCO-koder inkluderes og følges opp 30 dager (ett år ved implantatkirurgi) etter operasjonen.
- Følgende variabler fylles ut for alle inkluderte pasienter: Pasientidentitet, kjønn, alder, innleggelsesdato, antibiotikaprofylakse, NOMESCO- kode, operasjonsdato, akutt eller elektivt inngrep, reoperasjon, sårkontaminasjon, operasjonsvarighet (knivtid), ASA klassifikasjon, utskrivningsdato, siste oppfølgingsdato og evt. dato hvis død (for definisjon av variablene se kapittel 6).
- Infeksjonsstatus og eventuelt infeksjonstype registreres ved utskrivelse fra sykehuset/helseforetaket og 30 dager postoperativt (ett år ved implantatkirurgi)
- Postoperative sårinfeksjoner diagnostiseres i henhold til de epidemiologiske kriterier utarbeidet av CDC (se Vedlegg 3) av leger ved direkte observasjon. Etter utskrivelse godtar vi pasient diagnostisert overflatisk postoperativ sårinfeksjon.
- Smittevernpersonell bør sjekke for samsvar mellom registreringsdata og minst en av de følgende datakilder: Pasientens journal, antibiotikaforskrivningsrapporter, laboratoriesvar, røntgenbeskrivelse eller behandlende lege.
- Alle pasienter som ikke er innlagt eller er kontrollert poliklinisk 30 dager (ett år) etter operasjonen, skal returnere en egenerklæring (pasientbrev). Purring skjer ved purrebrev og evt. telefonhenvendelse.

Vedlegg 6 EuroSCORE

Pasientrelaterte faktorer				**Poengforklaring (tekst)**							
<60 år	0	60-64 år	1	65-69 år	2	70-74 år	3	75-79 år	4		
80-84 år	5	85-89 år	6	90-94 år	7						

Alle over 60 år får poeng for alder

Kjønn Kvinne	1	: Menn får 0 poeng for kjønn
KOLS	1	: Behandlet med broncholytica og/eller steroider
Perifer karsykdom	2	: Claudicatio, carotisstenose, utført eller planlagt karkirurgi eller røntgen intervensjon
Nevrologisk sykdom/sekvele	2	: Alvorlig bevegelseshemming, affiserer ADL funksjon
Nyresvikt	2	: Serum kreatinin > 200 mmol/l
Endocarditt, akutt	3	: Under medikamentell behandling
REDO	3	: Tidligere hjerteoperasjon hvor pericard er åpnet
Klinisk instabilitet	3	: Sirkulatorisk instabilitet (dvs VT, preoperativ hjertemassasje, resusitert pasient), intubert preoperativt, preoperativ inotopi, ABP, preoperativ akutt nyresvikt (<10ml/time)

Kardiale faktorer

Ustabil angina pectoris	2	: Pågående nitrater iv under anestesi-innledning
EF, moderat redusert	1	: EF 30-50%
EF, redusert betydelig	3	: EF < 30%
Hjerteinfarkt, nylig	2	: < 90 dager
Pulmonal hypertensjon	2	: PAP > 60 mmHg

Operative faktorer

Øhj operasjon	2	: Start innen begynnelsen av 1ste virkedag
Tillegg til ACB operasjon	2	: Alle større hjertekirurgiske prosedyrer forskjellig fra eller i tillegg til ACB operasjon
Kirugi av aorta thoracalis	3	: Ascendens, bue og descendens
Postinfarkt VSR	4	: Ventrikkel septum ruptur

Sum EuroSCORE poeng: _____

Kilde: European System for Cardiac Operative Risk Evaluation, oversatt av Ullevål universitetssykehus

App. VII

Description of the NARA-data file

(changed by Anne Marie on November 4th 2011)

Primary prosthesis = the first total hip prosthesis. Thus, insertion of cup, and insertion of cup and a new stem, in a hip previously operated with hemi prosthesis, is defined as a primary prosthesis.
Revision is here defined as replacement or removal of any component.
The three variables at the end (RevCause, DateRev and SurgProc) reflect first revision for a patient on a given laterality (left or right).

Variables included:

Variable	Position	Label	Measurement Level	Print Format	Write Format
Nation	1	Country	Nominal	F1	F1
PatID	2	Patient's unique serial number	Nominal	F8	F8
Age	3	Age at primary THR	Scale	F3	F3
Gender	4	Gender	Nominal	F1	F1
Laterality	5	Operated side	Nominal	F1	F1
DiaCode	6	Diagnosis code	Nominal	F2	F2
DatePri	7	Date of primary THR	Scale	SDATE10	SDATE10
HosCode	8	Hospital code (country-specific)	Nominal	F6	F6
FixType	9	Type of fixation	Nominal	F1	F1
Cup	10	Cup component (country-specific)	Nominal	F4	F4
Stem	11	Stem component (country-specific)	Nominal	F4	F4
TrocOst	12	Trochanteric osteotomy used?	Nominal	F1	F1
PostApp	13	Posterior approach used?	Nominal	F1	F1
HaCup	14	Hydroxyapatatite coating?	Nominal	F1	F1
HaStem	15	Hydroxyapatatite coating?	Nominal	F1	F1
CemCup	16	Type of bone cement cup component (country-specific)	Nominal	F4	F4
CemStem	17	Type of bone cement stem component (country-specific)	Nominal	F4	F4
DateDis	18	Date of death	Scale	SDATE10	SDATE10
RevCause	19	Cause of revision	Nominal	F1	F1
DateRev	20	Date of revision	Scale	SDATE10	SDATE10
SurgProc	21	Surgical procedure at revision	Nominal	F1	F1

The variables with country-specific encoding should not contain any SPSS value labels since the values probably will collide between countries, which would lead to misleading labels on some values.

HaCup and **HaStem** are included to give information if the components have a hydroxyapatatite coating or not.

CemCup and **CemStem** will contain the country-specific codes for bone cement. If the register does not have separate variables for bone cement in cup and stem, the two variables will be identical.

DiaCode: Split the DiaCode variable to include Rheumatoid arthritis and Ankylosing spondylitis in two separate labels of the variable. Split the Childhood diseases in three; DDH, slipped capital femoral epiphysis and Perthes disease.

SurgProc: Søren will make a suggestion for this. We want to include reoperation without change or removal of part(s).

Encoding of variables in the NARA data file:

Value	Label	
Nation	1	Denmark
	2	Norway
	3	Sweden
	4	Finland
Gender	1	Male
	2	Female
Laterality	1	Right
	2	Left
DiaCode	1	Primary osteoarthrosis
	3	Hip fracture
	5	Nontraumatic femoral head necrosis
	6	Rheumatoid arthritis
	7	Ankylosing spondylitis
	8	Other inflammatory
	9	Others
	10	DDH
	11	Slipped capital femoral epiphysis
	12	Perthes disease
	13	Combination of Slipped capital femoral epiphysis and Perthes
FixType	1	Cemented, both components
	2	Uncemented, both components
	3	Hybrid (Cemented stem, uncemented cup)
	4	Inverse hybrid (Uncemented stem, cemented cup)
	5	Resurfacing (uncemented cup, cemented caput)
TrocOst	0	No
	1	Yes
PostApp	0	No (anterior, anterolateral, and others)
	1	Yes (posterior approach)
HaCup	0	No Hydroxyapatatite coating
	1	With Hydroxyapatatite coating
HaStem	0	No Hydroxyapatatite coating
	1	With Hydroxyapatatite coating
RevCause	1	Aseptic loosening (W*ear and Osteolysis included)*
	2	Deep infection
	3	Periprosthetic femoral fracture
	5	Dislocation

	7	Pain only
	9	Others
SurgProc	1	Both cup and stem replaced
	2	Only stem replaced
	3	Only cup or liner replaced
	4	Extraction of the total prosthesis (Girdlestone), permanent or temporary
	9	Others (such as exchange of caput)

Paper I

Increasing risk of revision due to deep infection after hip arthroplasty

A study on 97,344 primary total hip replacements in the Norwegian Arthroplasty Register from 1987 to 2007

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Background and purpose **Over the decades, improvements in surgery and perioperative routines have reduced the incidence of deep infections after total hip arthroplasty (THA). There is, however, some evidence to suggest that the incidence of infection is increasing again. We assessed the risk of revision due to deep infection for primary THAs reported to the Norwegian Arthroplasty Register (NAR) over the period 1987–2007.**

Method **We included all primary cemented and uncemented THAs reported to the NAR from September 15, 1987 to January 1, 2008 and performed adjusted Cox regression analyses with the first revision due to deep infection as endpoint. Changes in revision rate as a function of the year of operation were investigated.**

Results **Of the 97,344 primary THAs that met the inclusion criteria, 614 THAs had been revised due to deep infection (5-year survival 99.46%). Risk of revision due to deep infection increased throughout the period studied. Compared to the THAs implanted in 1987–1992, the risk of revision due to infection was 1.3 times higher (95%CI: 1.0–1.7) for those implanted in 1993–1997, 1.5 times (95% CI: 1.2–2.0) for those implanted in 1998–2002, and 3.0 times (95% CI: 2.2–4.0) for those implanted in 2003–2007. The most pronounced increase in risk of being revised due to deep infection was for the subgroup of uncemented THAs from 2003–2007, which had an increase of 5 times (95% CI: 2.6–11) compared to uncemented THAs from 1987–1992.**

Interpretation **The incidence of deep infection after THA increased during the period 1987–2007. Concomitant changes in confounding factors, however, complicate the interpretation of the results.**

Improvements in surgical technique, perioperative routines, and prophylactic measures have reduced the incidence of infection from 5–10% in the late 1960s (Charnley 1972) to around 1% (Gaine et al. 2000, Zimmerli and Ochsner 2003, Phillips et al. 2006). There is, however, some evidence to suggest that the incidence of infection is increasing (Kurtz et al. 2008). Few publications have addressed time trends concerning postoperative infections after THAs, and large numbers of primary THAs are required to show changes in risk of infection. We assessed whether there have been any changes in risk of revision due to deep infection for THAs reported to the Norwegian Arthroplasty Register over the last 2 decades.

Patients and methods

Since its inception on September 15, 1987, the Norwegian Arthroplasty Register (NAR) has registered detailed data on primary THAs and THA revisions in Norway. The data gathered include information on patient identity, date of operation, indication for surgery, type of implant, method of fixation, duration of surgery, type of operating room ventilation, and the type of antibiotic prophylaxis used. The unique identification number of each inhabitant of Norway is used to link the primary THA to any revision (Havelin et al. 2000). Revision due to deep infection of the implant is defined as removal or exchange of the whole or parts of the prosthesis, with deep infection reported as the diagnosis. Isolated soft tissue revisions are not reported to the register. The register form is filled in by the surgeon immediately after surgery.

The period of inclusion and observation in this study was from the start of the NAR on September 15, 1987 to January 1, 2008. For this time period, the NAR contained data on 110,882 primary THAs. In order to have homogeneous subgroups concerning type of fixation, 4,392 hybrids and 3,727 reversed hybrids were excluded. 3,730 arthroplasties had incomplete data on fixation method or were registered with

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different brands of cement for different components, and were also excluded. 1,689 additional THAs were excluded because of missing values for other adjustment variables. There were 97,344 THAs with complete information where both components were either cemented or uncemented, and these were eligible for analysis.

All THAs were followed until their first revision due to deep infection or revision for other causes, until date of death or emigration of the patient, or until January 1, 2008. Thus, follow-up was 0–20 years. 4 time periods were compared: 1987–1992, 1993–1997, 1998–2002, and 2003–2007, with subanalyses on cemented and uncemented THAs.

As a control, we performed a subanalysis on Charnley prostheses fixed with antibiotic-loaded bone cement and given antibiotic prophylaxis systemically. This prosthesis was the most used in Norway from 1987 to 2008, and it was used extensively throughout the whole period of observation.

Statistics

Survival analyses were performed with a Cox regression model, with time period as main risk factor and revision due to deep infection as the endpoint. Revision rate ratios (RRs) for the time periods are presented with 95% confidence interval (CI) and p-values relative to the first time period. We adjusted for differences over time concerning sex, age (< 40, 40–59, 60–69, 70–79, ≥ 80 years), diagnosis (osteoarthritis, inflammatory disease, other), monoblock or modular prosthesis, type of fixation (uncemented, cemented with cement containing or not containing antibiotics), antibiotic prophylaxis systemically (yes, no), type of operation room ventilation (ordinary, laminar flow, greenhouse), and duration of surgery (< 70, 70–99, 100–129, or≥ 130 min). Cox regression analyses with time period as stratification factor were used to construct cumulative revision curves (1 minus cumulative survival) at mean values of the covariates, and to assess 5-year survival percentages. We also performed a separate Cox analysis with revision due to aseptic loosening as endpoint for all THAs, in order to be able to compare these findings with our findings for revision due to deep infection. Furthermore, to ensure similar potential follow-up for operations in all time periods, additional analyses were performed with follow-up restricted to 0–5 years.

We also investigated changes in the revision rate due to deep infection as a function of year of operation. These analyses gave a graphical display of the relationship based on a generalized additive model for survival data (Hastie and Tibshirani 1990). The curves are presented with 95% CI.

Risk ratio analyses were performed for the different risk factors and prophylactic measures for each time period separately, and for the whole 20-year period adjusted for year of primary surgery.

Values of p less than 0.05 were considered statistically significant. We used SPSS software version 15.0.

Table 1. Primary THAs included over the four 5-year time periods

Variable	1987–1992	1993–1997	1998–2002	2003–2007
No. of THAs	20,913	22,519	26,230	27,682
Sex (%)				
Male	30	30	29	31
Female	70	70	71	69
Age (%)				
< 40	2	2	2	1
40–59	15	14	15	14
60–69	31	27	26	26
70–79	41	43	41	39
≥ 80	12	14	17	19
Diagnosis (%)				
Osteoarthritis	67	70	73	77
Inflammatory	4	4	4	3
Other	29	26	23	20
Prosthesis (%)				
Monoblock	58	53	38	22
Modular	42	47	62	78
Duration (min) of surgery (%)				
< 70	11	10	11	15
70–99	41	45	45	45
100–129	31	31	31	29
≥ 130	18	15	13	12
Operation room ventilation (%)				
"Greenhouse"	12	2	1	1
Laminar flow	29	45	53	56
Ordinary	59	53	46	44
Antibiotic prophylaxis systemically (%)				
No	8	0	0	0
Yes	92	100	100	100
Method of fixation (%)				
Uncemented	15	15	14	16
Cement				
with antibiotics	38	56	82	83
without antibiotics	48	29	4	2

Results

97,344 primary THAs in 79,820 patients met the inclusion criteria for this study. 614 first revisions due to deep infection were reported in 610 patients. The 5-year survival was 99.46% with revision due to deep infection as endpoint.

The distribution of patient characteristics such as sex, age, and diagnosis of patients undergoing primary THA was stable throughout the period studied (Table 1), except for the group of primary uncemented THAs, where mean age increased from 52 (SD 12) in 1987–1992 to 61 (SD 13) in 2003–2007. There was a shift from monoblock towards modular THAs (Table 1). Duration of surgery decreased slightly, whereas the use of an operating room with laminar air flow increased through the 4 time periods (Table 1). Antibiotic-loaded bone cement was used more extensively, and cement containing antibiotics was used in most cemented THAs towards the end of the study period (Table 1). Except during the first time period, prophylactic antibiotics were administered systemically in almost all operations (Table 1).

Table 2. Risk ratios and 5-year survival estimates for revision due to deep infection. The risk ratios and survival estimates are adjusted for sex, age, diagnosis, prosthesis, operation room ventilation, duration of operation, and antibiotic prophylaxis

Prosthesis	Time period	No. of THAs included	No. of THAs revised due to infection	Risk ratio	p-value	95% CI	5-year survival
All THAs	1987–1992	20,913	134	1			99.7
	1993–1997	22,519	156	1.3	0.03	1.0–1.7	99.6
	1998–2002	26,230	150	1.5	0.003	1.2–2.0	99.5
	2003–2007	27,682	174	3.0	< 0.001	2.2–4.0	99.1
Cemented THAs	1987–1992	17,867	119	1			99.7
	1993–1997	19,191	133	1.3	0.04	1.0–1.7	99.5
	1998–2002	22,558	129	1.5	0.008	1.1–2.1	99.5
	2003–2007	23,380	136	2.7	< 0.001	1.9–3.7	99.2
Uncemented THAs	1987–1992	3,046	15	1			99.8
	1993–1997	3,328	23	1.2	0.6	0.6–2.4	99.8
	1998–2002	3,672	21	1.4	0.3	0.7–2.9	99.6
	2003–2007	4,302	38	5.3	< 0.001	2.6–10.7	98.9
Charnley with antibiotics in the cement and systemically	1987–1992	4,321	26	1			99.7
	1993–1997	7,776	46	1.1	0.6	0.7–1.9	99.6
	1998–2002	9,301	44	1.1	0.9	0.6–1.8	99.6
	2003–2007	5,925	37	2.0	0.02	1.1–3.5	99.3

Time trend: deep infection

For all primary THAs, we found an increase in the risk of revision due to deep infection, compared to the time period 1987–1992, for all 3 of the other consecutive time periods. The risk of revision due to infection was 1.3 times higher for 1993–1997, 1.5 times higher for 1998–2002, and 3.0 times higher for 2003–2007, respectively (Table 2, Figure 1). The risk of infection increased throughout the whole period of observation (Figure 2).

In the cemented group of primary THAs, with revision due to deep infection as endpoint, we found the same pattern of gradual increase in revision risk over time (Table 2, Figures 1 and 2). This was also found in the subgroup of Charnley prostheses fixed with antibiotic-loaded bone cement and given antibiotic prophylaxis systemically (Table 2).

Uncemented THAs had a 5.3 times higher risk of being revised due to deep infection in the last time period compared to 1987–1992 (Table 2, Figure 1). The 5-year survival (98.94%) was also inferior to that of the cemented group (99.20%) for this period (difference = 0.26%, CI: 0.22–0.30, $p < 0.001$). The increase in risk of revision due to deep infection was most pronounced after the year 2000 for uncemented THAs (Figure 2).

We had 0–20 years of follow-up in our study, but maximum follow-up varied for THAs in the different time periods. To determine whether this would have influenced the results, analyses were performed including only 0–5 year follow-up for each group. This did not change the findings.

Time trend: aseptic loosening

There were 4,437 primary THAs revised due to aseptic loosening in the entire period studied. The percentage revised due to aseptic loosening decreased significantly throughout the period (Figure 3). Relative to the time period 1987–1992, the risk of revision due to aseptic loosening was 0.4 times (CI: 0.3–0.4) for the time period 1998–2002 ($p < 0.001$) and 0.3 times (CI: 0.3–0.4) for 2003–2007 ($p < 0.001$). There was no statistically significant difference between the 2 latter time periods concerning risk of revision due to aseptic loosening (Figure 3).

Impact of risk factors and prophylactic measures on deep infection

We assessed the effect of the different risk factors and prophylactic measures that were adjusted for in the Cox analysis. These factors were adjusted for year of index surgery to adjust for unknown confounding and time-dependent factors.

Male sex was a significant risk factor for revision due to deep infection, but age and diagnosis did not influence the risk (Table 3). Laminar air flow was associated with a higher risk of revision due to infection postoperatively compared to ordinary ventilation (Table 3). There was also a higher risk of revision due to infection in the groups with an operating time of more than 100 min (Table 3). Uncemented THAs and THAs implanted with plain cement had a statistically significantly higher risk of revision due to infection compared to cemented THAs fixed with antibiotic-loaded cement (Table 3). Exclusion of monoblock prostheses from the cemented group did not alter these findings. In the small group of patients who did not receive antibiotic prophylaxis systemically, we found a 60% higher risk of THAs being revised due to infection (Table 3). Subanalyses of the risk factors and prophylactic measures performed for each time period separately showed similar effects in all 4 time periods.

Comparison of unadjusted and adjusted risk estimates for the 4 time periods showed that different covariates acted as

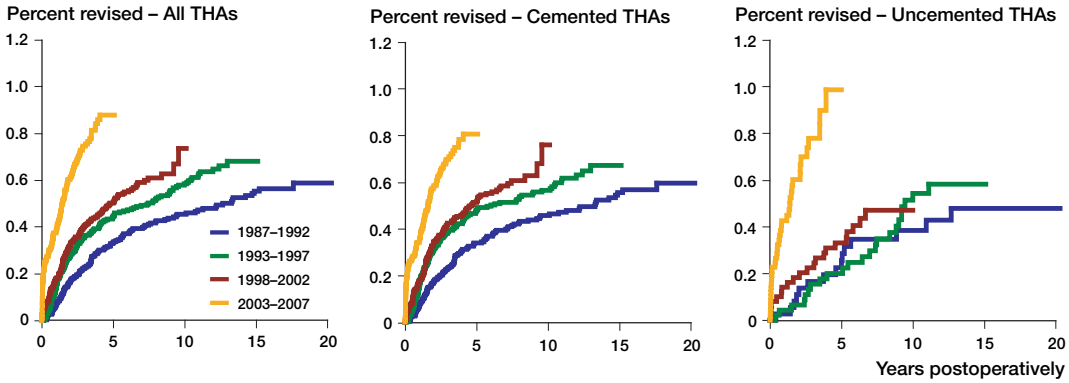

Figure 1. Percentage revision due to deep infection, for all THAs, for cemented THAs, and for uncemented THAs, for 4 periods of primary surgery, adjusted for sex, age, diagnosis, prosthesis, operation room ventilation, duration of operation, and antibiotic prophylaxis.

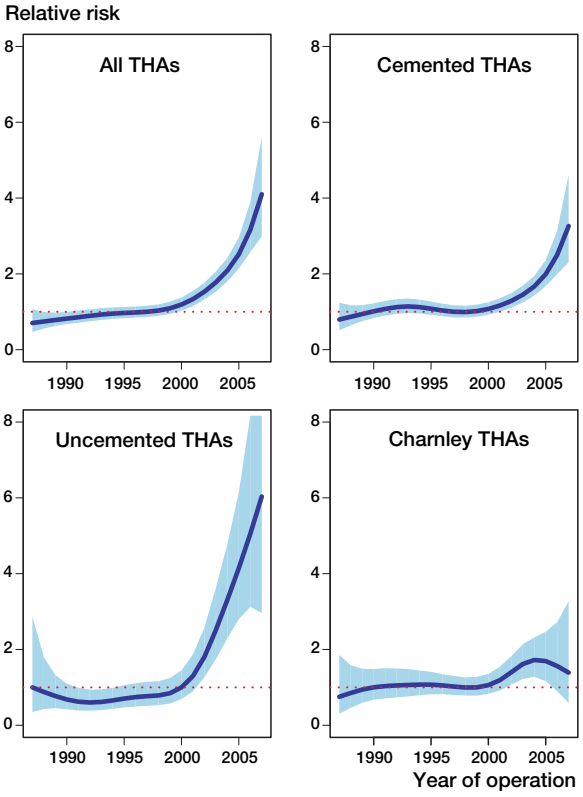

Figure 2. Graphical display of the relationship between year of primary surgery and risk of revision due to deep infection (with 95% CI) for all THAs, cemented THAs, uncemented THAs, and Charnley THAs with uniform antibiotic prophylaxis, adjusted for sex, age, diagnosis, prosthesis, operation room ventilation, duration of operation, type of fixation, and antibiotic prophylaxis.

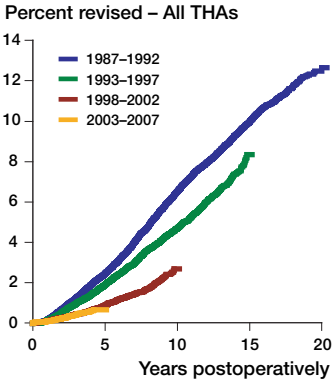

Figure 3. Percentage revision due to aseptic loosening, for all THAs, for 4 periods of primary surgery, adjusted for sex, age, diagnosis, prosthesis, operation room ventilation, duration of operation, type of fixation, and antibiotic prophylaxis.

confounders for cemented and uncemented THAs. Comparing the first and the last time period for cemented THAs, the risk of revision due to infection increased from 1.8 (CI: 1.4–2.3) ($p < 0.001$) to 2.7 (CI: 1.9–3.7) ($p < 0.001$). This change was mainly due to adjustment for use of cement containing antibiotics and explained by increased use over time and the protective ability of cement containing antibiotics. There was also a trend of shorter duration of surgery having a protective effect on cemented THAs. For Charnley prostheses inserted with cement containing antibiotics, the effect of adjustment was negligible. For uncemented THAs, the risk of revision due to infection was reduced from 5.7 (CI: 2.9–11.2) ($p < 0.001$) to 5.3 (CI: 2.6–10.7) ($p < 0.001$) for the

Table 3. Number of primary THAs included and number of reported first revisions due to deep infection. Adjusted risk ratio estimates for sex, age, diagnosis, type of prosthesis, duration of operation, operation room ventilation, antibiotic prophylaxis systemically, and type of fixation. The risk factors are adjusted for all the other risk factors in addition to year of surgery

	No. of THAs included	revised due to infection	Risk ratio	p-value	95% CI
Sex					
Male	29,216	311	2.5	< 0.001	2.1–2.9
Female	68,128	303	1		
Age					
< 40	1,721	9	0.5	0.1	0.3–1.1
40–59	14,240	95	0.8	0.2	0.6–1.1
60–69	26,336	196	1.1	0.3	0.9–1.3
70–79	39,812	241	1		
≥ 80	15,235	73	0.9	0.5	0.7–1.2
Diagnosis					
Osteoarthritis	70,134	440	1		
Inflammatory	3,522	22	1.1	0.6	0.7–1.7
Other	23,688	152	1.2	0.1	1.0–1.4
Prosthesis					
Modular	57,374	332	0.8	0.1	0.7–1.0
Monoblock	39,970	282	1		
Duration of surgery, min					
< 70	11,334	55	0.9	0.5	0.7–1.2
70–99	42,700	236	1		
100–129	29,679	211	1.3	0.01	1.0–1.5
≥ 130	13,631	112	1.5	0.001	1.2–1-9
Operation room ventilation					
Greenhouse	3,386	30	1.3	0.2	0.9–2.0
Laminar flow	45,620	324	1.3	0.006	1.1–1.5
Ordinary	48,338	260	1		
Antibiotic prophylaxis systemically					
No	1,820	15	1.6	0.1	0.9–2.7
Yes	95,524	599	1		
Method of fixation					
Uncemented	14,348	97	1.4	0.03	1.0–1.8
Cement					
with antibiotics	65,005	360	1		
without antibiotics	17,991	157	1.9	< 0.001	1.5–2.3

last time period relative to the first. The decrease was caused by adjustment for sex.

Discussion

Our main finding was an increased risk of revision due to deep infection after primary THA for the 3 consecutive 5-year periods after 1987–1992. The most pronounced increase was for the last time period. The increase was particularly high in the subgroup of uncemented THAs.

We have found no reports on an increased risk of infection for primary THAs. Kurtz et al. (2008) report a 2-fold increase in overall incidence of deep infection after THA from 0.66% in 1990 to 1.23% in 2004. This study on "total infection burden" was based on aggregated data, and both primary and revision arthroplasties were included in the analyses. For primary THAs only, they found a reduced incidence of infection. Mannien et al. (2008) also reported a 60% decrease in surgical site infection after THA between 1996 and 2006 in the Dutch national nosocomial surveillance network (PREZIES). The Cochrane collaboration has not evaluated THA infections.

To our knowledge, the finding that uncemented THAs have shown a larger increase in infection rate than cemented THAs in recent years has not been described previously. The most pronounced increase in risk of revision due to infection in uncemented THAs was after the year 2000. Engesaeter et al. (2006) concluded in their study from the Norwegian Arthroplasty Register, including THAs from the period 1987–2003, that the risk of revision due to infection was the same for uncemented THAs and THAs fixed with cement-containing antibiotics. THAs fixed with cement without antibiotics had a higher risk of deep infection. Based on our study, we have reason to believe that there is now a trend towards higher susceptibility to deep infection for uncemented THAs than for THAs implanted with cement-containing antibiotics. This confirms earlier findings that antibiotic-loaded bone cement protects against infection (Engesaeter et al. 2003, Block and Stubbs 2005, Parvizi et al. 2008b).

One possible explanation for the increased risk of infection could be that THA is now performed on patients with more comorbidity. Obesity and diabetes have an increasing incidence in the population, and these conditions are both risk factors for postoperative surgical site infections (Olsen et al. 2008, Pulido et al. 2008). These factors are not reported to our register, but if our material is similar to the general population, this could contribute to the increased risk of infection. Another independent risk factor is a higher American Society of Anesthesiologists score (ASA score) (Ridgeway et al. 2005, Pulido et al. 2008). In our register, ASA score was registered from 2005; thus, we only have data from the last 3 years of the study period (The Norwegian Arthroplasty Register 2008). During this short period, however, we found an increase in patients with higher ASA scores. There was an increase in mean age from the first to the last time period for the uncemented THAs, but this was adjusted for in the analyses. However, age was not found to be a statistically significant risk factor concerning risk of revision due to infection.

Parvizi et al. (2008a) reported on "the changing organism profile in periprosthetic infection", which is another risk factor not recorded in the NAR. The microbes causing periprosthetic infections could have become more virulent or resistant (Styers et al. 2006, Anderson et al. 2007). More extensive use of antibiotic prophylaxis systemically and in bone cement may have resulted in selection of more virulent or resistant microbes (Santos Sanches et al. 2000).

The clinical presentation of aseptic loosening and low-grade periprosthetic infection can be similar (Ince et al. 2004).

After revision surgery the diagnosis, reported immediately after surgery, will be based on preoperative blood and bacterial samples and peroperative evaluation by the surgeon. Unexpectedly positive peroperative bacterial cultures will be recognized postoperatively and are not reported to NAR. An incorrect reported diagnosis will therefore not be corrected in the register. Improved diagnostics and knowledge about the ability of microbes to cause infection would only affect our results if, with time, preoperative bacterial detection improved or changed surgeons' evaluation of the clinical diagnosis.

There have been improvements in procedures for diagnosis of periprosthetic infection, and more standardized techniques of sampling, culture, and analysis lead to less samples being false negative (Dempsey et al. 2007, Moojen et al. 2007, Neut et al. 2007). Also, bacteria such as Staphylococcus epidermidis have emerged as important agents of implant infection (Neu 1994, Raad et al. 1998, von Eiff et al. 2006, Anderson et al. 2007). Earlier in the period studied, these species were considered to be incapable of causing infections. This may have led to deep infection being suspected, and therefore reported, more frequently in recent years. The magnitude of this shift remains unclear, but with 4,437 revisions due to aseptic loosening and only 614 revisions due to infection, even small improvements in diagnostics and in our understanding of low-grade infections may have had an influence on the results. However, we found no change in percentage revision due to aseptic loosening between the last 2 time periods, whereas it was between these two time periods that we found the greatest increase in percentage revision due to deep infection (Figure 3).

We do not have information on what time the systemically administered antibiotics were given prior to surgery, or if there were changes in this routine over time. This has been shown to be of importance concerning the protective ability of antibiotic prophylaxis (van Kasteren et al. 2007). These factors may have influenced our results.

Because of the large numbers and the long period of observation, registry studies on deep infection can be a useful source of information regarding incidences and trends. The NAR has good-quality, detailed information about patients, primary surgery, and prophylactic measures, gathered uniformly over a long period of time. Our data are prospective, with 95–97% completeness for primary THA (Havelin 1995, Espehaug et al. 2006). We therefore have an excellent basis for a trend study on a relatively rare complication like periprosthetic infection. However, with 97,344 THAs available for analysis, there were only 614 revisions due to infection available for analysis. This restricts division into subgroups, and when this is done, marginal effects are difficult to assess.

Registry results are influenced by confounding factors. Changes in reporting, revision policy, diagnostics, surgeon awareness and surgery, selection of patients, and the virulence of microbiotic agents will also influence the results. These factors can only be partially elucidated. Completeness studies on the NAR have shown that there is 10–20% under-reporting of Girdlestone procedures, which is a common procedure in revision surgery for deep infection (Arthursson et al. 2005, Espehaug et al. 2006). These procedures will, however, be registered if a second stage in the revision is performed and reported. Under-reporting will only affect our findings if the degree to which it happens changes over the period studied. Awareness of the importance of thorough reporting probably improved the reporting of infection over the study period, but a time trend evaluation of this was not done.

We found an increase in the risk of revision due to infection during the first postoperative year for the 2002–2007 group. This shows that the infections were revised earlier after index surgery in recent years. This can either be explained by a change in revision policy, a change in surgeons' awareness, or more acute infections. Current recommendations for early surgical site infection involve early soft tissue debridement and exchange of prosthesis parts (Zimmerli and Ochsner 2003). In our material, we found a shift from use of monoblock prostheses to more frequent use of modular prostheses. Early revision due to infection in the case of modular prostheses will therefore involve the exchange of a femoral head, an acetabular liner, or both, and the procedure should therefore be reported to the registry. Early revisions for infection in the case of monoblock prostheses will not, however, be reported if a successful soft tissue debridement combined with antibiotic treatment heals the infection and the prosthesis is retained. We adjusted for monoblock or modular prosthesis in our Cox analysis, to adjust for changes in reporting of deep infection due to these changes in the use of implants. In addition, because of the possible "under-reporting" of deep infection in the monoblock group, we also performed separate analyses on Charnley monoblock prostheses and found an increase in risk of infection in this group as well.

Improvements in the design of prostheses and surgical technique have reduced the incidence of aseptic loosening in recent years (Herberts and Malchau 2000, Morscher 2003). This could affect surgeons' awareness of low-grade infection when deciding on the clinical diagnosis to report after surgery.

The problem of confounding factors and time-dependent risk factors in our registry study is the reason why we must interpret the evaluation of the risk factors and prophylactic measures in Table 3 with caution. The evaluation was made to illustrate the effect of these factors in this study, and the study was not set up to assess each covariate independently.

Due to the small numbers of infections, large numbers of primary THAs are needed to study different aspects of periprosthetic infections. There is a need for improved monitoring of time trends and evaluation of prophylactic measures concerning deep infection. For this purpose, surveillance programs such as the National Nosocomial Infections Surveillance (NNIS) System Reports (USA) and the European surveillance HELICS-SSI database could be of value, as could the increasing number of national arthroplasty registries and improved collaboration between these. Concentration on

and improvement of prophylaxis, diagnostics, and treatment of these infections will be of great importance to limit any increase in this serious complication.

The first author performed data analysis and wrote the manuscript. All authors contributed to the conception and design of the study, critical analysis of the data, interpretation of the findings, and critical revision of the manuscript.

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Paper II

Infection after primary hip arthroplasty

A comparison of 3 Norwegian health registers

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Background and purpose **The aim of the present study was to assess incidence of and risk factors for infection after hip arthroplasty in data from 3 national health registries. We investigated differences in risk patterns between surgical site infection (SSI) and revision due to infection after primary total hip arthroplasty (THA) and hemiarthroplasty (HA).**

Materials and methods **This observational study was based on prospective data from 2005–2009 on primary THAs and HAs from the Norwegian Arthroplasty Register (NAR), the Norwegian Hip Fracture Register (NHFR), and the Norwegian Surveillance System for Healthcare–Associated Infections (NOIS). The Norwegian Patient Register (NPR) was used for evaluation of case reporting. Cox regression analyses were performed with revision due to infection as endpoint for data from the NAR and the NHFR, and with SSI as the endpoint for data from the NOIS.**

Results **The 1–year incidence of SSI in the NOIS was 3.0% after THA (167/5,540) and 7.3% after HA (103/1,416). The 1–year incidence of revision due to infection was 0.7% for THAs in the NAR (182/24,512) and 1.5% for HAs in the NHFR (128/8,262). Risk factors for SSI after THA were advanced age, ASA class higher than 2, and short duration of surgery. For THA, the risk factors for revision due to infection were male sex, advanced age, ASA class higher than 1, emergency surgery, uncemented fixation, and a National Nosocomial Infection Surveillance (NNIS) risk index of 2 or more. For HAs inserted after fracture, age less than 60 and short duration of surgery were risk factors of revision due to infection.**

Interpretation **The incidences of SSI and revision due to infection after primary hip replacements in Norway are similar to those in other countries. There may be differences in risk pattern between SSI and revision due to infection after arthroplasty. The risk patterns for revision due to infection appear to be different for HA and THA.**

Increasing incidence of revision due to infection after primary total hip arthroplasty (THA) has been observed in different countries during the last decade (Kurtz et al. 2008, Dale et al. 2009, Pedersen et al. 2010). There have been several studies on incidence of and risk factors for infection based on data from surveillance systems (Ridgeway et al. 2005, Mannien et al. 2008), arthroplasty (quality) registers (Berbari et al. 1998, Dale et al. 2009, Pedersen et al. 2010), and administrative databases (Mahomed et al. 2003, Kurtz et al. 2008, Ong et al. 2009). There have been reviews on incidence of and risk factors for infection after hip arthroplasty, based on publications from databases with different definitions of infection (Urquhart et al. 2009, Jämsen et al. 2010a). Superficial surgical site infections (SSIs) may have risk factors that are different from those of full surgical revisions due to infection. Furthermore, THA and hip hemiarthroplasty (HA) may have different patterns of risk of infection (Ridgeway et al. 2005, Cordero–Ampuero and de Dios 2010).

In the present study, we used data from 3 national health registries in Norway to assess incidence and some risk factors for infection after primary hip arthroplasty. Differences in risk patterns between SSI and revision due to infection were investigated for HA and THA.

Material and methods

In Norway, 3 national health registries representing 2 different surveillance systems record information on primary hip replacement surgery and postoperative infections: the Norwegian Arthroplasty Register (NAR) and the Norwegian Hip Fracture Register (NHFR). These are quality registers, while the Norwegian Surveillance System for Healthcare–Associated Infections (NOIS (Norwegian acronym)) is an infection surveillance system. We compared these registries for

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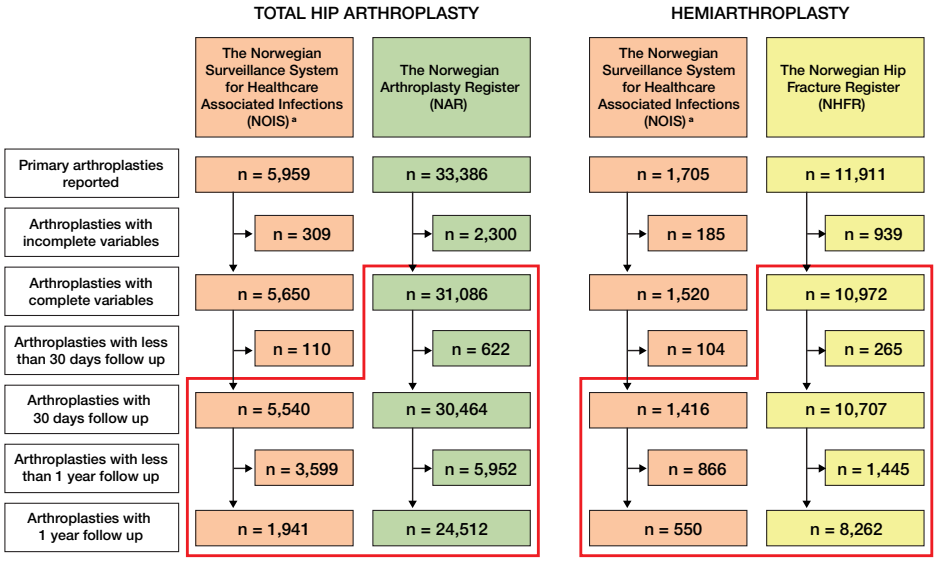

Number of primary THAs and HAs (red squares) included in the NOIS, the NAR, and the NHFR, including number of arthroplasties with missing data on the confounders and incomplete 30–day and 1–year follow–up.
[a] The NOIS registers arthroplasties 3 months every year. Not all hospitals that reported to the NAR and the NHFR reported to the NOIS. (NOIS is a Norwegian acronym).

infectious endpoints after primary THA or HA over the years 2005–2009. In addition, data from a fourth health registry, the Norwegian Patient Register (NPR), were used to assess the reporting of primary procedures to the 3 registries.

The Norwegian Surveillance System for Healthcare–Associated Infections (NOIS)

The NOIS is based on a modified version of Hospitals in Europe Link for Infection Control through Surveillance (HELICS 2004). The aims are to survey, describe, and evaluate the incidence of surgical site infection (SSI) after certain procedures. Furthermore, the intention is to assess effects of prophylactic interventions and discover variations in SSI. Since 2005, it has been mandatory for all Norwegian hospitals to report arthroplasty and 4 other procedures (Caesarean section, coronary bypass, appendectomy, and cholecystectomy) over a 3–month period every year (September to November). The data are collected either electronically from the patients' medical records or manually (by infection–control nurses) into a standardized case report form. The information collected includes hospital affiliation, patient characteristics, date of admission, surgery, discharge, first infection and last follow–up, type of arthroplasty, type of infection, the source of diagnosis (patient or physician), and reoperations. For this study, only infections verified by a medical doctor were included. Verification of SSI was from a form signed by a general physician or from the hospital medical records if the patient had SSI diagnosed at a hospital. The endpoint in the NOIS was SSI, defined according to the CDC guidelines. The CDC–defined organ/space SSI category was combined with the deep incisional SSI category. Reoperations reported to the NOIS comprised all types of surgical procedures due to infection. If no infection was recorded, the patient was censored at death or last date of surveillance. Endpoint evaluation was done at discharge, by questionnaire to the patient, and by evaluation of the medical records at 30 and 365 days postoperatively. 30 days were defined as the minimum follow–up time for inclusion. The procedures included were primary THAs and HAs with the NOMESCO codes NFB 02, –12, –20, –30, and –40. In the NOIS, 6,956 hip arthroplasties, including 5,540 THAs and 1,416 HAs, were eligible for analysis (Figure 1). In contrast to the NHFR, the NOIS also includes HAs inserted for causes other than femoral neck fracture. With this exception, THAs in the NOIS should also be reported to the NAR whereas HAs should be reported to the NHFR.

The Norwegian Arthroplasty Register

Since its inception in 1987, the NAR has registered data on primary THAs and THA revisions. This includes the patient's identity and characteristics, the indication for THA, the surgical procedure, the implant, and revisions. The unique identification number of each Norwegian citizen can be used to link the primary THA to a later revision (Havelin et al. 2000).

Revision due to deep infection of the implant was the infection endpoint in the NAR in the present study, and was defined as removal or exchange of the whole or part of the prosthesis with deep infection reported as the cause of revision. Isolated soft tissue revisions were not reported. The case report form is filled in by the surgeon immediately after surgery. Detailed information on the arthroplasty was transformed into the following NOMESCO groups: cemented THAs (NFB 40), uncemented THAs (NFB 20), and hybrid THAs (NFB 30). The NAR does not register HAs. All THAs were followed until their first revision due to deep infection or revision for other causes, until the date of death or emigration of the patient, or until December 31, 2009. In the NAR, 31,086 THAs were eligible for analysis (Figure).

The Norwegian Hip Fracture Register

The NHFR has the same administrative foundation and purpose as the NAR. Since January 1, 2005, all hip fractures treated surgically and later revisions have been reported on a similar case report form to that for registration in the NAR (Gjertsen et al. 2008). Procedures included were HAs performed as a primary operation for a femoral neck fracture and HAs inserted secondary to failure of the primary osteosynthesis of a femoral neck fracture. THAs as primary emergency treatment or secondary planned treatment of femoral neck fractures were registered in the NAR. As for the NAR, the endpoint was revision of the implant due to infection. The groups cemented HA (NFB 12) and uncemented HA (NFB 02) were defined based on detailed information about the implant type and fixation reported to the NHFR. HAs inserted for causes other than hip fracture or complications after hip fracture (i.e. osteoarthritis or malignancies) were not registered in the NHFR. All HAs were followed until their first revision due to deep infection or revision for other causes, until the date of death or emigration of the patient, or until December 31, 2009. In the NHFR, 10,972 HAs were eligible for analysis (Figure).

The Norwegian Patient Register

The NPR is a national administrative health register. It is compulsory by law to report medical treatment to the NPR, and it is the basis of funding in Norwegian hospitals. Primary THAs and HAs with the NOMESCO codes NFB 02, –12, –20, –30, and –40 were included for the assessment of case reporting, regardless of diagnosis.

Statistics

Descriptive statistics were used for demographics and surgery–related data. Data from NOIS and the merged NAR and NHFR data were analyzed separately. The 1–year incidences of SSI, reoperation, and revision due to infection were estimated by dividing the number of events reported during the first postoperative year by the number of primary arthroplasties. Cox regression analyses were performed to establish risk factors for revision due to deep infection or SSI, and also 1–year probabilities (risks) of these events (1 minus 1–year survival (%)). Adjusted hazard rate ratios, hereafter called risk ratios (RRs), were estimated for each risk factor with 95% confidence intervals (CIs). The risk factors evaluated were age, sex, American Society of Anesthesiologists classification (ASA class), duration of surgery, type of surgery (emergency or planned), and method of fixation of the prosthesis (Table 1). Adjusted risk of SSI after HA relative to THA was assessed in the NOIS, whereas adjusted risk of revision due to infection after HA relative to THA was analyzed in the merged NAR–NHFR data. In addition, we calculated and assessed the National Nosocomial Infection Surveillance (NNIS) risk index, which comprise duration of surgery (> 75th percentile for the procedure), co–morbidity of the patient (ASA class > 2), and contamination of the wound peroperatively (Mangram et al. 1999). In the NAR and NHFR, we assumed that there was no contamination. The 75 percentile duration of surgery as reported was used (in the NOIS, HA 94 min and THA 108 min; in the NHFR, HA 90 min; and in the NAR, THA

Table 1. Distribution of the assessed risk factors in the registers: THAs and HAs included from the Norwegian Surveillance System for Healthcare Associated Infections (NOIS), THAs included from in the Norwegian Arthroplasty Register (NAR) and HAs included from in the Norwegian Hip Fracture Register (NHFR).

	Total hip arthroplasty		Hemiarthroplasty	
Register	NOIS	NAR	NOIS	NHFR
Number of procedures	5,540	31,086	1,416	10,972
Risk factor %				
Agegroup (years)				
<60	19	20	2	1
60–69	31	30	4	5
70–79	34	34	22	24
80–89	15	15	56	54
≥90	1	1	16	15
Sex				
female	66	67	74	74
male	34	33	26	26
ASA score				
1	18	29	2	5
2	65	52	42	35
≥3	17	19	56	60
Duration of surgery (Min)				
<60	6	7	19	22
60–89	41	40	50	47
90–119	33	35	22	24
≥120	19	19	8	8
Type of surgery				
emergency	3	2	74	86
planned	97	98	26	14
Method of fixation				
cemented	64	65	81	81
uncemented	16	16	19	19
hybrid	20	18		
NNIS index				
0	63	64	32	31
1	32	31	54	56
≥2	5	5	14	13

Table 2. 1-year incidence of SSI and reoperation after primary arthroplasties as reported to the Norwegian Surveillance System for Healthcare Associated Infections (NOIS) and 1-year incidence of revisions due to infection after THAs as reported to the Norwegian Arthroplasty Register (NAR) and after HAs as reported to the Norwegian Hip Fracture Register (NHFR)

Register[a] Endpoint	Total hip arthroplasty 1–year incidence	Hemiarthroplasty 1–year incidence
NOIS		
Sugical Site Infection	3.0% (167/5,540)	7.3% (103/1,416)
Superficial SSI	1.7% (94/5,540)	2.2% (31/1,416)
Deep SSI	1.3% (73/5,540)	5.1% (72/1,415)
SSI reoperated	1.0% (58/5,540)	3.6% (51/1.416)
NAR / NHFR		
Revision due to infection	0.7% (182/24,512)	1.5% (128/8,262)

[a] The NOIS and the NAR/NHFR represents different selections of cases

110 min), and not the 120 min estimated for HA and THA in the HELICS guidelines. Follow–up for the NAR and the NHFR analyses was 0–5 years and for the NOIS it was 0–1 year. However, to ensure similar follow–up for all 3 registries, additional analyses were performed with follow–up restricted to 1 year for all available cases. Stratified analyses were performed on the NOIS data with deep SSI as separate endpoint. Any p–values of less than 0.05 were considered statistically significant. SPSS software version 18.0 and PASS 2008 software were used for statistical analysis.

Results

Case reporting and distribution of risk factors

32 hospitals reported THAs to the NPR and the NAR during the study period. 30 hospitals reported THAs to the NOIS; there was an increase in hospitals reporting THA, from 8 in the first year.

29 hospitals reported HAs to the NPR, whereas 27 reported HAs to the NHFR and 26 reported HAs to the NOIS over the study period. The number of hospitals reporting HAs increased from 5 to 26 in the NOIS and from 26 to 27 in the NHFR. 33,466 primary THAs and 12,069 primary HAs were reported to the NPR during the study period. The comparable number of procedures reported to each of the other registries is presented in Figure 1. The distribution of risk factors was similar for THAs in the NOIS and the NAR, and for HAs in the NOIS and the NHFR (Table 1). The exception was ASA classification (Table 1).

Incidence and risk of infection

The 1–year incidence of SSI was 3.0% after primary THA (Table 2). 6/94 of the superficial SSIs and 52/73 of the deep SSIs after THA in the NOIS were reported to have been reoperated due to the infection, whereas in the NAR the 1–year incidence of revision due to infection was 0.7% (Table 2).

In primary HAs, the 1–year incidence of SSI was 7.3% (Table 2). 50/51 of the reoperations due to infection after HA in the NOIS were due to deep SSIs, and 50/72 of the deep SSIs were reported to have been reoperated. 1.5% of the HAs were reported to the NHFR to have been revised due to infection (Table 2).

In the NOIS, the adjusted risk of SSI after HA compared to THA was 1.2 (CI: 0.8–1.9). The adjusted risk of revision due to infection was 1.8 times higher for HAs (CI: 1.2–2.7) than for THA in the merged NAR/NHFR data.

Time to SSI and revision due to infection

For THAs, the median postoperative time to diagnosis of SSI was 16 (2–214) days. Median time to revision due to infection was 29 (4–343) days, when restricting follow–up to 1 year, and 47 (4–1,782) days with 0–5 years of follow–up. For HAs, the median postoperative time to SSI was 15 (2–79) days. Median time to revision due to infection was 20 (4–304) days with 1–year follow up and 20 (4–701) days with 0–5 years of follow–up. 72% of the SSIs in the NOIS were identified in the post discharge surveillance, but only 9 cases of SSI were identified between 30 and 365 days postoperatively.

Risk factors for infection after THA

The following factors were associated with increased risk of revision due to infection: 70–89 years of age, male sex, and ASA class higher than 1 (Table 3). Emergency surgery as opposed to planned surgery and a National Nosocomial Infection Surveillance Systems (NNIS) risk index of > 1 were also associated with a higher risk of revision due to infection after THA. Uncemented fixation of the prosthesis had a 50% higher risk of revision due to infection compared to cemented THAs.

Risk factors for SSI after THA were short duration of surgery (< 60 min), which was also the finding when cemented, uncemented, and hybrid fixations were analyzed separately. Patients older than 80 years of age also had higher risk of SSI than those who were less than 60 years of age. The risk patterns for SSI and revision due to infection were different regarding effects of gender, duration of surgery < 60 min, and method of fixation. Separate analyses of all cases with 1–year follow–up in the NOIS and restricted follow–up of 1 year for the NAR as in the NOIS did not change the findings concerning risk factors for SSI or revision due to infection. Restriction to deep incisional SSI in the NOIS had only minor effects on the risk estimates.

Risk factors for infection after HA

In the NHFR, age less than 60 years and duration of surgery of less than 60 min were associated with increased risk of revision due to infection (Table 4). No risk factors were identified for SSI after HA. HA had a different risk profile from that of THA, for both SSI and revision due to infection (Tables 3 and 4).

Table 3. Risk factors for infection after THA: Adjusted risk of surgical site infection (SSI) after primary THAs in the Norwegian Surveillance System for Healthcare Associated Infections (NOIS), and adjusted risk of revision due to infection in the Norwegian Arthroplasty Register (NAR) for different risk factors. Each risk factor was adjusted for the other risk factors in the table except NNIS index

	Total hip arthroplasty											
Register:			NOIS						NAR			
Number infected / included:			167 / 5,540 (3.0%)						236 / 31,086 (0.8%)			
Risk factor	A	B	C	D	E	F	G	H	I	J	K	L
Age group (years)												
< 60	1,067	23	1			2.4	6,114	34	1			0.4
60–69	1,740	46	1.2	0.7–2.1	0.5	2.7	9,320	61	1.3	0.8–1.9	0.3	0.4
70–79	1,882	59	1.4	0.8–2.4	0.2	3.3	10,703	95	1.7	1.1–2.6	0.02	0.6
80–89	816	36	1.9	1.1–3.5	0.03	4.2	4,766	45	1.8	1.1–3.0	0.02	0.8
≥90	35	3	3.8	1.1–13	0.04	7.4	183	1	1.0	0.1–7.4	1.0	0.5
Sex												
female	3,676	103	1			2.7	20,922	113	1			0.4
male	1,864	64	1.3	0.9–1.8	0.1	3.6	10,164	123	2.4	1.8–3.1	<0.001	1.0
ASA score												
1	1,010	18	1			2.1	8,964	46	1			0.4
2	3,608	109	1.5	0.9–2.5	0.1	3.1	16,148	125	1.5	1.1–2.2	0.02	0.6
≥3	922	40	1.9	1.0–3.4	0.04	4.1	5,974	65	2.0	1.3–2.9	0.001	0.7
Duration of surgery (min)												
<60	357	20	2.4	1.4–4.0	0.001	6.8	2,045	15	1.0	0.6–1.8	0.9	0.6
60–89	2,294	56	1			2.4	12,427	84	1			0.5
90–119	1,822	59	1.3	0.9–1.9	0.1	3.2	10,745	84	1.1	0.8–1.5	0.5	0.5
≥120	1,067	32	1.2	0.8–1.9	0.4	3.2	5,869	53	1.3	0.9–1.8	0.2	0.5
Type of surgery												
emergency	183	10	1.8	0.9–3.4	0.08	6.6	609	9	2.2	1.1–4.3	0.02	1.3
planned	5,357	157	1			2.9	30,477	227	1			0.5
Method of fixation												
cemented	3,547	111	1			2.9	20,308	159	1			0.5
unemented	902	25	1.0	0.7–1.7	0.8	3.5	5,110	43	1.5	1.0–2.2	0.03	0.8
hybrid	1,091	31	1.1	0.7–1.7	0.7	3.4	5,668	34	1.1	0.7–1.6	0.7	0.6
NNIS index [a]												
0	3,480	94	1			2.8	19,729	129	1			0.5
1	1,784	64	1.3	0.9–1.7	0.2	3.8	9,760	87	1.3	1.0–1.7	0.08	0.6
≥2	267	9	1.0	0.5–2.0	1.0	3.5	1,597	20	1.7	1.1–4.4	0.02	0.6

A Number of primary arthroplasties included
B Number of SSIs
C Adjusted risk of SSI
D 95% CI
E P-value
F Adjusted 1–year SSI percent
G Number of primary THAs included
H Number of revisions due to infection
I Adjusted risk of revision due to infection
J 95% CI
K P-value
L Adjusted 1–year revision percent
[a] Adjusted for sex, age, type of surgery and method of fixation

Discussion

The 3.0% incidence of SSI after primary THA is similar to incidences of SSI reported from other European countries with similar surveillance systems to those of Norway (range 0.9–4.6%) (Ridgeway et al. 2005, HELICS 2006, The Health Protection Agency 2007, Mannien et al. 2008). The 1–year incidence of revision due to infection (0.7% for THA) in the NAR is similar to results from other Scandinavian arthroplasty registries (Havelin et al. 2009). Comparisons of incidence of infection after arthroplasty across countries are complicated due to differences in definitions, in completeness of case reporting, and in post–discharge surveillance (Wilson et al. 2007).

The 1–year incidence of SSI of 7.3% after primary HA appears to be high compared to the results reported from the English mandatory surveillance (3.6–5.0%), which has also reported that HA patients had 2.5 times greater risk of developing SSI than THA patients (Ridgeway et al. 2005, The Health Protection Agency 2007). Similar differences between SSI after HA and SSI after THA were also reported by Wilson from the HELICS collaboration (2007). One explanation for the higher infection rates after HA may be differences in patient population, including how frail individuals are from a

Table 4. Risk factors for infection after HA: Adjusted risk of surgical site infection (SSI) after primary HAs in the Norwegian Surveillance System for Healthcare Associated Infections (NOIS), and adjusted risk of revision due to infection in the Norwegian Hip Fracture Register (NHFR) for different risk factors. Each risk factor was adjusted for the other risk factors in the table except NNIS index

						Hemiarthroplasty						
Register:			NOIS						NHFR			
Number infected / included:			103 / 1,416 (7.3%)						167 / 10,972 (1.5%)			
Risk factor	A	B	C	D	E	F	G	H	I	J	K	L
Age group (years)												
<60	22	1	0.8	0.1–5.8	0.8	4.0	145	7	3.6	1.6–7.8	0.001	5.1
60–69	51	4	1.2	0.4–3.4	0.7	6.7	566	8	1.0	0.5–2.1	1.0	1.4
70–79	318	19	1.0	0.6–1.6	0.9	6.0	2,634	41	1.1	0.8–1.7	0.5	1.6
80–89	796	54	1			6.2	5,946	80	1			1.4
≥90	229	25	1.6	1.0–2.6	0.06	8.7	1,681	31	1.4	1.0–2.2	0.08	2.1
Sex												
Female	1,053	82	1			7.0	8,085	115	1			1.5
Male	363	21	0.8	0.5–1.3	0.3	4.8	2,887	52	1.3	1.0–1.9	0.08	2.0
ASA score												
1	25	0					523	7	1			1.3
2	592	43	1			7.3	3,854	58	1.2	0.5–2.6	0.6	1.5
≥3	799	60	1.1	0.7–1.6	0.8	8.2	6,595	102	1.3	0.6–2.8	0.5	1.6
Duration of surgery (min)												
<60	271	26	1.9	1.0–3.9	0.06	7.8	2,371	47	1.4	0.9–2.0	0.1	2.2
60–89	709	53	1.7	0.9–3.2	0.08	7.2	5,152	77	1			1.6
90–119	317	13	1			3.7	2,598	30	0.8	0.5–1.2	0.2	1.2
≥120	119	11	2.2	1.0–4.9	0.06	8.0	851	13	0.9	0.5–1.7	0.7	1.4
Type of surgery												
Emergency	1,041	81	1.3	0.8–2.0	0.8	6.9	9,459	137	0.8	0.5–1.1	0.2	1.5
Planned	375	22	1			5.4	1,513	30	1			2.0
Method of fixation												
Cemented	1,141	74	1			6.0	8,849	127	1			1.5
Unemented	275	29	1.4	0.9–2.3	0.1	8.5	2,123	40	1.2	0.8–1.7	0.4	1.8
NNIS index [a]												
0	452	32	1			7.2	3,436	54	1			1.6
1	759	56	1.1	0.7–1.7	0.7	8.2	6.113	92	1.0	0.7–1.4	1.0	1.6
≥2	190	15	1.2	0.6–2.2	0.6	7.9	1.423	21	0.9	0.6–1.6	0.8	1.5

A–L: See table 3.
[a] Adjusted for sex, age, type of surgery and method of fixation

medical standpoint (Gjertsen et al. 2008, Hahnel et al. 2009). HA patients were generally older, with more co–morbidity than the THA patients, and the majority of HA patients had had surgery due to a trauma (hip fracture). Ridgeway found, as in the present study, that there was no difference in the risk of SSI between HA and THA patients after adjusting for ASA score, age, duration of surgery, and procedures performed after trauma. In contrast, we found an increased risk of revision due to infection after HA as compared to after THA.

Male sex was a risk factor for revision due to infection after THA, as shown in some other studies (Ong et al. 2009, Pedersen et al. 2010), whereas yet other studies have not found this (Mahomed et al. 2003, Ridgeway et al. 2005). It also appears that males have a relatively high risk of revision due to infection—as compared to SSI. One reason may be different thresholds for referral or revision surgery, or the fact that surgery on males can cause a greater degree of surgical trauma and tissue damage (Franks and Clancy 1997, Borkhoff et al. 2008, Pedersen et al. 2010). There may also be differences in bacterial flora or carriage between men and women (Skramm et al. 2007).

The risk of infection increased with age, for both SSI and revision due to infection after THA, and this was also found to be the trend for the oldest HA patients. The exception was HAs in patients aged less than 60 years, who had greater than 3 times higher risk of revision due to infection than patients between 80 and 90 years of age. In Norway, the common policy is to use HA in young patients only if they have many risk factors for complications or have a short life expectancy. High age has been found to be an independent risk factor for SSI in some other studies (Ridgeway et al. 2005, Geubbels et al. 2006). In contrast, without adjustment for ASA class, high age was not found to be a risk factor for revision due to infection in a previous publication from the NAR involving THAs from the period 1987–2007 (Dale et al. 2009). A recent large Danish study, adjusted for co–morbidity, did not find age to be a risk factor (Pedersen et al. 2010). Having a primary THA at a young age may indicate co–morbidity, and thereby increased susceptibility to infection. Among very old patients the most healthy are selected to undergo THA, and may therefore have reduced susceptibility to infection compared to the average population at that age (Lie et al. 2000). Furthermore,

a revision operation on hip arthroplasty is extensive surgery, and surgeons may sometimes choose a nonoperative approach in old and frail patients—an option that is not reported to the NAR and NHFR.

ASA class is a crude approximation of physical status, and works poorly at the individual level where there will be large inter–observer variability. In addition, different co–morbidities may have different effects on infection rates. However, ASA class has predictive value for complications in epidemiological studies like the present one, where the number of cases is large (Ridgeway et al. 2005, Bjørgul et al. 2010). Thus, all 3 registries have chosen the ASA classification as their measure of physical state. An ASA score higher than 1 had an increased risk of revision due to infection after THAs. This indicates that even minor co–morbidities may increase the risk of postoperative infection. For patients with an infected prosthesis, the treatment strategy may be nonoperative for higher ASA classes. In the latter case, some surgeons may choose lifelong antibiotic suppression rather than reoperation for a low–grade implant infection. This may be one explanation for why higher ASA scores had no increased risk of revision due to infection after HA in our study. It may also be that ASA class does not capture frailty in the elderly in a sufficient way in our study population (Makary et al. 2010).

We could not confirm findings from previous studies that longer duration of surgery is associated with higher risk of SSI and higher risk of revision due to infection after THA (Småbrekke et al. 2004, Ridgeway et al. 2005, Dale et al. 2009, Ong et al. 2009, Pedersen et al. 2010). However, duration of surgery less than 60 min was associated with higher risk of SSI after arthroplasty and risk of revision due to infection after HA. Similar findings were reported for SSI after revision arthroplasties, but not primary HA or THA, by Ridgeway (2005). Rapid surgery may result in inferior soft tissue treatment and hemostasis, thereby leading to increased risk of infection.

Primary arthroplasty performed as an emergency procedure after a femoral neck fracture increased the risk of both SSI and revision due to infection after THA. Ridgeway (2005) also found trauma to be a risk factor for SSI after THA. This may be due to local or systemic reactions to the trauma itself, to frailty of the patients, or to other confounders not reported to the registers. For HAs, there was no difference in the risk of revision due to infection between arthroplasty performed in the acute phase and planned surgery. A primary arthroplasty performed as planned surgery caused by a failed osteosynthesis is a reoperation, and may therefore resemble a revision arthroplasty more than a genuine primary arthroplasty. Revision arthroplasty and arthroplasty secondary to fractures are found to have higher susceptibility to infection (Berbari et al. 1998, Ridgeway et al. 2005, Jämsen et al. 2009a).

Cementless fixation had a higher risk of revision due to deep infection after THA, but not a higher risk of SSI. In Norway, nearly all cemented THAs are inserted with cement containing antibiotics (The Norwegian Arthroplasty Register 2010). Uncemented THAs can only be protected by antibiotic prophylaxis given systemically, and this was administered in nearly all hip arthroplasties in Norway over the study period (The Norwegian Arthroplasty Register 2010). Antibiotic eluted from cement is delivered locally, and protects the implant and periprosthetic tissue (Espehaug et al. 1997, Engesæter et al. 2003, Hendriks et al. 2005, Dale et al. 2009). This local antibiotic treatment appears to be less effective for protection against SSI.

The NNIS risk index is a combined surgery–related assessment tool developed to identify high–risk patients, and to evaluate the risk of SSI (Mangram et al. 1999). The NNIS index combines ASA class of greater than 2, duration of surgery longer than the 75th percentile for the procedure, and contamination of the wound. Considering our findings on ASA class and duration of surgery, and that arthroplasty is a clean procedure, the NNIS does not appear to be optimal for identification of patients who are at risk of infection after arthroplasty.

All data on completeness of case reporting to the NAR, the NHFR, and the NOIS, indicate that there would be minor selection bias in our study. The arthroplasties reported to the NOIS were similar, regarding the characteristics of patients and procedures, to the all–year–round registrations in the NAR and the NHFR. SSIs may have been underreported to the NOIS, just as revision due to infection has been to the NAR and other registers (Arthursson et al. 2005, Espehaug et al. 2006, Huotari et al. 2007, Jämsen et al. 2009b, Jämsen et al. 2010b). There is also a possibility of overestimation of SSI in surveillance systems, as superficial infections may be difficult to distinguish from aseptic wound complications (Walenkamp 2009). The lack of validation of endpoints is therefore a weakness in our study, even though we performed separate analyses on overall and deep infections without any major changes in risk assessment. This should be addressed in future studies. Surgical policy was also a possible confounder in the present study on the NHFR and the NAR, since different subgroups—such as patients with higher ASA classes and advanced age—may have been subject to different treatment strategies. For the NOIS and the NHFR, the number of cases included makes statistical power an issue when differences between subgroups are small or the numbers are low.

The 2 endpoints of infection in our study may reflect different types of infections, or at least different stages of infection. The NOIS is more likely to capture the acute virulent postoperative infections whereas the NAR/NHFR is more likely to capture either a more advanced stage of infection or more low–grade, late infections. This fact will affect the findings of incidence and risk patterns of infection, and it is important for the interpretation of results of studies with different definitions of infection and different follow–up.

The majority of SSIs were identified after discharge, which confirms earlier findings that post–discharge surveillance is important to capture the true incidence of SSI after hip

replacement (Huenger et al. 2005, Huotari and Lyytikainen 2006, Mannien et al. 2008). Infection surveillance appears to reduce the incidence of SSI (Brandt et al. 2006), which is also the aim for the NOIS. The NAR has improved THA surgery in Norway over the last 25 years (Fevang et al. 2010). In 2005, the NHFR was established on the same basis with the same methodology. This has led to changes in the treatment of femoral neck fractures towards more use of HA (The Norwegian Hip Fracture Register 2010, Gjertsen et al. 2010). Adverse effects of such changes, such as infection, should be evaluated, which requires good–quality surveillance through registers like the NOIS, the NAR, and the NHFR.

HD performed the data analysis and wrote the manuscript. BE, HLL, HME, FES, LIH, LBE, and OF contributed to the conception and design of the study, critical analysis of the data, interpretation of the findings, and critical revision of the manuscript through all stages of the study. IS contributed to critical evaluation of the analyses, and to revision of the manuscript.

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Paper III

Increasing risk of prosthetic joint infection after total hip arthroplasty

2,778 revisions due to infection after 432,168 primary THAs in the Nordic Arthroplasty Register Association (NARA)

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Background and purpose The risk of revision due to infection after primary total hip arthroplasty (THA) has been reported to be increasing in Norway. We investigated whether this increase is a common feature in the Nordic countries (Denmark, Finland, Norway, and Sweden).

Materials and methods The study was based on the Nordic Arthroplasty Register Association (NARA) dataset. 432,168 primary THAs from 1995 to 2009 were included (Denmark: 83,853, Finland 78,106, Norway 88,455, and Sweden 181,754). Adjusted survival analyses were performed using Cox regression models with revision due to infection as the endpoint. The effect of risk factors such as the year of surgery, age, sex, diagnosis, type of prosthesis, and fixation were assessed.

Results 2,778 (0.6%) of the primary THAs were revised due to infection. Compared to the period 1995–1999, the relative risk (with 95% CI) of revision due to infection was 1.1 (1.0–1.2) in 2000–2004 and 1.6 (1.4–1.7) in 2005–2009. Adjusted cumulative 5–year revision rates due to infection were 0.46% (0.42–0.50) in 1995–1999, 0.54% (0.50–0.58) in 2000–2004, and 0.71% (0.66–0.76) in 2005–2009. The entire increase in risk of revision due to infection was within 1 year of primary surgery, and most notably in the first 3 months. The risk of revision due to infection increased in all 4 countries. Risk factors for revision due to infection were male sex, hybrid fixation, cement without antibiotics, and THA performed due to inflammatory disease, hip fracture, or femoral head necrosis. None of these risk factors increased in incidence during the study period.

Interpretation We found increased relative risk of revision and increased cumulative 5–year revision rates due to infection after primary THA during the period 1995–2009. No change in risk factors in the NARA dataset could explain this increase. We believe that there has been an actual increase in the incidence of prosthetic joint infections after THA.

The outcome of hip replacement surgery and the survival of implants have improved during the last decades (Herberts and Malchau 2000, Liu et al. 2009, Fevang et al. 2010). However, an increase in the risk of revision due to infection after THA has also been reported in recent years (Kurtz et al. 2008, Dale et al. 2009, Pedersen et al. 2010b). We wanted to assess whether the increase in risk of revision due to infection is a common feature in the Nordic countries, and we therefore assessed time trends and risk factors for revision due to infection after primary total hip arthroplasty (THA) in the Nordic countries (Denmark, Finland, Norway, and Sweden). The aim was to compare revision rates due to infection in different time periods and different patient and implant groups, and to investigate factors that influence the risk of revision due to infection.

Materials and methods

The Nordic Arthroplasty Register Association dataset

The NARA dataset contains merged individual-based data from the Danish, Finnish, Norwegian, and Swedish arthroplasty reg-

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isters (Herberts et al. 1989, Havelin et al. 2000, Lucht 2000, Puolakka et al. 2001, Malchau et al. 2005, Havelin et al. 2009). In each register, the data selected were transformed according to a common set of definitions, and revisions were linked to the primary procedures. The data were de-identified nationally before the anonymous data were merged into the NARA dataset. The data were treated in full confidentiality and in compliance with the regulations of each country (Havelin et al. 2009).

The inclusion criteria in the present study were primary THAs and first revisions from the period 1995 through 2009, with complete information on the following parameters: year of primary surgery and first revision, age, sex, diagnosis (osteoarthrosis (OA), inflammatory hip disease, hip fracture, childhood hip disease, femoral head necrosis, or other diagnoses), prosthesis (monoblock or modular), and type of fixation (uncemented, cemented, hybrid, or inverse hybrid, with plain or antibiotic-loaded cement). Primary THA was defined as the first total hip prosthesis regardless of cause of the arthroplasty. The endpoint was revision due to infection, and revision was defined as removal or exchange of the whole or part(s) of the prosthesis. Infection as the cause of revision was determined and reported by the surgeon immediately after surgery, based on the preoperative clinical manifestations and samples in addition to peroperative evaluation. The national datasets were harmonized according to these definitions. Of the 459,540 primary arthroplasties in the NARA dataset, 7,450 resurfacing arthroplasties were not considered as THAs. Of the 452,090 THAs, 3,397 were excluded due to unknown type of fixation, as were 16,525 THAs due to incomplete information on the risk factors. 432,168 THAs met the inclusion criteria. Denmark contributed 83,853 primary THAs, Finland 78,106, Norway 88,455, and Sweden 181,754 (Table 1).

Table 1. Patient and procedure characteristics for the primary THAs included, and number of primary THAs excluded over the 3 time periods

	1995–1999	2000–2004	2005–2009	1995–2009
Number of THAs included	113,280	147,823	171,065	432,168
Age (%)				
<40 years	2	1	1	1
40–59 years	17	18	17	17
60–69 years	29	29	32	30
70–79 years	38	37	35	36
80–89 years	14	15	15	15
≥90 years	1	1	1	1
Sex (%) Female	63	62	61	61
Diagnosis (%)				
Osteoarthritis	76	80	83	80
Hip fracture	10	7	6	8
Inflammatory disease	5	4	2	4
Childhood hip disease	4	4	3	3
Femoral head necrosis	2	2	2	2
Other diagnoses	2	3	3	3
Prosthesis (%)				
Monoblock	22	10	2	10
Modular	78	90	98	90
Fixation (%)				
Uncemented	13	16	30	21
Cemented	76	71	56	67
Hybrid	10	10	6	9
Inverse hybrid	1	3	8	4
Cement (%)				
No cement	13	16	30	21
With antibiotics	71	79	69	73
Without antibiotics	15	5	1	6
Country (%)				
Denmark	14	20	22	21
Norway	23	21	19	20
Sweden	45	42	41	42
Finland	19	17	18	18
Number of THAs excluded	10,540	3,303	6,169	9,922 (4.4%)

Statistics

Descriptive statistics were used for presentation of the patient and procedure characteristics. Adjusted Cox regression analyses were performed to assess relative risk of revision due to infection and to estimate adjusted cumulative 5-year probability (risk) of revision. Unadjusted cumulative 5-year risks of revision due to infection were estimated by the Kaplan-Meier (KM) method. The study population was divided into 5-year periods (1995–1999, 2000–2004, and 2005–2009). The cases were observed until first revision, death, emigration, or December 31, 2010. We also investigated changes in the revision rates due to deep infection as a function of the year of operation, to give a graphical display of the relationship based on a generalized additive model for survival data (Hastie and Tibshirani 1990). Adjusted hazard rate ratios, as a measure of relative risk, were estimated, with 95% confidence intervals (CIs) for time periods and risk factors. In the Cox analyses we adjusted for age, sex, diagnosis, modularity of the prosthesis, and fixation, and the influence on revision risk of each of these factors was assessed. Separate Cox analyses were performed on a homogenous subgroup of hips with cemented modular THAs with antibiotics in the cement on patients with OA, as this combination was common throughout the 3 time periods in all 4 countries.

The Cox survival analyses were performed with 1–16 years of follow-up, but the last time period had only 1–6 years of follow-up. To ensure that there was similar follow-up for operations in all 3 time periods, we performed additional analyses with follow-up restricted to 1–6 years for each time period. In addition, we performed separate time trend analyses of revision due to infection for men and women, all age groups, and groups of diagnoses separately. Also, the risk factors were studied in each country separately. Finally, we assessed the risk factors separately within each of the 3 time periods to

Table 2. Relative risk of revision due to infection of primary THAs in the NARA with 1–16 years of follow–up. Adjusted for age, sex, diagnosis, prosthesis, and cement

	Period	Number of THAs included	Number of THAs revised due to infection	Adjusted risk ratio for revision due to infection	95% confidence interval	p–value
All THAs	1995–1999	113,280	778	1		
	2000–2004	147,823	937	1.1	1.0–1.2	0.03
	2005–2009	171,065	1,063	1.6	1.4–1.7	<0.001
Uncemenxted THAs	1995–1999	15,177	87	1		
	2000–2004	23,553	147	1.4	1.0–1.8	0.03
	2005–2009	51,445	308	1.9	1.5–2.5	<0.001
Cemented THAs	1995–1999	86,177	538	1		
	2000–2004	105,421	641	1.2	1.1–1.3	0.006
	2005–2009	96,455	619	1.7	1.5–2.0	<0.001
Hybrid THAs	1995–1999	11,369	149	1		
	2000–2004	15,163	125	0.8	0.6–1.0	0.02
	2005–2009	10,390	63	0.8	0.6–1.1	0.2
Inverse hybrid THAs	1995–1999	556	4	1		
	2000–2004	3,685	24	1.3	0.4–4.0	0.6
	2005–2009	12,775	73	1.6	0.5–4.6	0.4
Cemented modular THAs with antibiotics in cement inserted due to OA [a]	1995–1999	37,848	208	1		
	2000–2004	69,052	374	1.1	0.9–1.3	0.2
	2005–2009	75,929	467	1.7	1.4–2.0	<0.001

[a] Adjusted for age and sex.

minimize time-dependent confounding. Additional Cox analyses with the endpoints revision due to aseptic loosening and revision for any cause were performed to relate these to our findings on revision due to infection.

The analyses were performed in accordance with the guidelines for statistical analyses of arthroplasty register data (Ranstam et al. 2011). The proportional-hazard assumptions of the Cox survival analyses were not completely fulfilled. We therefore assessed the proportionality of the main risk factors by smoothed Schoenfeld residuals (Figure 3) (Ranstam et al. 2011). This resulted in assessment of the risk factors before and after 1 year, since adjusted revision rates of the 3 time periods were not fully proportional. Potential overestimation of incidence of revision due to infection through the effect of competing risks (death and revision due to causes other than infection) was assessed by the cumulative incidence function (Gillam et al. 2010). The 3.9% of THAs that were revised for causes other than infection and the 21% of THA patients who died during the follow-up had a negligible effect on the Cox analyses.

Bilateral THAs are not independent observations, but were included. The extent of bilaterality was estimated to be 18% and the incidence of revision due to infection was 0.6% in both the first and second hip. Only 0.05% of the bilateral THAs were identified to have had revisions due to infection in both hips. We therefore considered bilaterality to have a negligible influence on the results (Lie et al. 2004, Ranstam and Robertsson 2010, Ranstam et al. 2011).

Values of $p < 0.05$ were considered to be statistically significant. SPSS software version 18.0 and the R statistical software package were used for the analyses.

Results

2,778 primary THAs (0.6%) were revised due to deep infection. The cumulative 5-year revision rate due to infection, adjusted for year of primary surgery, was 0.62% (0.60–0.65) for the study population and 0.99% (0.83–1.15) for the excluded THAs (4.4% of the total). The implants at use had changed during the study period. In the last 5-year period, there were more uncemented THAs and inverse hybrid THAs and nearly all of the cemented THAs were modular and inserted with cement containing antibiotics (Table 1). There were only minor changes in the distribution of patient-related risk factors over the study period, with the exception that fewer THAs were performed due to inflammatory disease and hip fracture later in the study period (Table 1).

Time trend of revision due to infection

The risk of revision due to infection increased in the period 2005–2009 relative to the period 1995–1999 in the total study population (Table 2; Figures 1 and 2), and in each of the 4 countries separately (Denmark: RR = 1.3 (CI 1.0–1.6); Norway: RR = 1.7 (1.2–2.3); Sweden: RR = 1.5 (1.2–1.9); and Finland: RR = 1.2 (1.0–1.5)). For the period 2000–2004, the risk of revision due to infection only increased in Norway (RR = 1.3 (1.1–1.6)). The overall cumulative 5-year revision rate due to infection also increased, despite the fact that the revision rate for the period 2005–2009 might be an underestimate due to incomplete 5-year follow-up (Table 3 and Figure 1). The subgroup of cemented modular THAs with antibiotic-loaded bone cement in OA patients showed similar results (Tables 2 and 3; Figures 1 and 2).

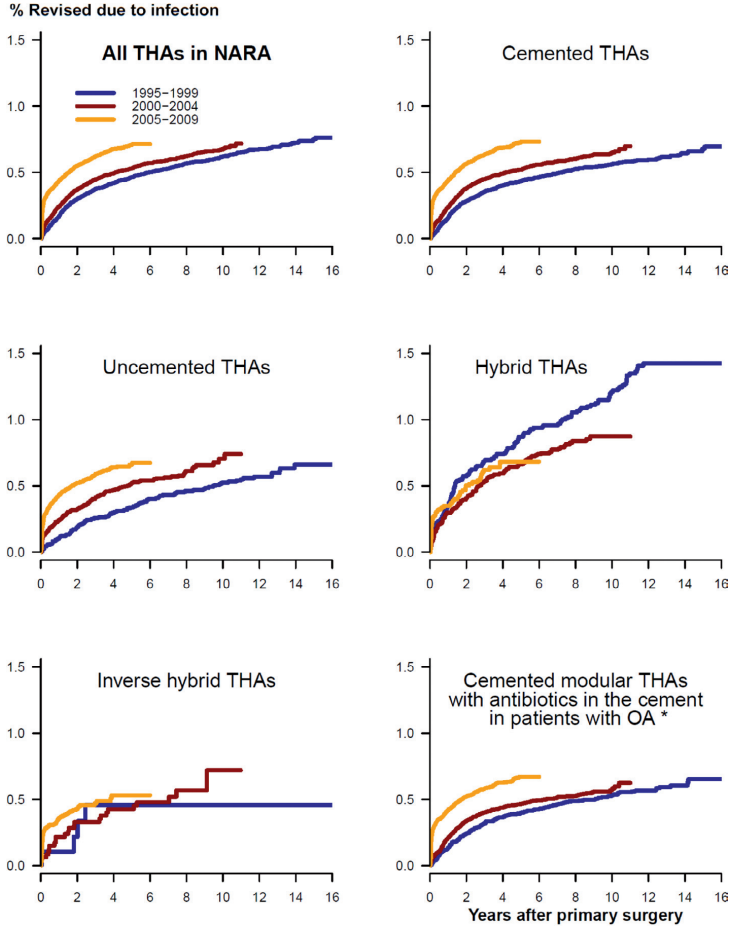

Figure 1. Adjusted cumulative revision rates for THAs revised due to infection in 3 time periods of primary surgery, for all THAs (upper left panel) and 5 subgroups of THAs. Adjusted for age, sex, diagnosis, prosthesis, and cement. *Adjusted for age and sex only.

The entire increase in risk of revision due to infection occurred within 1 year of primary surgery, and most notably within the first 3 months after surgery (Table 4; Figures 1 and 3). The increased risk of revision due to infection was found for cemented and uncemented THAs, but not for hybrid THAs and inverse hybrid THAs (Table 2; Figures 1 and 2). The increase in risk of revision due to infection was more gradual through the time periods for uncemented THAs than for cemented THAs, where the main increase in relative risk of revision and cumulative 5-year revision rate was in the last time period (Tables 2 and 3; Figures 1 and 2).

The risk of revision due to infection increased similarly for men and women, in all age groups and for the different diagnoses, as well as for the excluded cases.

Time trend of revision due to aseptic loosening and revision for any cause

The adjusted cumulative 5-year revision rate due to aseptic loosening was lower in 2000–2004 and 2005–2009 than in 1995–1999, but the last time period did not have complete 5-year follow-up and would have been an underestimate (Table 3). For uncemented THAs, the cumulative 5-year revision rate due to aseptic loosening did not improve during the study period (Table 3). For revisions due to any cause, there was no improvement in cumulative 5-year revision rate during the study period, except for hybrid THA, despite the incomplete 5-year follow-up in 2005–2009 (Table 3). Compared to other methods of fixation, cemented THA had the lowest cumulative 5-year revision rate for any cause in 2005–2009 (Table 3).

Risk factors for revision due to infection

Male sex and THA performed due to inflammatory disease, hip fracture, or femoral head necrosis were the patient-related risk factors associated with increased risk of revision due to infection (Table 5). Implant-related risk factors that increased the relative risk of revision due to infection were hybrid fixation and plain bone cement (Table 5). The findings were similar when we assessed the risk factors within each time period separately and before and after 1 year after primary surgery. The exception was patients of advanced age at primary THA, who had a higher risk of revision due to infection within the first year after surgery, whereas they had a lower risk of revision due to infection more than 1 year postoperatively.

Discussion

Our main finding was the higher risk of revision due to infection after primary uncemented and cemented THAs in the 4 Nordic countries for the period 2005–2009 than for the period

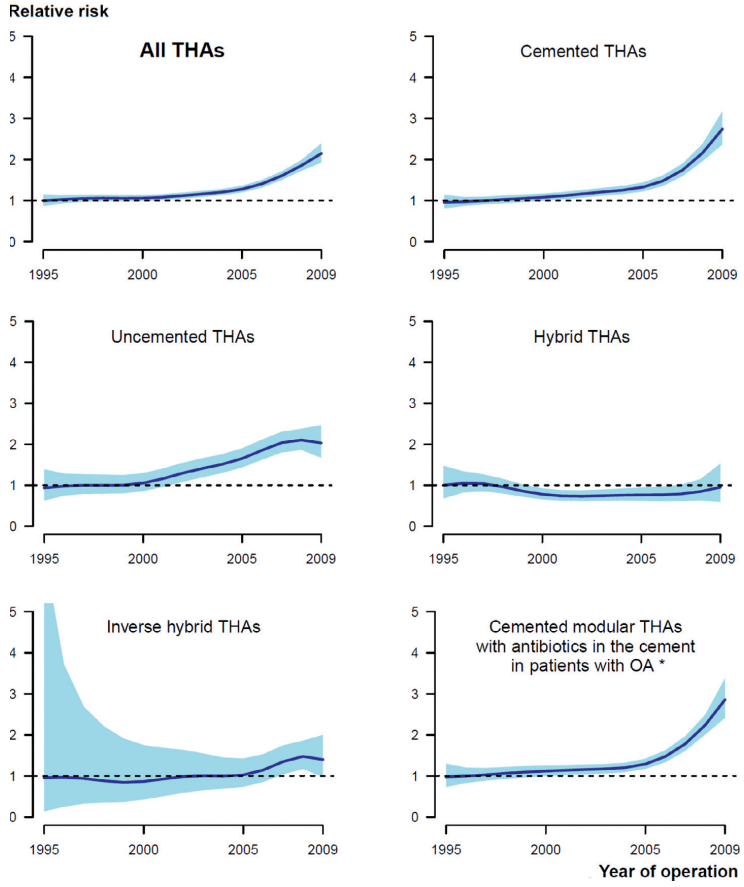

Figure 2. Graphical display of the relationship between year of primary surgery and relative risk of revision due to infection (with 95% CI), for all THAs (upper left panel) and 5 subgroups of THAs. The broken lines represent no difference in relative risk from the beginning of the period (RR = 1). Adjusted for age, sex, diagnosis, prosthesis, and cement. *Adjusted for age and sex.

1995–1999. This confirms earlier reports from Norway and Denmark (Dale et al. 2009, Pedersen et al. 2010b). The cumulative 5-year revision rate due to infection was also higher in 2005–2009 than in the previous 2 time periods. This was the case even though the revision rates for 2005–2009 probably were underestimates due to the incomplete 5-year follow-up, and they might therefore have been expected to be even higher.

None of the risk factors that we assessed could explain the increased risk of revision due to infection. The incidence of unfavorable risk factors (male sex, hybrid fixation, cement without antibiotics, and THA performed due to inflammatory disease, hip fracture, or femoral head necrosis) did not increase during the study period. In addition, these confounders were adjusted for in the analyses. An increased incidence of prosthetic joint infection would therefore have to be caused by factors that are not registered in the NARA dataset. These may include changes in patient-related factors (i.e. more comorbidity), changes in microbiology (i.e. increased bacterial virulence or more resistant strains), or changes in surgery-related factors (i.e. duration of surgery or changed surgical technique).

The common NARA dataset contains only limited information on comorbidity, which is a well-documented risk factor for infection after THA (Ridgeway et al. 2005, Pulido et al. 2008, Pedersen et al. 2010b, Dale et al. 2011). If THA was performed on more patients with poor health in the later parts of the study period, an increased incidence of prosthetic joint infections could result. In Norway, the comorbidity at THA increased during 2005–2009 (The Norwegian Arthroplasty Register 2010). The incidence of specific comorbidities associated with increased risk of infection after THA, like obesity and diabetes, is increasing in several countries (Pedersen et al. 2010a, Danaei et al. 2011, Haverkamp et al. 2011, Mraovic et al. 2011, Doak et al. 2012, Iorio et al. 2012). Given that the THA patients reported to the NARA are representative of the general population, an increased incidence of prosthetic joint infections requiring revision could result.

Surgery-related risk factors such as duration of surgery, and timing and type of systemic antibiotic prophylaxis are also not included in the NARA dataset. However, both short and long duration of surgery have been shown to be risk factors for infection (Ridgeway et al. 2005, Pulido et al. 2008, Dale et al. 2009, Pedersen et al. 2010b, Dale et al. 2011). Less compliance to guidelines for optimal systemic prophylaxis could also have contributed to an increased incidence of prosthetic joint infections, as could an increase in bacterial resistance to antibiotic prophylaxis (Kerttula et al. 2007, Stefansdottir et al. 2009a, b, Lutro et al. 2010). Finally, changes in operation room ventilation or changed adherence to guidelines of prophylactic routines may also have influenced the trend of revision due to infection (National Institute of Health and Clinical Excellence (NICE) 2008, Dale et al. 2009).

Table 3. Adjusted cumulative 5-year revision rates of primary THAs in the NARA. Adjusted for age, sex, diagnosis, prosthesis, and cement

	Period	Number of THAs included	Cumulative 5-years revision rate							
			Kaplan–Meier infection		Adjusted infection		Adjusted aseptic loosening		Adjusted all revisions	
All THAs	1995–1999	113,280	0.54	(0.49–0.58)	0.46	(0.42–0.50)	1.41	(1.34–1.49)	3,34	(3.22–3.45)
	2000–2004	147,823	0.57	(0.53–0.61)	0.54	(0.50–0.58)	0.81	(0.77–0.86)	3.01	(2.92–3.10)
	2005–2009 [b]	171,065	0.73	(0.68–0.77)	0.71	(0.66–0.76)	1.00	(0.93–1.07)	3.30	(3.19–3.41)
Uncemented THAs	1995–1999	15,177	0.36	(0.26–0.45)	0.34	(0.25–0.44)	1.32	(1.13–1.50)	4.39	(4.05–4.72)
	2000–2004	23,553	0.55	(0.45–0.65)	0.52	(0.43–0.61)	0.85	(0.73–0.97)	4.28	(4.02–4.54)
	2005–2009 [b]	51,445	0.70	(0.61–0.78)	0.65	(0.57–0.74)	1.21	(1.08–1.34)	4.24	(4.02–4.45)
Cemented THAs	1995–1999	86,177	0.51	(0.47–0.56)	0.43	(0.38–0.48)	1.34	(1.25–1.43)	2.82	(2.70–2.94)
	2000–2004	105,421	0.56	(0.51–0.60)	0.52	(0.48–0.57)	0.74	(0.68–0.79)	2.53	(2.43–2.63)
	2005–2009 [b]	96,455	0.74	(0.68–0.81)	0.74	(0.67–0.80)	0.85	(0.77–0.94)	2.93	(2.80–3.07)
Hybrid THAs	1995–1999	11,369	0.94	(0.76–1.12)	0.88	(0.70–1.06)	1.82	(1.55–2.09)	4.92	(4.50–5.34)
	2000–2004	15,163	0.72	(0.58–0.85)	0.67	(0.53–0.80	0.98	(0.81–1.14)	3.79	(3.48–4.10)
	2005–2009 [b]	10,390	0.72	(0.54–0.90)	0.67	(0.50–0.85)	1.00	(0.75–1.25)	3.86	(3.41–4.31)
Inverse hybrid THAs	1995–1999	556	0.77	(0.02–1.51)	0.36	(0–1.38)	2.36	(0.97–3.75	5.59	(3.65–7.54)
	2000–2004	3,685	0.53	(0.29–0.77)	0.34	(0–1.27)	1.64	(1.19–2.09)	3.98	(3.31–4.64)
	2005–2009 [b]	12,775	0.66	(0.50–0.83)	0.43	(0–1.58)	1.37	(1.02–1.72)	3.67	(3.20–4.14)
Modular THAs with antibiotics in cement in patients with OA [a]	1995–1999	37,848	0.43	(0.36–0.49)	0.40	(0.33–0.46)	1.18	(0.67–1.69)	2.60	(2.44–2.77)
	2000–2004	69,052	0.49	(0.44–0.55)	0.47	(0.41–0.52)	0.69	(0.39–0.99)	2.21	(2.10–2.32)
	2005–2009 [b]	75,929	0.71	(0.64–0.77)	0.67	(0.60–0.73)	0.78	(0.44–1.12)	2.60	(2.46–2.75)

[a] Adjusted for age and sex.
[b] Cumulative 5-year revision rates probably were underestimates due to incomplete 5-year follow-up.

Table 4. Adjusted relative risks of revision due to infection for 4 different time intervals after primary surgery, for the 3 time periods. Adjusted for age, sex, diagnosis, prosthesis, and cement

Time after primary surgery	Number of THAs included	Number of THAs revised due to infection	Adjusted risk ratio for revision due to infection	95% CI	p–value
0–3 months					
1995–1999	113,280	74	1		
2000–2004	147,823	175	1.9	1.4–2.4	<0.001
2005–2009	171,065	535	4.8	3.7–6.2	<0.001
3–12 months					
1995–1999	111,607	142	1		
2000–2004	145,625	206	1.3	1.0–1.6	0.05
2005–2009	168,019	216	1.2	1.0–1.5	0.09
1–2 years					
1995–1999	109,178	164	1		
2000–2004	142,589	195	1.1	0.9–1.3	0.6
2005–2009	164,758	175	1.0	0.8–1.3	0.9
> 2 years					
1995–1999	105,338	398	1		
2000–2004	138,270	361	0.9	0.8–1.1	0.5
2005–2009	126,131	137	0.9	0.7–1.1	0.2

Other confounders not reported to the NARA may have contributed to an increase in reporting of revision due to infection to the registers without reflecting a corresponding increase in true incidence of prosthetic joint infection. Such confounders could be improved reporting of revisions due to infection, changes in revision policy and in the threshold of revision (i.e. new surgical methods), or changes in diagnostics (i.e. improved microbiological detection methods and changed definitions) (Dale et al. 2009, Pedersen et al. 2010b).

Since 2000, in Norway there has been an increase in the reporting of minor revision procedures, such as soft tissue debridement procedures with exchange of removable parts of modular implants and retention of the femoral stem and acetabular cup (Engesæter et al. 2011). Such procedures were reported to the registers as revision procedures because prosthesis parts were exchanged. These minor revisions may have different indications or a lower threshold to be performed than full exchange revisions. Such minor revisions may also be performed and reported earlier postoperatively than full exchange revisions. This may be the reason for the increased risk of revision due to infection in the first year after primary surgery, as found for the latter 2 time periods. In addition, similar operations performed on monoblock prostheses would not be reported because heads and liners were not exchanged. We adjusted for this potential under-reporting of infected monoblock prostheses in the analyses. In addition, the minor partial revisions were most likely used as alternatives to complete exchange procedures

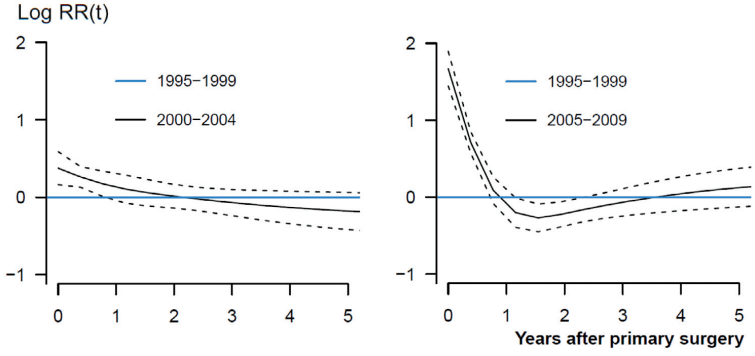

Figure 3. A graphical display of the relationship between relative risk of revision due to infection and time after primary THAs for the period 2000–2004 (left panel) and 2005–2009 (right panel) compared to 1995–1999 (blue lines). Smoothed Schoenfeld residuals adjusted for age, sex, diagnosis, prosthesis and cement (solid lines) with 95% confidence intervals (broken lines).

rather than alternatives to no revision at all. This is supported by the finding of a higher risk of revision due to infection in 2005–2009 than in 1995–1999 both for the uncemented THAs, which were all modular, and for the more homogenous subgroup of modular THAs inserted with cement containing antibiotics in patients with OA. In addition, in Norway the incidence of major revision due to infection increased during 1995–2009 as well (Engesæter et al. 2011). Thus, we do not think that increased use of modular implants and the changes in revision policy could explain the increased risk of revision due to infection.

There have been improvements in the diagnostics of prosthetic joint infections. Some bacteria such as coagulase-negative staphylococci have been increasingly acknowledged for their pathogenicity (von Eiff et al. 2006). In addition, improvements in bacterial sampling and identification may also have increased the number of infections being identified preoperatively (Trampuz and Widmer 2006, Moojen et al. 2007). The clinical presentation of an aseptic loosening and a low-grade periprosthetic infection may also be similar (Tunney et al. 1998, Ince et al. 2004, Moojen et al. 2010). If

Table 5. Adjusted relative risks and adjusted cumulative 5–year revision rates for risk factors for revision due to infection. All risk factors were adjusted mutually for the other risk factors in addition to the year of primary surgery. Follow–up in the risk analyses was 1–16 years

	Number of THAs included	Number of THAs revised due to infection	Adjusted risk ratio for revision due to infection	95% confidence interval	p–value	Adjusted cumulative 5-years revision rate, infection
Age (years)						
<40	5,590	39	1			0.47
40–51	74,107	515	1.1	0.8–1.5	0.6	0.59
60–69	129,134	854	1.1	0.8–1.5	0.7	0.58
70–79	157,292	1,021	1.1	0.8–1.5	0.6	0.62
80–89	63,034	337	0.9	0.7–1.3	0.8	0.52
≥90	3,011	12	0.7	0.4–1.4	0.3	0.32
Sex						
Female	266,42	1,312	1			0.46
Male	165,748	1,466	1.9	1.8–2.1	<0.001	0.87
Diagnosis						
Osteoarthritis	345,925	2,090	1			0.54
Hip fracture	33,572	327	2.1	1.9–2.4	<0.001	1.12
Inflammatory disease	15,771	118	1.4	1.1–1.7	0.001	0.72
Childhood hip disease	14,983	80	0.9	0.7–1.2	0.6	0.51
Femoral head necrosis	9,671	92	1.7	1.4–2.1	<0.001	0.87
Other diagnoses	12,246	71	1.3	1.0–1.6	0.06	0.65
Prosthesis						
Modular	388,371	2,475	1			0.58
Monoblock	43,797	303	1.1	1.0–1.3	0.09	0.69
Fixation						
Uncemented	90,177	542	1			0.54
Cemented	288,053	1,798	1.1	1.0–1.2	0.09	0.58
Hybrid	36,922	337	1.6	1.4–1.8	<0.001	0.79
Inverse hybrid	17,016	101	1.0	0.8–1.3	0.7	0.53
Cement						
With antibiotics	316,072	1,997	1			0.58
Without antibiotics	25,921	239	1.5	1.3–1.8	<0.001	0.96

knowledge and awareness changed during the study period, there may have been a corresponding change in reporting of infection as the cause of the revision. Unexpectedly positive peroperative bacterial samples would be identified postoperatively and would not be reported to the registers. Some prosthetic joint infections may therefore have been erroneously registered as aseptic loosening in the NARA, but possibly to a lesser extent in the later stages of the study period due to improvements in diagnostics.

Our finding of increased risk of revision due to infection, which is the definition of infection used by the NARA, most probably reflects a true increase in incidence of prosthetic joint infections. To our knowledge, there have been no publications on time trends of the incidence of prosthetic joint infections after primary THA. Kurtz et al. (2008) reported a 2-fold increase in overall incidence of deep infection after THA from 0.66% in 1990 to 1.23% in 2004. This study on "total infection burden" was based on aggregated data, without any linkage between primary THA and revision after discharge and with both primary and revision arthroplasty included in the analyses. For primary THAs only, the authors found a reduced incidence of infection, most probably due to shorter length of hospital stay.

Another manifestation of infection after THA is surgical site infection, which a subject of interest in large infection surveillance programs. The definition of surgical site infection is wider than those of prosthetic joint infection and revision due to infection: the risk pattern is different and the follow-up is more limited than in arthroplasty registers (HELICS 2004, Dale et al. 2011). It may be that the treatment strategy for early postoperative soft tissue infections has become more aggressive in recent years, resulting in an increased revision rate. However, only one fifth of the surgical site infections reported to the Norwegian Surveillance System for Healthcare Associated Infections after primary THAs were reported to the Norwegian Arthroplasty Register for revisions due to infection in the period 2005–2009 (Dale et al. 2011). Both revision due to infection and surgical site infection will be surrogate endpoints of true prosthetic joint infections (Parvizi et al. 2011).

The Dutch National Nosocomial Surveillance Network (PREZIES) reported a decrease in surgical site infections after primary THA between 1996 and 2006 (Mannien et al. 2008), as did the British mandatory surveillance of SSI between 2004 and 2010 (Health Protection Agency 2011). Capture of surgical site infections is highly dependent on length of stay after primary THA or type and length of post-discharge surveillance (Huotari and Lyytikainen 2006). For instance, low-grade prosthetic joint infections, presenting as pain and loosening of the implant at a later stage, will generally be missed in surveillance programs for surgical site infection. The reported decrease in the incidence of surgical site infections may therefore be due to shorter length of stay and limited post-discharge surveillance, and not to a reduction in the incidence of prosthetic joint infections in need of revision (Mannien et al. 2008, Health Protection Agency 2011).

A previous study from Norway found that uncemented THAs had a higher risk of revision due to infection than cemented THAs (Dale et al. 2009). A study from Denmark, in contrast, found that cemented THAs had higher risk of revision due to infection than uncemented THAs (Pedersen et al. 2010b). In the present study, the overall risk of revision due to infection was similar for cemented, inverse hybrid, and uncemented THAs.

We found an incidence of revision due to infection of 0.6%; it is therefore a relatively rare complication after THA. Large populations are required for the study of time trends and risk factors for such rare events. The large NARA dataset offers an opportunity for in-depth studies of revision due to infection even in subgroups with sufficient power. The data are prospective and have a high degree of completeness (Soderman et al. 2000, Pedersen et al. 2004, Espehaug et al. 2006). The completeness of the NARA dataset and the small proportion of cases excluded in the present study (4.4%) also indicate that there was minimal selection bias, even if the relative risk of revision due to infection was higher in the excluded group. The time trend of revision due to infection was similar for the included cases and the excluded cases. The number of variables in the NARA dataset is limited, however, and even though we adjusted for several well-known confounders in our analyses, unmeasured confounding would still be a problem.

Considering the size and quality of the NARA dataset, and the adjustment for several clinically important risk factors, we believe that there has been a true increase in the risk of prosthetic joint infections. The largest increase in relative risk of revision due to infection was for uncemented THAs, but the overall risk of revision due to infection was similar for cemented, uncemented, and inverse hybrid THAs. Male sex, hybrid fixation, cement without antibiotics, and THA performed due to inflammatory disease, hip fracture, or femoral head necrosis were risk factors for revision due to infection.

HD and AMF performed the analyses. HD wrote the manuscript. All the authors contributed to interpretation of the analyses and to critical revision of the manuscript.

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