THE DEPARTMENT OF CLINICAL SCIENCES, DANDERYD HOSPITAL

Karolinska Institutet, Stockholm, Sweden

IMPROVING THE QUALITY OF CARE FOR HIP FRACTURE PATIENTS

STUDIES ON FAST-TRACK TO SURGERY AND ADVERSE EVENTS

Paula Kelly-Pettersson

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IMPROVING THE QUALITY OF CARE FOR HIP FRACTURE PATIENTS: STUDIES ON FAST-TRACK TO SURGERY AND ADVERSE EVENTS

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By

Paula Kelly-Pettersson

Principal Supervisor:
Associate Prof. Olof Sköldenberg, MD, PhD
Karolinska Institute
Department of Clinical Sciences
Danderyd Hospital
Division of Orthopaedics

Co-supervisor(s):
Bodil Samuelsson, RN, PhD
Karolinska Institute
Department of Clinical Sciences
Danderyd Hospital
Division of Orthopaedics

Professor André Stark, MD, PhD
Karolinska Institute
Department of Clinical Sciences
Danderyd Hospital
Division of Orthopaedics

Olav Muren, MD, PhD
Karolinska Institute
Department of Clinical Sciences
Danderyd Hospital
Division of Orthopaedics

Opponent:
Associate Professor Anna Nilsdotter MD, PhD
Lund University
Faculty of Medicine
Department of Clinical Sciences
Division of Orthopaedics

Examination Board:
Associate Professor Pelle Gustafson
Karolinska Institute
Department of Learning, Informatics, Management and Ethics (LIME)

Associate Professor Liisa Byberg, MD, PhD
Uppsala University
Department of Surgical Sciences, Orthopaedics

Associate Professor Ann-Charlotte Falk, RN, PhD
Karolinska Institute
Department of Neurobiology, Care Sciences and Society
Division of Nursing

For Anders

ABSTRACT

Hip fractures in the elderly are common and are associated with high comorbidity and mortality. Their care and treatment present challenges for nurses and other healthcare professionals and impose a substantial burden on healthcare resources.

The general aim of this thesis was to examine how a new enhanced fast-track system to operation, waiting time to surgery, and depression influence outcomes in patients after hip fracture, with particular interest in adverse events.

In study I, we examined the effects of the implementation of a new enhanced fast-tracking system for the management of hip-fracture patients compared to an already existing system in 415 patients. Data was collected prospectively and a record review was carried out. Our results showed that the time to surgery was reduced by an average of 3 hours in patients admitted via the new fast-track system compared to the existing system. We found no difference in the 3-month mortality or the length of stay (LOS) between the groups. There was a trend toward a lower incidence of adverse events (AEs) in the invention group at 3 months, but this difference did not reach statistical significance. We were able to show that the introduction of an enhanced fast-track management system to surgery could reduce waiting time to surgery for this patient group.

In study II, we investigated how waiting time to surgery influenced the risk of serious adverse advents (SAEs) in patients with hip fracture and how time affected risk. A retrospective record review was conducted. Outcomes were the occurrence of SAEs, the LOS and one-year mortality rate. A cohort of 576 patients was included (577 hip fractures) in the study. We found that around 20.6% suffered at least one SAE during the hospital stay (range 1-5). Risk of SAE increased by 12% with every 10 hours of waiting time and the length of the hospital stay was prolonged by 0.6 days with every 24 hours of waiting time to operation. No optimal cut-off times for waiting time to surgery were found and no correlation between waiting time to surgery and one-year mortality. Those patients at greatest risk of SAEs were patients with pre-existing health problems, males and those with subtrochanteric fractures.

In study III we explored the incidence, preventability and nature of adverse events occurring in hip-fracture patients up to 90 days after surgery. A structured retrospective record review, using the Swedish version of Global Trigger Tool methodology was carried out on prospectively collected data from 163 patients. Sixty-two of the patients (38%) suffered at least one AE during their hospital stay and up to 90 days post-operatively (range 1-7). The most common types of AEs were infections such as pneumonia and urinary tract infections, but pressure ulcers and AEs associated with surgery were also common. AEs were more common in older patients and those with pre-existing health conditions. About 60% of these AEs were judged to be preventable.

In study IV, we investigated the influence of depression on patient-reported outcome up to one year after hip fracture. A cohort of 162 patients with intact cognitive function were included into either the depression or control group and were followed from baseline, to 3-months and 12-months. Using questionnaires, patients reported on their pain levels, hip function and quality of life. The depression group had significantly poorer hip function at baseline but this had improved at 3-months. The depression group experienced a lower health-related quality of life at baseline compared to the control group. At 12 months, neither group had returned to their pre-fracture level of function. Both groups experienced a decline in their health-related quality of life. The one-year mortality rate was higher in the depression group compared to the control group but the difference was not statistically significant. In this study we did not find that depression had a bearing on patient-reported outcome one year after hip fracture in patients without cognitive impairment.

In conclusion, the results of these studies demonstrate that the introduction of a new fast-track can reduce waiting time to surgery. Long waiting time to surgery is correlated with increased risk for SAEs and prolonged hospital stay. No optimal cut-off times exist, the risk for SAEs increases linearly over time. Patients at greatest risk of suffering SAEs are those with a higher American Society of Anaethesiologist's (ASA) classification score, males and those with subtrochanteric fractures. We have also shown that many hip-fracture patients suffer AEs and the majority of these are preventable. We found no correlation between the presence of depression pre-fracture and poorer functional outcome one year after hip fracture.

Key Words: Hip fracture, adverse events, preventable adverse events, retrospective record review.

SAMMANFATTNING (SUMMARY IN SWEDISH)

Att drabbas av höftfraktur är vanligt speciellt bland äldre och är förenat med hög samsjuklighet och dödlighet. Vård och behandling utgör därför utmaningar för sjuksköterskor och annan vårdpersonal och tar en betydande del av vårdresurserna inom ortopedisk och geriatrisk vård.

Det övergripande syftet med avhandlingen var att undersöka hur ett nytt snabbspår till kirurgi, väntetid till operation och depression kan påverka patientutfall, med särskilt intresse för skada på patienten.

I studie I, undersökte vi effekterna av införandet av ett nytt snabbspår för det preoperativa omhändertagandet av patienter med misstänkt höftfraktur jämfört med ett redan existerande. I studiekohorten ingick 415 patienter med verifierad höftfraktur. En journalgranskning på prospektivt insamlade data gjordes. Resultaten visade att tid till operationen minskades med i genomsnitt tre timmar hos patienter som följde det nya snabbspåret jämfört med det befintliga. Vi fann ingen skillnad i 3-månaders mortalitet eller vårdtidens längd mellan grupperna. Det fanns en trend mot en lägre förekomst av skador på patienter i gruppen som ingick i det nya snabbspåret efter tre månader. Vi kunde visa att införandet av det nya snabbspåret inför kirurgi kan minska väntetiden till operation för denna patientgrupp.

I studie II undersöktes hur väntetid till kirurgi påverkade risken för allvarliga skador hos patienter med höftfraktur. En retrospektiv journalgranskning gjordes. Utfallsvariablerna var förekomst av allvarlig skada under vårdtiden, vårdtidens längd och mortalitet ett år efter kirurgi. I studien inkluderades 576 patienter (577 höftfrakturer). Vi fann att 20,6% av patienterna drabbades av minst en allvarlig skada under vårdtiden (1-5 skador per drabbad patient). Risken för allvarlig skada ökade med 12% för varje period om 10 timmars väntetid och längden på vårdtiden ökade med 0,6 dagar för varje dygns väntetid. Inga optimala gränser för väntetid till kirurgi hittades, inte heller någon korrelation mellan väntetid till operation och mortalitet inom ett år efter kirurgi. De patienter som hade störst risk att drabbas av allvarliga skada var de med redan existerande komorbiditet, män och patienter med subtrochantära frakturer.

I studie III var syftet att undersöka förekomst, typ och unvikbarhet avseende skador som inträffade hos patienter med höftfraktur upp till 90 dagar efter operation. En strukturerad retrospektiv journalgranskning gjordes med hjälp av Markörbaserad journalgranskning på prospektivt insamlade data från 163 patienter. Av dessa drabbades 62 (38%) av minst en skada som var relaterade till det ortopediska vårdtillfället (1-7 skador per drabbad patient). Av de 102 identifierade skadorna bedömdes 61% vara undvikbara. De vanligaste typerna av skador var infektioner som urinvägsinfektion, sårinfektion och lunginflammation, men också trycksår och skador associerade till operation var vanligt förekommande. Äldre patienter och patienter med redan existerande komorbiditet drabbades i högre utsträckning av skador.

I studie IV undersökte vi om depression påverkade patientrapporterade utfall upp till ett år efter höftfrakturen. En kohort av 162 patienter med intakt kognitiv funktion inkluderades i en depressionsgrupp eller i en kontrollgrupp. Patientrapproterade data samlades in vid inklusion och efter tre respektive tolv månader. Patienterna fyllde i enkäter angående deras upplevda smärtnivåer, höftfunktion och livskvalitet. Depressionsgruppen hade signifikant sämre höftfunktion vid inklusion men detta förbättrades vid 3 månader. Depressionsgruppen upplevde en lägre hälsorelaterad livskvalitet vid inklusion jämfört med kontrollgruppen. Vid 12 månader hade ingen av grupperna återfått sin höftfunktion som före frakturen och båda grupperna upplevde en försämring av sin hälsorelaterade livskvalitet. Mortalitet efter ett år och förekomst av skada och allvarliga skada var högre i depressionsgruppen jämfört med kontrollgruppen men skillnaderna var inte statistiskt signifikanta. I denna studie fann vi att depression hos patienter med intakt kognitiv funktion inte hade påverkan på de patientrapporterade utfallen ett år efter höftfraktur.

Sammanfattningsvis visar resultaten av dessa studier att snabbspår till operation kan minska väntetiderna till operationen. Lång väntetid till kirurgi är korrelerad med ökad risk för SAE och förlängd sjukhusvistelsen. Inga optimala tidsgränser finns, risken för SAE ökar linjärt över tiden. Patienter med störst risk att drabbas av SAE är de med komorbiditet, män och de med subtrochanteriska frakturer. Vi har också visat att många patienter med höftfrakturer drabbas av skador och många av dessa bedöms kunna förebyggas. Vi hittade ingen korrelation mellan förekomsten av depression före fraktur och dålig funktionellt utfall ett år efter höftfrakturen.

Nyckelord: Höftfrakturer, skador på patient, vårdskador, journalgranskning

LIST OF SCIENTIFIC PAPERS

This thesis is based on the following four papers, which are denoted in the text using the Roman numerals I-IV:

I. ‘Straight to bed’ for hip-fracture patients: A prospective observational cohort study of two fast-track systems in 415 hips.
Martin Eriksson, Paula Kelly-Pettersson, André Stark, Anna K. Ekman, Olof Sköldenberg
Injury, International Journal of the Care of the Injured; 43 (2012) 2126-2131

II. Waiting time to surgery is correlated with an increased risk of serious adverse events during hospital stay in patients with hip-fracture: A cohort study.
Paula Kelly-Pettersson, Bodil Samuelsson, Olle Muren, Maria Unbeck, Max Gordon, André Stark, Olof Sköldenberg
International Journal of Nursing Studies; 69 (2017) 91-97

III. The identification of adverse events in hip-fracture patients using the global trigger tool: A prospective observational cohort study.
Paula Kelly-Pettersson, Olof Sköldenberg, Bodil Samuelsson, Andreas Stark Olav Muren, Maria Unbeck
Manuscript

IV. The influence of depression on patient-reported outcomes for hip-fracture patients 1 year after surgery: A prospective cohort study.
Paula Kelly-Pettersson, Bodil Samuelsson, Maria Unbeck, Olav Muren, Martin Magnéli, Max Gordon, André Stark, Olof Sköldenberg
Manuscript

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LIST OF ABBREVIATIONS

AE	Adverse Event
A&E	Accident & Emergency Department
ASA-score	American Society of Anaesthesiologist's classification of health status
ADL	Activities of Daily Living
BMD	Bone Mineral Density
CT	Computed Tomography
EQ-5D	EuroQol Health-Related Quality of Life (5 dimensions)
EUPAP	European Pressure Ulcer Advisory Panel
DAG	Directed Acyclic Graphs
GTT	Global Trigger Tool
HADS	Hospital Anxiety and Depression Scale
HHS	Harris Hip Score
ICU	Intensive Care Unit
ICH-GCP	International Conference on Harmonisation of Technical Requirements of Pharmaceuticals in Human Use-Harmonised Tripartite Guideline for Good Clinical Practice
IHI	Institute for Healthcare Improvement
LOS	Length of Stay
MRI	Magnetic Resonance Imaging
NCC MERP	National Co-ordinating Council for Medication Error Reporting and Prevention
PNRS	Pain Numerical Rating Scale
PROM	Patient-Reported Outcome Measures
RRR	Retrospective Record Review
RCT	Randomized Clinical Trial
RN	Registered Nurse
SAE	Serious Adverse Event
SPMSQ	Short Portable Mental Status Questionnaire
WHO	World Health Organization

1 INTRODUCTION

1.1 HIP FRACTURES

Hip fractures are one of the commonest fracture types occurring in the elderly worldwide[1]. There are differences in the incidence of hip fracture between countries; the lowest rates are recorded in African countries whilst the highest rates have been found in Scandinavia[2,3]. In 2012, the proportion of individuals 60 years and over in the global population was around 11% and this is predicted to rise to 20% by the year 2050[4]. As life expectancy increases and the proportion of elderly in the global population increases, the number of individuals at risk of sustaining an osteoporotic fracture is also expected to rise sharply in the future[5]. By 2025, it is estimated the number of hip fractures worldwide will reach 2.6 million, and this number is predicted to increase to 4.5 million by the year 2050[6].

The risk of suffering a hip fracture increases with advancing age[7]. In Sweden, approximately 18,000 individuals sustain a hip fracture each year, and almost half of these occur in patients aged between 80-89 years[8]. The number of hip fractures in Sweden is predicted to almost double by the year 2050[9]. In Norway too, the number is expected to rise, as a 22% increase is predicted by the year 2040[10].

There is a difference in the distribution of hip fractures between the sexes. They are more common in women[11] and this is related to both the post-menopausal osteoporotic changes in bone quality[12] and the longer life expectancy that women enjoy compared to men[5].

In Sweden, just over two-thirds or 68% of hip-fractures occur in women compared to 32% in men[8]. The average age at fracture is 83.4 years in women and slightly lower at 80.7 years in men, while the overall age is 82 years[8]. Over the last few decades, the proportion of hip fractures amongst men has increased[13], it has risen from around a quarter (28%) of the hip fractures in the 1990s to nearly a third (32%) of all hip fractures today[8].

1.2 CAUSES OF HIP FRACTURE

Hip fractures are normally caused by low-energy trauma. Usually from a fall, often indoors whilst the individual is engaged in daily activities such as walking, sitting or rising from a seated to an upright position[14-16]. They account for nearly one-fifth of all osteoporotic fractures[1]. Osteoporosis is a disorder of the skeleton associated with a decrease in the density of the bone. This results in a weakening of the bone tissue, causing it to become porous and fragile. This weakening or fragility of the bone leaves the individual susceptible to bone fracture. Osteoporosis is a common condition in post-menopausal women[17]. The World Health Organization (WHO)[18] defines osteoporosis as having a bone mineral density (BMD) score 2.5 standard deviations or more under the average value for young healthy women, that is a T-score of <-2.5 SD. Statistics from the WHO suggest that the lifetime risk for hip fracture is greater than 20% for women over 50 years of age in countries in the developed world, while for men the risk is approximately half this number[18]. Though the problem is potentially greater, as many patients who suffer fragility fractures have BMD scores above the level given in the WHO definition[19].

1.3 COMORBIDITY AND MORTALITY

Hip fractures are associated with high co-morbidity and mortality. It is a condition that predominately affects the elderly, who usually have pre-existing or underlying medical conditions[20-22]. Cognitive impairment is common in these patients[23-25] and can have a detrimental influence on outcome after hip fracture[26-28]. Male gender, increasing age and pre-existing health conditions reflected in a higher ASA score, have been shown to be factors that influence the in-hospital mortality[29]. The one-year mortality after hip fracture is high, studies have reported results ranging from between 14% to 36%[21,30-33]. Hip-fracture patients run double the risk of death in the first year post fracture compared to age-matched controls[34].

1.4 TYPES OF HIP FRACTURE

The hip joint is a ball and socket joint located at the proximal end of the femur. It is enclosed in the capsule, which is the soft tissue that surrounds the hip joint. Hip fractures are classified according to the anatomical position of the fracture on the femur bone i.e. intra-capsular or extra-capsular fractures. The most common hip-fractures are cervical, trochanteric and subtrochanteric fractures and the least common are the basocervical fractures. Cervical or femoral neck fractures are intra-capsular fractures, occurring below the head of the femur or in the neck of femur. Basocervical fractures occur in the region at the base of the neck of the femur, at its junction with the trochanter. The extra-capsular fractures are the trochanteric and subtrochanteric fractures. Trochanteric fractures occur in the area between the greater and lesser trochanters. Subtrochanteric fractures are breaks beneath the lesser trochanter and up to 5 cm lower down on the femur shaft (Figure 1).

Cervical fractures are the most common accounting for 51% of hip fractures, intertrochanteric fractures are the next largest group comprising 38%, the subtrochanteric fractures make up 8% of hip fractures while the least common is the basocervical fractures which accounts for about 3% of hip fractures[8].

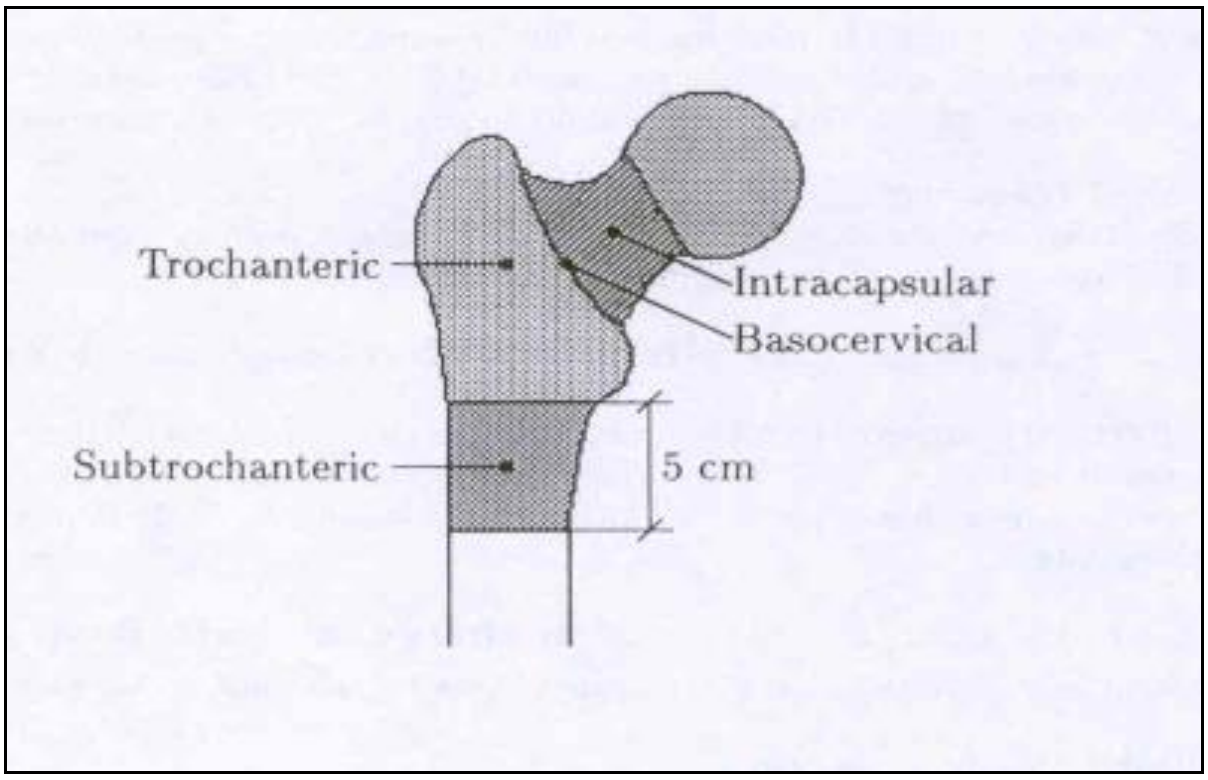

Figure 1. Types of fractures (Source: RIKSHÖFT).

1.5 TREATMENT AND NURSING CARE

The treatment of choice for hip fracture is surgery. Cervical fractures, if undisplaced, are usually treated using osteosynthesis with cannulated screws or pins, while displaced fractures are treated with either partial or total hip replacement, that is, a hemi- or total arthroplasty. Trochanteric and subtrochanteric fractures are treated with the dynamic hip screw or sliding screw fixation or the intramedullary nail.[8,35]

Sustaining a hip fracture is a devastating experience for the individual. It is invariably accompanied by pain, stress and loss of mobility and independence in the acute phase. It also can potentially adversely affect the individual's mobility, independence, quality of life and social functioning after the fracture. Patients with a hip fracture are a group that require a substantial amount of healthcare resources. As the treatment is surgery, all patients require admission to an acute care hospital, which necessitates pre-, per and post-operative care and rehabilitation. In Sweden, the cost of care and rehabilitation for these patients is around 1,5 billon Swedish crowns per annum[8].

The nursing care of these elderly patients focuses on the pre-operative, per-operative and post-operative phases of patient management. It encompasses assessing and providing adequate pain relief, reducing anxiety, preventing pressure ulcers, assessment of cognitive function and recognising and preventing escalation of acute confusional states. It also involves maintaining adequate fluid balance, assessing and promoting good nutrition, as well as monitoring and maintaining adequate elimination and helping to prevent urinary tract infections. The nursing care also includes monitoring and reporting any deterioration in the patient's condition and implementing measures to counteract this. Encouraging and facilitating mobilization post-operatively and promoting recovery and rehabilitation are also integral parts of their nursing management.[36-38]

The ultimate goal for the nursing care and medical treatment of patients with hip fracture is to return the individual back to their pre-fracture level of functioning and to their usual place of residence.

1.6 WAITING TIME TO SURGERY

In recent years, time to surgery has emerged as one of the major modifiable risk factors influencing complications in hip fracture patients[39]. Early surgery is associated with decreased risk for pressure ulcers and post-operative pneumonia[40] reduced length of hospital stay, and a reduction in complications and mortality[41]. Surgery within 12 hours significantly reduces the in-hospital mortality[42] and 30-day mortality[43] while delays of 48 hours or more have been found to increase the mortality risk[44,45]. No unfavourable outcomes of early surgery have been reported[41].

There are international recommendations for waiting time to surgery for hip fracture patients. The British, Australian and New Zealand recommendation is for surgery on the day of or day after admission[46,47]. The American guidelines advocate surgery within 48 hours of admission as it is associated with better outcomes[48]. In Sweden, the goal is for hip-fracture patients to undergo surgery on the day of their arrival or within 24 hours after their admission to hospital[35]. Although, some differences exist between these recommendations, the common denominator is timeliness to surgery.

1.7 FAST TRACK SURGERY

With the advent of new evidence-based knowledge over the last few decades regarding the care of patients undergoing surgery, the concept of fast-track surgery has been established[49]. It was developed as a comprehensive approach to care of the surgical patient, combining new concepts of patient information, advances in anaesthetic techniques and analgesics, as well as, minimally invasive surgery with a view to reducing stress and pain and enabling rapid recovery and rehabilitation after surgery[50]. It requires a multi-disciplinary and comprehensive approach toward patient care and management where new evidenced-based routines are incorporated into the standardized care of the patient[51]. Studies have shown that many traditional practices previously used in surgical care, were not supported by science, for example, routine use of drains after hip or knee joint replacement[52,53], complete bed rest[54], extended use of urinary catheters[55].

The initial fast-track concept encompassed the peri-operative and post-operative care of surgical patients. During the perioperative phase of care, it involves the use of prophylactic antibiotics, regional anaesthesia, minimally invasive surgery and maintaining body warmth during surgery. Post-operatively, the use of prophylactic anti-coagulant therapy, promotion of pain relief, reduction of nausea, correction of post-operative hypoxia and the commencement of early oral nutrition, all of which help to promote a satisfactory outcome for the patient.[50]

Fast-track surgery was first implemented in the care of patients undergoing elective or planned short-term surgery, but is now being used to facilitate early recovery and rehabilitation after major surgery, and the knowledge gained can even have application in acute trauma settings[56]. Today, the fast-tracking concept, in the form of optimized clinical pathways[57,58] and integrated care pathways[59,60] has been embraced in the care of hip-fracture patients. In some hospitals, orthogeriatric care is being incorporated into the pathways[61,62].

1.8 FAST-TRACK TO SURGERY AT DANDERYD HOSPITAL

1.8.1 The Hip Process

At Danderyd hospital fast-track to surgery was integrated into the acute management of hip-fracture patients in an effort to reduce waiting time to surgery and improve care. In 2006, the first fast-track system for the management of hip-fracture patients, the *Hip process* was implemented. The focus was on the reducing the time spent by patients in the Accident and Emergency Department (A&E), by rapid transport to the Radiology Department and then on to the orthopaedic ward. This was a multi-disciplinary and pan-departmental process involving staff from all hospital departments engaged in the care of these patients. Prior to its inception, the proportion of patients who underwent surgery within 24 hours was around 50%, and after its introduction this figure rose to around 75%.

Hip-fracture patients were not a prioritized group. Despite their age, fragility and comorbidity, traditionally they were regarded as sub-acute patients. Their surgery could be postponed to allow for surgery on more acute cases. In 2010, in Sweden this changed, as the focus altered and waiting time to surgery, specifically for hip-fracture patients, became an indicator of the quality of care delivered. The goal was that 80% of these patients would undergo surgery within 24 hours of arrival at hospital or economic sanctions would be incurred. This created the impetus and prompted the introduction, in early 2010, of a new improved system, the *Ambulance process.*

1.8.2 The Ambulance Process

This involved the incorporation of the ambulance personnel in the management process. Hip-fracture patients bypassed the A&E completely and were transported directly to the Radiology Department by ambulance personnel. To be eligible for admission via the *Ambulance process,* the patient had to meet specific criteria laid down in the checklist (Appendix 1). Initially, only one ambulance provider Samariten, had implemented the fast-track system. It was later adopted by all the ambulance providers transporting hip-fracture patients to Danderyd Hospital. Patients with a suspected hip fracture after a fall, presenting

with pain in the hip or groin and with the leg externally rotated were eligible to follow the *Ambulance process*.

Patients with head injuries, multiple fractures, those where diagnostic doubts existed, those with life threating conditions e.g. stroke, myocardial infarction, or those who had undergone previous hip surgery on the affected side were exempted from the *Ambulance process*.

The ambulance personnel gave initial analgesia. On arrival at the hospital the patient was registered and transported directly to Radiology for x-rays. An orthopaedic bed was taken to Radiology and the patient was transferred from the x-ray table to the bed and then transported to the ward. Pre-operative blood tests and electrocardiogram were taken by nursing staff on the ward. The admitting doctor assessed and admitted the patient on the ward. The advantages of this process were not only the time gained but also for the patient it entailed bypassing the stressful A&E environment. This meant the pre-operative care could begin sooner, for example, pressure ulcer prevention, optimization prior to surgery and pre-operative showering.

1.9 ADVERSE EVENTS

There are many definitions of a complication. It has been defined in the Oxford Dictionary[63] (p.177) as "a secondary disease or condition aggravating an already existing one" and in Balliere's Nurses' Dictionary[64] (p 90) as "an accident or second disease process arising during the course of or following the primary condition; may be fatal". In the literature there are also many classifications of complications, for example, major or minor, early or late, general or disease specific, but within the medical nomenclature there is no comprehensive standardized definition. The term adverse event (AE) has been used in clinical trials and in the fields of quality assurance and patient safety. In national and international studies, one common definition of an adverse event is "an unintended injury or complication, which results in disability, death or prolonged hospital stay and is caused by healthcare management rather than the patient's disease"[65,66]. The Swedish Patient Safety Act (SFS 2010:659)[67] defines a preventable adverse event as suffering, physical or psychological harm or disease as well as death which could have been prevented if adequate measures had been taken in the patient's contact with healthcare. Using these definitions, what we normally regard as a complication in healthcare, would be considered an adverse event but not necessarily a preventable adverse event.

In studies I and II, we have investigated the occurrence of AEs in patients with hip fracture in relation to fast track to surgery and waiting time to surgery and in study III we examined the types and preventability of AEs in these patients.

1.10 DEPRESSION AND HIP FRACTURE

Depression is a major health problem worldwide and the global estimate for suffers is around 300 million[68]. From a Swedish perspective the prevalence of depression is around 10.8% in the general population[69] and in 65- 80 year olds about 9.8%, with the largest proportion of suffers in the 75-80 year age group[70]. It often affects patients with conditions of the musculoskeletal system[71]

In elderly patients with hip-fracture, depression is common[72] and the occurrence has been reported to range from between 9% to 47%[73]. Depression has been associated with increased risk of mortality in hip-fracture patients[74,75] and combined with impaired cognitive status has been found to be a significant predictor of poorer outcomes in the recovery of these patients[76,77]. In addition, it has been reported that one out of every five individuals who are not depressed at the time of their hip fracture is likely to develop depressive symptoms after eight weeks[78].

While some studies have found that the presence of depression or depressive symptoms can adversely affect functional outcome after hip-fracture[76,79-83], other studies have not shown this association[84-87], so uncertainty still exists. The evidence is conflicting, and as the question is still a moot point further investigation is warranted.

2 AIMS

General Aim

The general aim of this thesis was to examine how a new enhanced fast-track system to operation, waiting time to surgery, and depression influence outcomes in patients after hip fracture, with particular interest in adverse events.

Specific Aims

Study I

To evaluate whether the implementation of an improved fast-tracking system for hip-fracture patients could reduce waiting time to surgery.

Study II

To investigate how waiting time to surgery influenced the risk of serious adverse events in hip-fracture patients during the hospital stay and to examine how the risk increased over time.

Study III

To explore the incidence, nature and preventability of adverse events occurring in hip-fracture patients up to 90 days after surgery.

Study IV

To examine the influence of depression on patient-reported outcome up to 1 year after acute hip fracture.

3 METHODS

3.1 DESIGN

Studies 1, III and IV were prospective observational cohort studies and study II was a retrospective observational single cohort study. All the studies were conducted at the Orthopaedic Department of Danderyd Hospital. This is one of the four large acute care hospitals servicing the Stockholm metropolitan area. It has a catchment area of approximately 500,000 inhabitants and around 650 hip-fracture patients are admitted to the hospital annually.

3.2 PATIENTS AND METHODS

3.2.1 Studies I, III and IV

The patients included in studies I, III and IV were included between 2010 and 2012 (Figure 2). In study I, 415 hip-fracture patients were included consecutively during the period April 2010 to January 2011. During this period, a new enhanced fast-tracking system for patients with suspected hip fracture had been implemented at Danderyd Hospital, thus patients were admitted to hospital either via the existing hip process or the new ambulance process. All patients admitted with a suspected hip-fracture were eligible for inclusion, no age limits were used and cognitive impairment was not en an exclusion criteria. Patients with dislocations, pelvic rim fractures, contusions, other lower extremity fractures, degenerative hip disease, peri-prosthetic and pathological fractures were excluded. Patients requiring either Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) scanning for diagnosis or those requiring stabilization in the Intensive Care Unit (ICU) pre-operatively were also excluded. Data was collected prospectively during the hospital stay and up to 3 months post-operatively. A record review was conducted to identify adverse events.

In studies III and IV, 163 patients who gave their informed consent to participate in the studies were included between 2010 and 2012. Patients with cognitive impairment, pathological or peri-prosthetic fractures were not eligible for inclusion. Those unable to speak or understand Swedish and those patients from other health authority districts were also ineligible. The study patients were followed up at 3 and 12 months after operation.

3.2.2 Study II

The 576 hip-fracture patients with 577 hip fractures were admitted consecutively between 1st June 2007 and 1st June 2008 (Figure 2). One patient suffered both a right and left hip-fracture during the inclusion period. All patients, including those with cognitive impairment, were eligible for inclusion. No age limits were imposed but those patients with peri-prosthetic

fractures or pathological fractures were excluded from the study. The patients' charts were reviewed for the occurrence of serious adverse events (SAEs) during the hospital stay.

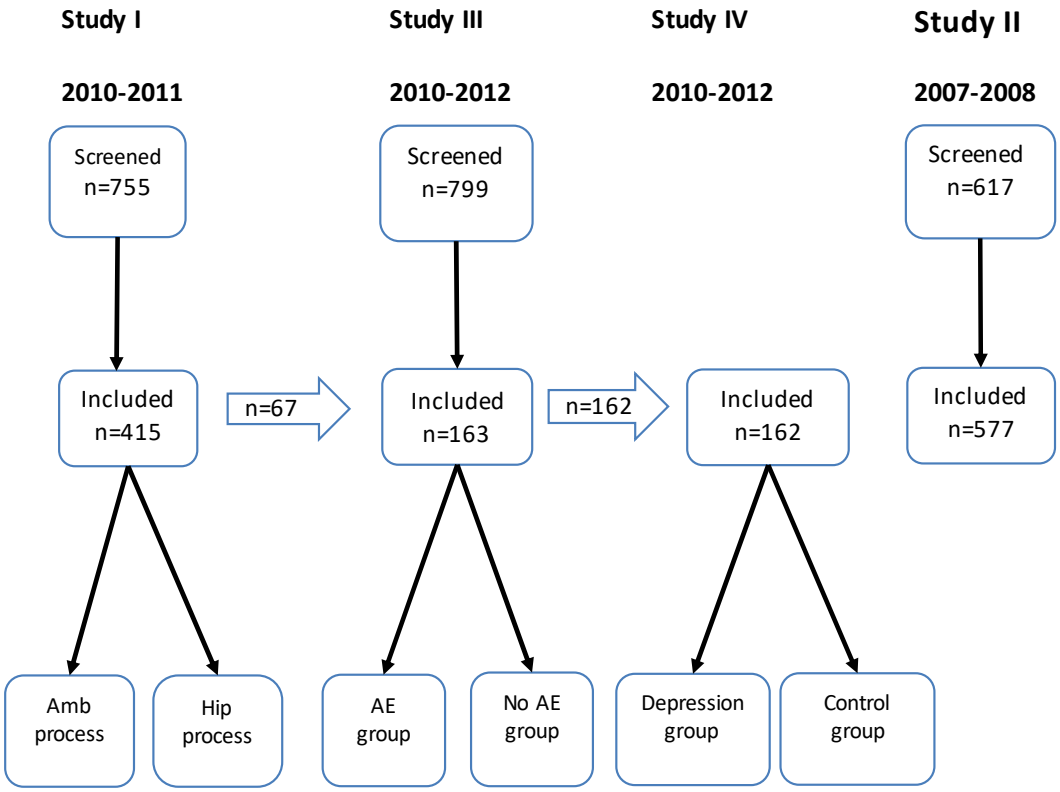

Figure 2. Flow diagram of the patients in the four studies.

3.3 DEFINITIONS

The World Health Organization definitions within patient safety for an adverse event (AE) and serious adverse event (SAE) were used in study I. An AE was defined as any unfavourable or unintended sign including abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure. An SAE was defined, as any medical occurrence that results in death, is life threatening, requires hospitalization, prolongs an existing hospitalization or results in persistent or significant disability.[88]

In study II, an SAE was defined as any unfavourable or unintended sign, symptom or disease associated with the use of a medical treatment or procedure and that also was either life-threatening, prolonged an existing hospitalization, resulted in death or in a persistent or significant disability or incapacity[89]

In study III, the definition of an adverse event used was based on the Swedish version[90] of the GTT methodology and was defined as suffering, physical harm or disease, as well as death related to the index admission which was not considered to be the inevitable consequence of the patient's underlying medical condition or treatment.

A preventable adverse was defined as an event which could have been prevented if adequate actions had been taken during the patient's contact with the healthcare system.

In study IV, depression was defined as ≥ 8 points on the HADS depression subscale and /or a diagnosis of depression irrespective of current use of anti-depressant medication at the time of inclusion.

3.4 OUTCOME VARIABLES

Study I

The primary outcomes in study I were the time in hours from arrival at the hospital to time of first incision and the proportion of patients undergoing surgery within 24 hours. The secondary outcomes were the 3-month mortality rate, the length of stay and the incidence of adverse events (AEs) and serious adverse events (SAEs). The reasons for delay to surgery were also examined.

Study II

The main outcome variables in study II were the occurrence of any SAEs during the hospital stay, the length of the hospital stay and the mortality rate at one-year post surgery.

Study III

The outcome variables in study III were the incidence of adverse events, the frequency of preventable adverse events, the types, severity and timing of adverse events. An estimate of the number of extra hospital days caused by these events was also calculated.

Study IV

The functional outcome variables in study IV were the modified Harris Hip Score (HHS), the pain numerical rating scale (PNRS), the quality of life score EQ-5D (3L) and the Hospital Anxiety and Depression Scale (HADS), depression subscale.

3.5 INSTRUMENTS

3.5.1 ASA Classification

Prior to surgery, the physical health status of the patient is assessed by the anaesthetist using the American Society of Anaesthesiologists' (ASA) classification [91]. This instrument gives an indication of the patient's health status pre-operatively. The score has 5 stages, each stage denoted by a number ranging from 1-5. A score of 1 indicates a normally healthy person, 2 indicates that the person is suffering from mild systemic disease, 3 indicates the presence of severe systemic disease, a score of 4 indicates severe systemic disease that is a constant threat to life whilst the highest score 5 indicates the person is seriously ill or moribund and is not expected to survive without surgery. All the patients included in the four studies were assessed as to their ASA score prior to surgery. The score was used as a proxy to indicate the level of the comorbidity the patient suffered.

3.5.2 Short Portable Mental Status Questionnaire (SPMSQ)

The Short Portable Mental Status Questionnaire SPMSQ [92] is a validated assessment instrument for screening cognitive function in different patient populations. It consists of 10 questions that test both short and long term memory and take between 1-5 minutes to complete. The questions are normally posed orally, but they can be completed in written form. In Sweden, it is usually referred to as the "Pfeiffer" test. The results range from 0-10; a score of 8-10 is indicative of an intact cognitive functioning, 6-7 indicates mild impairment, 3-5 indicates moderate impairment and 0-2 indicates severe cognitive impairment. It has been previously used in research relating to hip-fracture patients[26,93].

The 10 questions that constitute the test are the following:

1	What are the date, month and year?
2	What day of the week is it?
3	What is the name of this place?
4	What is your telephone number or address?
5	How old are you?
6	When were you born?
7	Who is the current prime minister?
8	Who was the prime minister before him or her?
9	What was your mother's maiden name?
10	Can you count backwards from 20 by 3's?

3.5.3 Pressure Ulcer Categorization

The European Pressure Ulcer Advisory Panel (EUPAP)[94] defines pressure ulcer as localized damage to the skin and or the underlying tissues, caused by pressure, or combined pressure and shear. The EUPAP categories for the classification of pressure ulcers are the following:

Category 1	Non-blanchable area with redness of intact skin, particularly over bony protuberances. Individuals with darker skin may not exhibit blanching. There may be pain, hardness, softness, warmth or coolness compared to surrounding tissue.
Category 2	Partial thickness loss of dermis showing as a shallow open ulcer with a pink wound bed without sloughing or as an intact or open serum filled blister. Skin tears, tape burns, perineal dermatitis, maceration or excoriation are not included in this category
Category 3	Full thickness tissue loss. Subcutaneous fat may be visible but not bone, tendon or muscle. Sloughing may be present but does not obscure the depth of tissue loss. May include undermining and tunneling.
Category 4	Full thickness tissue loss with exposed bone, tendon or muscle. Slough or eschar may be present on some parts of the wound bed. Often include undermining and tunneling.

The classification system was used in studies I, II and III to classify pressure ulcers identified as adverse events.

3.5.4 Charnley Classification

The Charley hip classification[95] is used to assess walking ability and it has three grades designated by the letters A, B, C. A indicates that one hip is involved, B both hips are involved but no other joints and C indicates that some other factor is contributing to impede normal walking ability, for example, hemiplegia, rheumatoid arthritis, Parkinson's disease or a cardiovascular or respiratory condition that impinges upon the patient's walking ability. A pre-operative value was used in the demographic data of studies III and IV.

3.5.5 Activities of Daily Living (ADL)

The Activities of Daily Living (ADL) index as described by Katz et al[96] was used to evaluate the level of the patients functional independence or dependence in carrying out six everyday functions: bathing, dressing, going to the toilet, transferring from bed or chair, continence and feeding. The indices range from A – G, where A indicates independence in all six activities, B indicates independence in all but one of the activities, C independent in all but bathing and one additional function, D independent in all but bathing, dressing, and one additional activity and through to index G which indicates dependence in all of the six functions. The ADL index was used to describe baseline characteristics in studies III and IV.

3.5.6 Patient-Reported Outcome Measures (PROM)

In recent years, in both healthcare and research there has been move toward using patient-centred outcomes and asking patients to evaluate elements of their own health, quality of life and functioning using questionnaires. The data collected is then used to assess how healthcare interventions and treatments impact on the everyday life of patients[97]. In study VI of this thesis, patients were asked to complete the following PROM questionnaires: Harris Hip Score, Pain numerical rating scale, EQ-5D 3L quality of life questionnaire, and the Hospital Anxiety and Depression Score.

3.5.7 Harris Hip Score (HHS)

The Harris Hip Score (HHS)[98] is a disease-specific instrument used to assess hip function and was initially developed for the evaluation of hip function in patients undergoing arthroplasty for traumatic arthritis after luxation or acetabular fractures.

The score is comprised of the following domains: pain; function; the absence of deformity and the range of motion. The pain domain indicates the severity of the pain experienced and its influence on normal activity, as well as the need for analgesia. The function domain covers daily activities (climbing stairs, sitting, putting on and taking off shoes and socks and using public transport) and gait (the presence and severity of a limp, the use of walking aides for support and walking distance). The absence of deformity domain covers hip flexion, adduction, internal rotation and leg length discrepancy. The range of motion assesses hip flexion, abduction, external and internal rotation and adduction.[98]

It has been used extensively in the evaluation of hip function in patients who have undergone hip arthroplasty and has been shown to be a valid and reliable score in the assessment of hip function in these patients[99].

The original HHS score gives a maximum of 100 points in the domains: pain (0-44 points); function (0-47 points); absence of disability (0-4 points) and range of motion (0-5 points). A high score indicates a better hip function. The domains of the score with the heaviest weighting are those of pain and function, giving at maximum 44 and 47 points. In its original form the orthopaedic surgeon carried out the assessment, but the instrument has since evolved into a self-reporting score for patients in which the surgeon–assessed absence of deformity and range of motion domains are not included. Excellent agreement has been found to exist between the modified self-reported version and the surgeon-assessed HHS[100]. The modified version has been validated for use in hip-fracture patients with neck of femur fractures[100,101]. In study IV of this thesis, the modified version of the HHS was used, where HHS is used as a self-reporting score and is completed by the patients. The maximum score that can be accrued is 91 points from the pain and function domains. For ease of comparison the score is then recalculated to maximum 100 points using a factor of 100/91 x individual score. The score is easily used and takes only a few minutes to complete (Appendix 2). This instrument was used in study IV to assess hip function at baseline, 3 and 12 months.

3.5.8 Pain Numerical Rating Scale (PRNS)

The Pain Numerical Rating Scale (PRNS) is a score used to assess levels of pain. It is a 10-point numeric scale ranging from 0 (no pain) to 10 (worst pain imaginable) and has been found to have a good correlation to other pain scores, for example, the visual analogue scale VAS [102]. The instrument is used widely and is quick to administer and easily used by patients. (Appendix 3) This instrument was used in study IV to assess pain levels.

3.5.9 EuroQol EQ-5D

The EuroQol 5-dimension (EQ-5D) is a generic or non-disease specific instrument developed by the EuroQol group[103,104] to measure health-related quality of life and health status. The EuroQol group is an international association of researchers from different academic fields interested in measuring and studying health status. The EuroQol consists of four sections: The first two, the health status questionnaire (EQ-5D) and the visual analogue scale (EQ-VAS) are used to collect data. Accompanying these are the valuation section and the background data section, which are used in evaluating the different states of health. The EQ-5D 3L[104] is a standardized questionnaire, which consists of 5 dimensions: pain/discomfort, usual activities, self-care, mobility, anxiety/depression, and for each dimension there are three levels or alternatives (3L), one of which best describes the patient's current situation. The alternatives indicate either no problems, some problems or severe problems. There is also a vertical visual analogue scale (EQ-VAS), which is used to register the patient's perceived current health status on a scale from 0-100, where 0 indicates the worst imaginable health status and 100 the best imaginable or optimal health status. The EQ-5D is widely used and has been translated into many languages, including Swedish[105]. The questionnaire, once completed, is scored by attaching set weights or values to each of the alternatives in each dimension, and then this is converted using a scoring algorithm to a single summary index. The value 1 indicates full health. Value sets of scores are available for representative samples of the general population in different countries, and it is against these that the index score is compared. (Appendix 4)

In study IV, the EQ-5D, 3L questionnaire with EQ-VAS was used. Today, a questionnaire with 5 levels or alternatives, the EQ-5D 5L[106] is available and is being taken into use.

3.5.10 Hospital Anxiety and Depression Scale (HADS)

The Hospital Anxiety and Depression Scale (HADS)[107] is a self-evaluating instrument consisting of a 14-item questionnaire that was initially used as a screening tool to assess and detect levels of anxiety and depression in patients in a primary health care setting. When developing the HADS instrument, items giving reference to somatic symptoms relating to physical disorders, for example, headache, dizziness or insomnia were excluded, as these could have other causes than emotional states. The creators also endeavoured to separate the concepts of depression and anxiety. The score was not intended as a tool for clinical diagnosis[108], as other clinical symptoms need to be assessed before a diagnosis can be made.

It consists of two subscales, each with 7 questions relating to depressive symptoms (HADS D) and 7 questions relating to anxiety (HADS A). Each question gives a four-point rating scale from 0-3, thus the subtotals for each of the subscales, anxiety and depression, can generate a score between 0-21 points (Appendix 5). The cut-off limits for the subscales of anxiety and depression[109] are categorized as follows:

0-7 points is within normal range and indicates no depression or anxiety

8-10 points indicates mild depression or anxiety

11-14 points indicates moderate depression or anxiety

15-21 points indicates severe depression or anxiety

The questionnaire is easily administered and takes around 2-5 minutes for patients to complete. The results of subscales can be used independently[110,111]. Although HADS has not been validated specifically for hip-fracture patients, it has been widely used and in a Swedish population sample has been found to be useful in gauging the presence of depression and anxiety symptoms[112,113]. In addition, a large meta-analysis of 747 articles examining the validity of the instrument showed it to perform well in the assessment of symptom severity for both depression and anxiety states in the general population, as well as for patients assessed in medical, psychiatric and primary care settings[114]. The HADS D subscale was used in study IV.

3.5.11 Structured Record Review

The structured review of records is an established methodology widely used in studies to detect the occurrence of AEs[115]. It involves using a structured method to peruse patient records to identify AEs with the assistance of predetermined screening criteria or the use of triggers. Retrospective record review (RRR) was utilised in studies I, II and III. In study III the Swedish version of the Global Trigger Tool[90] methodology was used.

3.5.12 Global Trigger Tool (GTT)

The Global Trigger Tool (GTT) is a methodological instrument first developed in 2003 by the Institute for Healthcare Improvement (IHI), Cambridge Massachusetts, and subsequently updated with a second edition in 2009[116,117]. It is used for conducting record reviews of medical charts to detect, measure and monitor the occurrence of AEs. The GTT was initially developed to monitor AE rates over time and measure the effectiveness of patient-safety interventions[118,119]. The GTT has been used internationally for retrospective reviews in patient safety initiatives, initially within hospital care[120-122], but it is now spreading to other healthcare settings[123,124].

This method involves screening patient records using a structured review process to search for predefined triggers, which act as pointers or clues indicating the occurrence of a potential AE. The GTT has 6 modules into which the triggers are grouped. The modules are the following: care, medication, surgical, intensive care, perinatal, emergency department. (Appendix 6)

The record review process has two stages, and involves carrying out an initial review by the primary reviewer who scans the record searching for the triggers. This process normally takes up to 20 minutes. The secondary reviewer's task is to adjudicate on whether the potential adverse event actually constitutes an AE. Once it is judged that an AE has occurred, the reviewers then assign a category of harm to the event using the severity ratings from E-I as described by the National Co-ordinating Council for Medication Error Reporting and Prevention (NCC MERP) [125]. There are 5 categories: category E – temporary harm to the patient; category F – temporary harm requiring an initial or prolonged hospitalization; category G – permanent harm to the patient; category H – intervention required to save life; category I – contributed to patient death.

The definition of an AE used in the original version of GTT is an "unintended physical injury resulting from or contributed to by medical care that requires additional monitoring, treatment or hospitalization, or results in death"[116].

The Swedish version of GTT[90] *(markörbaserad journalgranskning)* used in studies normally has 44 triggers but in this study only 38 triggers were used, as the perinatal triggers were superfluous. The Swedish version is based on the original GTT methodology, but has been further developed. The Swedish Patient Safety Act[67] requires judgements to be made as to the preventability of an AE. The Swedish version of GTT has thus incorporated the concept of preventability into its terminology. A preventable AE is defined as an event, which could have been prevented if adequate actions had been taken during the patient's contact with the healthcare system. A 4-point scale is used to assess the preventability of the AE. (1 indicates the AE was not preventable, 2 that the AE was probably not preventable, 3 indicates the AE was probably preventable, and 4 that the AE was preventable). A score of 3 or 4 indicates a preventable AE. AEs that would be judged as preventable are for example: (1) a patient with deep vein thrombosis who did not receive routine thrombosis prophylaxis postoperatively, (2) all pressure ulcers, category 1-4 are considered preventable, (3) Urinary tract infections in patients where indwelling catheters were not removed within 2 days of insertion as per routine guidelines (4) Urinary retention with ≥1000 ml in the bladder or two occasions during the admission with ≥ 500 ml is considered harmful and preventable (5) Joint dislocation or luxation of the hip joint post-operatively are AEs and deemed to be preventable.

4 STATISTICAL METHODS

An overview of the statistical methods used in the four studies

	Study I	Study II	Study III	Study IV
Pearson's Chi-square	X		X	X
Independent Student's t-test	X	X	X	X
Kolmogorov-Smirnov test	X			
Levene's test	X			
Cox & Snell R square test		X		
Nagelkerke R square test		X		
Logistic regression	X	X		
Linear regression				X
Piecewise logistic regression		X		
Cohen's kappa value		X	X	

The statistical analysis for study I was carried out using the statistical software PASW Statistics software for Windows (SPSS Inc., Chicago IL, USA). The analyses for study II were conducted using R3.3.1 for Macintosh with the segmented package version 0.5-0.0 for the piecewise logistic regression. For studies III and IV the analyses were done using SPSS software for Macintosh (SPSS, Chicago Illinois) version 25.0.

In all the studies a p-value of <0.05 was considered statistically significant and a 95% confidence interval (CI) was accepted for the level of the uncertainty estimate. The mean, median, standard deviation, range, mean difference and percentages were used for descriptive purposes. Proportions were given in percentages.

In study I, the Kolmogorov-Smirnov and the Levene's tests were used to test for normality and homogeneity of variance of the data. For categorical variables Pearson's Chi-square test was used to detect differences between the ambulance and control groups. In some instances, it was necessary to dichotomize variables, for example, time to surgery < 24hrs or > 24hrs. Differences in continuous data were tested using Student's t-test, for example, time to surgery in hours, length of stay in days.

In study I, a multivariate logistic regression model was used to evaluate differences between the two groups and adjust for potentially confounding factors, for example, age, gender, ASA classification, cognitive impairment and surgical method. It was also used to calculate the adjusted risk for mortality and AEs.

A power analysis was conducted in study I, which determined that with a power of 85%, a sample size of 300 patients with 75% admitted via the hip process and 25 % via the ambulance process would be sufficient to yield a statistically significant result.

A logistic regression analysis was used in study II, to identify risk factors, which in combination with waiting time to surgery had the potential to increase the risk for SAEs. The Cox & Snell R Square and Nagelkerke R Square tests were used to test the robustness and fit of the logistic regression model. Both crude and adjusted figures are shown. For identification of possible optimal cut-off times for SAEs, a piecewise logistic regression or segmented regression was used in study II.

The Cohen's kappa value (κ) was calculated to test inter-rater reliability in the record reviews in studies II and III. It was calculated to assess the level of consensus achieved between pairwise reviewers when identifying AEs and SAEs. The kappa values indicate the following levels of agreement if $\kappa < 0$ poor, 0-0.20 slight, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 substantial, > 0.80 almost perfect [126,127]

In study III, comparisons between the groups (AE compared to no AE) were carried out using the Student's t-test, and comparisons of categorical data were tested using the Pearson's Chi-square test.

In study IV, the Student's t-test was used for scale data to detect differences in functional outcome between the groups (depression versus control group) and categorical data was tested with Chi-Square test. A linear regression model was used to test, identify and to adjust for factors that could influence the patient-reported outcome at one year.

5 ETHICAL CONSIDERATIONS

Ethical approval was obtained for all the studies from the Regional Ethics Committee in Stockholm at the Karolinska Institutet. The studies were conducted in accordance with the guidelines set down in the Helsinki Declaration[128]. Patients in study III and IV were asked to sign an informed consent form and gave their written permission to participate in the studies. The studies have the following registration numbers at the Ethics Committee.

Studies I, III and IV: 2009/1657-31/2, Amendment: 2010/685-32

Study II: 2010/81-31/3, Amendment 1: 2010/2029-32, Amendment 2: 2015/311-32

6 SUMMARY OF RESULTS

6.1 STUDY I

Patient flow and baseline data

A total of 755 patients were admitted via either the Hip or Ambulance process with a suspected hip fracture between April 2010 and January 2011. Of these, 311 patients had injuries or conditions other than a hip fracture. 3 patients required stabilization in the Intensive Care Unit (ICU) before surgery and were therefore ineligible to follow any of the admission processes and were not included. A further 26 patients were excluded, 5 patients who had suffered pathological fractures and 21 patients had experienced lengthy diagnostic delays due to the need for magnetic resonance imaging (MRI) or computed tomography (CT). (Figure 3)

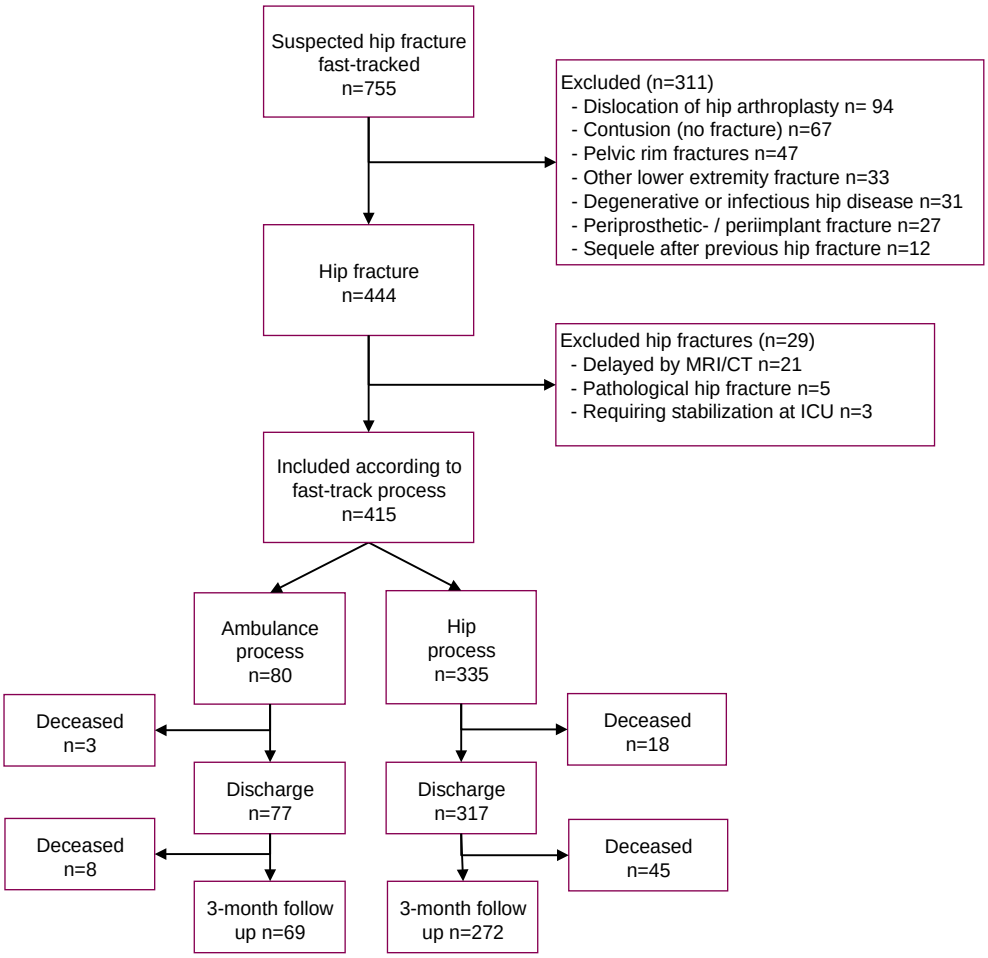

Figure 3. Flow of patients in study I

Primary Outcomes

The remaining 415 patients with a mean age of 83 years, of whom 292 (70.3%) were females, were divided into two groups depending upon which of the fast-track systems they were admitted to the orthopaedic ward; the Hip process (control group, n=335) and the Ambulance process (intervention group, n=80). There were no clinically significant differences between the groups at inclusion, although, there was a larger proportion of females in the Ambulance group 65 (81%) versus 227 (68%) in the Hip process group.

Table 1. Main results of study I

	Ambulance process ***(n = 80)***	**Hip process** ***(n = 335)***	**p-value** ***(p = 0.05)***
Time to Surgery (h) [a]	18 (4-47)	21 (4-72)	0.035
Proportion op < 24h[b]	70 (88)	250 (75)	0.015
Delays > 24h [c]			
Administrative	5 (50)	59 (69)	0.2
Medical	5 (50)	26 (31)	0.2
Length of stay [d]	6 (2-37)	6(1-51)	0.6
During admission			
Mortality [b]	3 (4)	18 (5)	0.6
AE [b, e]	49(61)	230 (69)	0.2
SAE [b, f]	12 (15)	65 (19)	0.4
3-months			
Mortality [b]	11 (14)	63 (19)	0.3
AE [b, e]	22 (28)	127 (38)	0.08
SAE [b, f]	16 (20)	83 (25)	0.4

[a] Mean (Range), p-value derived from Student's t-test. [b] n (%), p-value derived from Chi-square test.
[c] n (%) 10 patients delayed in Ambulance process & 85 in Hip process, p-value derived from Chi-square test.
[d] Median (Range), p-value derived from Student's t-test. [e] The AEs were death, pressure ulcers, pneumonia, any cardiac event, any thromboembolic event, wound infections, septicaemia, urinary tract infection or retention, acute renal failure, post-operative anaemia, dislocation or fracture, stroke, gastrointestinal bleeding, and any other minor medical complication. [f] The SAEs were death, pneumonia, acute myocardial infarction, cardiac failure, arrhythmi-as, pulmonary embolism, acute renal failure, stroke, gastrointestinal bleeding, p-value derived from Chi-square test.

Time to Surgery

The waiting time to surgery for all patients in the study was mean 20 hours (range, 4-72). The time to surgery was mean 3 hours ([95% CI 1 to 5]; p=0.035) shorter in the intervention

group and in this group, 88% (70/80) of the patients underwent surgery ≤ 24 hours compared to 75% (250/335) in the control group (Table 1). The risk ratio for surgery ≤24h was in favour of the intervention group (1.2 [95% CI 1.1 to 1.3]; p=0.014). After the multivariate logistic regression analysis was conducted, adjusting for age, gender, cognitive impairment, ASA-classification and type of surgery, the probability for surgery within 24 hours remained more favourable for the intervention group, with an odds ratio of 2.2 ([95% CI 1.1 to 4.5]; p=0.03).

Types of Delays

95 patients (85 control, 10 intervention) experienced a delay to surgery > 24 hours, 67% (64/95) of these delays were judged to be administrative delays and 33% (31/95) were determined to be medical delays. Administrative delays were more common in the control group. The most common reasons for administrative delays were either a surgeon, an anaesthetist or an operating theatre was not available. (Table 1)

Secondary Outcomes

Mortality and Length of Stay

The mortality rate at 3 months for all the patients was 18% (74/415) and similar results were found in both groups (intervention group 14% (11/80) versus control group 19% (63/335), p=0.3. The length of stay was median 6 days (range, 1-87) and did not differ between the groups. (Table 1) We found that age and ASA-class were significantly associated with increased risk of mortality, whereas surgery >24 hours was not (OR 1.4 [95% CI 0.8 – 2.5]).

Adverse events and serious adverse events

The incidence of AEs and SAEs during the hospital stay was 67% (279/415) and 19% (77/415) and did not differ between the groups. The incidence of AEs and SAEs at the 3-month follow-up was 36% (150/415) and 24% (99/415) respectively. There was a trend toward fewer AEs in the in the intervention group 28% (22/80) compared to the control: 38% (127/335) at 3 months, but this difference did not reach statistical significance (p=0.08). After adjusting for co-morbidity factors, age and ASA-class were found to be associated with increased risk for AE's, whereas the risk reduction for admission via the *Ambulance process* was no longer statistically significantly (OR 0.6 [95% CI 0.4 to 1.1]; p=0.1).

6.2 STUDY II

Baseline data

A total of 617 hip-fracture patients who were admitted consecutively to Danderyd Hospital were screened for inclusion in the study between June 2007 and June 2008. Patients with pathological fractures (n=6) and peri-prosthetic fractures (n=34) were excluded. The remaining 577 fractures in 576 patients were included in the study. The mean age was 82 years; the majority were women and most patients had pre-existing medical conditions (Table 2).

Table 2. Demographics for study II, n=577

Variable			
Age – years[1]		82	(10)
Sex[2] - n (%)	Female	418	72.4%
	Male	159	27.6%
American Society of Anaesthesiologists classification score (ASA)[2]	1 A normal healthy patient	20	3.5%
	2 A patient with mild systemic disease	199	34.5%
	3 A patient with severe systemic disease	307	53.2%
	4 A patient with severe systemic disease that is a	48	8.3%
	5 A moribund patient	3	0.5%
Cognitive dysfunction[2]	No	388	67.2%
	Yes	189	32.8%
Fracture type[2]	Femoral neck fracture	311	53.9%
	Intertrochanteric	222	38.5%
	Subtrochanteric	44	7.6%
Length of stay – days[1]		7	(6)
Time to surgery - hours[1]		29	(20)

[1] = mean (SD), [2] = n (%)

Outcomes

Serious adverse events and waiting time to surgery

A total of 119 patients (20.6%) suffered 397 SAEs during their hospital stay and the median number of SAEs for each patient was 1 (range, 1-5). The most common SAEs were respiratory infections, post-operative bleeding requiring major transfusions, cardiac and circulatory conditions and death.

The mean time to surgery for these patients was 29 hours, with a range from 4-167 hours. Every 10 hours of waiting time to surgery increased the risk for SAEs by 12% (odds ratio [OR] 1.12 [95%CI 1.02-1.23]). In addition, male sex (OR 1.7), increasing ASA classification (OR 2.3) and surgery for subtrochanteric fracture (OR 2.3) also increased the risk. (Table 3) The piecewise logistic regression model was unable to identify any optimal cut-off times for waiting time to surgery.

Table 3. Logistic regression for SAEs outcome for study II

	Crude		**Adjusted [a]**	
Variable	OR	2.5% to 97.5%	OR	2.5% to 97.5%
Time to surgery	1.16	1.06 to 1.27	1.12	1.02 to 1.23
Age (per 10 yrs)	1.27	1.03 to 1.58	1.22	0.96 to 1.55
Sex				
Female (ref)	1.00		1.00	
Male	1.59	1.03 to 2.45	1.69	1.06 to 2.67
ASA class (per increment)	2.43	1.77 to 3.35	2.26	1.62 to 3.17
Cognitive dysfunction				
No (ref)	1.00			
Yes	0.86	0.56 to 1.34	0.68	0.43 to 1.09
Fracture type				
Femoral neck (ref)	1.00		1.00	
Intertrochanteric	1.20	0.78 to 1.84	1.21	0.77 to 1.91
Subtrochanteric	2.30	1.16 to 4.58	2.32	1.13 to 4.79

[a] = Adjusted for age, sex, ASA classification, fracture type and the presence of cognitive dysfunction, ref = this is the reference group

Length of stay

The mean length of stay was 7.2 (range 44, 1- 45) days. We found that for every 24 hours of waiting time the length of stay after operation was increased by 0.6 days (p=0.016).

Mortality

The in-hospital mortality rate was 3.5% (n=20) and the one-year mortality rate was 23.4% (n=135). We found no correlation between waiting time to surgery and the one-year mortality rate.

6.3 STUDY III

Demographic data

The study cohort consisted of 163 patients, the majority were women (n =111, 68.1%) and the mean age was 76.4 ((±11.5) range 29.7-95.3) years. The majority of the patients had an ASA score in lower range 1-2. Cervical fractures were the most common type of fracture and arthroplasty (total or hemi) was the most frequent surgical treatment. The majority of patients were non-smokers, lived at home, cohabitated and were independent in the activities of daily living.

Statistically significant differences (p=<0.05) were found between the group of patients who experienced an AE and those who did not (Table 4). Those who suffered an AE were older, 80.4 (±11.5) compared to 74.0 (±11.8) years (p=0.001). They had an ASA score in the higher range i.e. 3-4 (59.7% compared to 37.6%) indicating a higher level of comorbidity. For patients who suffered AEs, the length of hospital stay (LOS) was longer 7.2 compared to 5.4 days, as was their time in surgery 75 compared to 63 minutes The time to surgery was comparable between the groups (AE group 20:34 versus No AE group 19:29 h:m) and no significant difference was found.

Table 4. Baseline demographics for study III

	Total group	**AE**	**No AE**	
	n =163	n=62	n=101	
Age, years				
Mean (SD)	76.4 (±11.5)	80.4 (±11.8)	74.0 (±11.8)	p = 0.001
Median (Range)	78.8 (29.7–95.3)	83.2 (29.7-91.7)	76.1 (46.0-95.3)	
Sex, n (%)				
Female	111 (68.1)	72 (71.3)	39 (62.9)	
Male	52 (31.9)	29 (28.7)	23 (37.1)	
ASA Class, n (%)				
1-2	88 (54.0)	25 (40.3)	63 (62.4	p=0.006
3-5	75 (46.0)	37 (59.7)	38 (37.6)	
Length of stay (LOS) days				
Mean, (M, SD) days	6.09 (±3.3)	7.2 (±4.4)	5.4 (±2.0)	p= 0.003
Median (Range)	6.0 (2.0 – 33.0)	7.0 (3.0-33.0)	5.0 (2.0-14.0)	
Operation time (min)				
Mean (SD)	67 (±36)	75 (±39)	63 (34)	p= 0.032
Median (Range)	63 (7-180)	72 (12-168)	60 (7-149)	

AE, adverse event; ASA, American Society of Anaesthesiologists' physical status classification system Independent t-test and Chi-square test, p=<0.05 statistically significant

Outcomes

Frequency, cumulative incidence, preventability and type of adverse events

A total of 102 unique AEs were identified in the records of 62 (38.0%) of the 163 patients (Figure 4). This corresponds to a mean 1.6 (median 1.0, range 1− 7) AEs per patient affected. Of the 102 AEs, 62 (60.8%) of these occurring in 38 (23.3%) patients were judged to be preventable. The most frequently occurring AEs were healthcare-associated infections, e.g. urinary tract infections and pneumonia. These accounted for 19.6% of the AEs identified and 65.0% of these were judged to be preventable. Pressure ulcers (18.6%), of which all were deemed to be preventable, were the next most common AE, followed by AEs related to surgery such as reoperation and fractures/fissures (14.7%) and acute confusional states (7.8%). Distension of the urinary bladder was also a common AE and in 57% of cases were judged to be preventable.

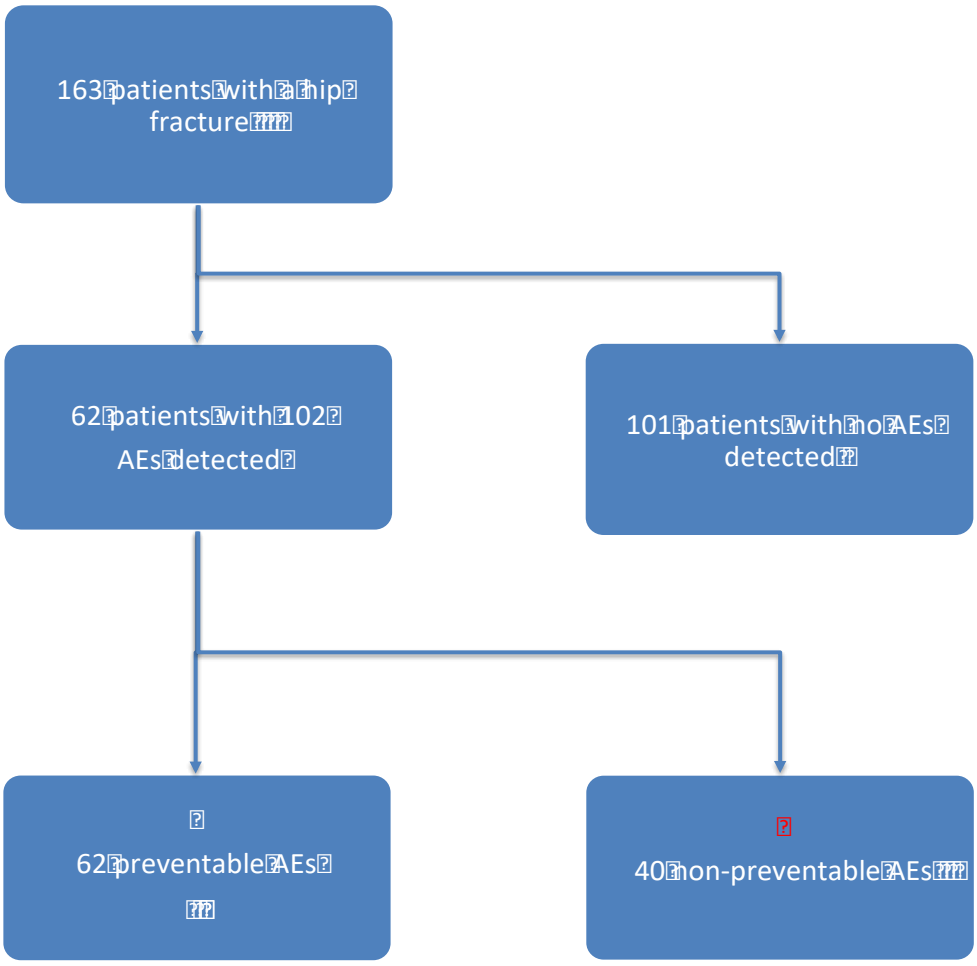

Figure 4. Flowchart of study III

Severity of harm

Of the total number of 102 AEs, the majority 84 (82.4%) were judged to have either caused temporary harm (n=58, 56.9%) or required outpatient care, hospitalization or prolonged an existing hospitalisation (n=26, 25.5%) (NCC MERP categories E and F). The remaining 18 AEs were judged to have caused permanent patient harm in 11 (10.8 %) cases, required an intervention to sustain life in 3 (2.9%) cases and in 4 (3.9%) cases contributed to the patient's death. All AEs in the H category were deemed to be preventable. (Table 5)

Table 5. Severity rating and preventability of AEs in study III

NCC MERP Category	All AEs n=102	Preventable AEs n=62
E: Temporary harm to patient	58 (56.9%)	40 (69.0%)
F: Temporary harm to the patient which required out-patient care, readmission or prolonged hospitalization	26 (25.5%)	10 (38.5%)
G: Permanent harm to patient	11 (10.8%)	7 (63.6%)
H: Intervention required to sustain life within 60 minutes	3 (2.9%)	3 (100.0%)
I: Contributed to patient death	4 (3.9%)	2 (50.0%)

AE, adverse event

Timing of adverse events

Most of the AEs, 86 (84.3%) of 102 occurred in the post-operative period, 7 (6.9%) AEs occurred in the pre-operative period and 9 (8.8%) occurred per-operatively.

Extra days

The estimated number of extra hospital days due to AEs was calculated at 185 days.

6.4 STUDY IV

Participants and descriptive data

Initially 163 patients were included in the study. One patient in the control group was excluded at surgery as this patient had both a fracture and a joint infection requiring a girdlestone operation. This operation limits the patient's ability to return to normal walking capacity in the short term until the infection is healed. As the main outcome was the return to functional capacity this patient was excluded. A total of 162 patients were included and the characteristics for the depression group (n=35) and control group (n=127) were similar with no statistically significant differences between the two groups in demographic data at baseline. Four patients withdrew from the study before the 3-month follow-up, 1 in the depression and 3 in the control group.

Outcomes and main results

The HHS scores for the depression group compared to the control were significantly poorer at baseline (85 vs. 91 points; p=0.021). At three months, this difference had levelled out (68 versus 69 points) and although the HHS had improved in both groups at 12 months, (74 versus 78 points), the patients did not regain their pre-fracture levels (Table 6). There was deterioration in hip function over time in both groups, a 13 point drop in the control group as opposed to an 11 point drop in the depression group from the baseline level. The depression group had a poorer function from the outset at baseline and this remained consistent throughout the study period.

A statistically significant difference in the EQ-5D scores at baseline was seen (0.85 vs. 0.73; p=0.011), the control group score was higher. The scores at both 3 and 12 months were somewhat lower than the baseline score, so patients in both groups experienced a decline in their quality of life over the duration of the study. (Table 6)

The PRNS scores were marginally lower in the depression group at baseline and 3-months indicating less pain was experienced pre-fracture in this group. By 12 months the depression group score was higher, although the differences never reached statistical significance. There were statistically significant differences between the groups in HADS Depression subscale throughout the study (Table 6).

Table 6. Differences in functional outcomes between the two groups during the study period.

	Control group Mean ± SD (n)	**Depression gr Mean ± SD (n)**	**Mean difference (95%CI)**	**P-value**
HHS				
Baseline	91 ± 11 (127)	85 ±13 (35)	5 (1 – 9)	**0.021**
At 3 months	69 ± 17 (120)	68 ±15 (32)	1 (-6 – 7)	0.852
At 12 months	78 ± 17 (117)	74 ±18(28)	3 (-4 – 10)	0.391
EQ-5D				
Baseline	0.85 ± 0.23 (127)	0.73 ± 0.26 (35)	-0.08 (-0.19 – 0.02)	**0.011**
At 3 months	0.71 ± 0.25 (121)	0.69 ± 0.22 (32)	0.02 (-0.07 – 0.12)	0.633
At 12 months	0.74 ± 0.26 (118)	0.66 ± 0.24 (30)	0,08 (-0.02 – 0.19)	0.117
PNRS				
Baseline	0.40 ± 1.6 (127)	0.38 ± 1.3 (35)	-0.25 (-0.94 – 0.45)	0.474
At 3 months	2.59±1.93 (120)	1.88 ±1.79 (32)	0.72 (-0.03 –1.46)	0.060
At 12 months	1.71 ± 1.86 (119)	2.04 ± 2.17 (28)	-0.32 (-1.12 –0.48)	0.426
HADS				
Baseline	2 ± 2 (127)	6 ± 3 (35)	-4.37 (-5.50 – -3.25)	**0.000**
At 3 months	2 ± 3 (118)	4 ± 0.79 (32)	-2.75 (-4.46 – -1.03)	**0.002**
At 12 months	2 ± 2 (114)	6 ± 3 (28)	-3.40 (-4.71 – -2.09)	**0.000**

Variables are presented as the mean with standard deviation and the mean difference is presented with 95% confidence intervals. P-values were derived from the Student´s T-test. HHS=Harris hip score, EQ-5D=European quality of life five dimensions, PNRS=pain numerical rating scale. HADS=Hospital Anxiety and Depression Score, depression subscale.

Linear regression model

Those factors that were found to influence the functional outcome at 1 year were the pre-fracture HHS and the pre-fracture EQ-5D score (Table 7). To which group the patients belonged did not affect the 1-year functional outcome. In the crude (unadjusted) model for HHS, we found a statistical significance for pre-fracture HHS score, age and ASA-classification but once the figures were adjusted only the significance of pre-fracture HHS remained. A similar pattern was seen in the model for the EQ-5D values. None of the variables tested in the model reached statistical significance with regard to the PRNS score.

Table 7. Linear regression model for functional outcomes at 1-year

	Crude			**Adjusted**		
Variable	Units	95% CI	P-value	Units	95% CI	P-value
Harris Hip Score						
Group	-3.2	-10.4 – 4.1	0.391	-0.6	-7.0 – 5.8	0.851
Pre-fracture score	0.7	0.5 – 0.9	**<0.001**	0.7	0.4 – 0.9	**<0.001**
Age	-0.3	-0.6 – 0.1	**0.007**	-0.2	-0.4 – 0.0	0.099
Sex	-2.2	-8.4 – 4.1	0.488	-1.6	-7.1 – 3.9	0.566
ASA	-8.6	-14.2 - -3.0	**0.003**	-1.1	-4.9 – 2.9	0.596
EQ-5D index						
Group	-0.08	-0.19 – 0.02	0.117	-0.02	-0.11 – 0.07	0.672
Pre-fracture score	0.52	0.37 – 0.67	**<0.001**	0.47	0.31 – 0.62	**<0.001**
Age	-0.00	-0.01 – -0.00	**0.016**	-0.00	0.01 – 0.00	0.230
Sex	-0.01	-0.01 – 0.08	0.888	0.01	-0.07 – 0.09	0.853
ASA	-0.16	-0.24 – -0.08	**<0.001**	-0.05	-0.11 – 0 00	0.063
PNRS						
Group	0.3	-0.5 – 1.1	0.426	0.3	-0.5 – 1.1	0.500
Pre-fracture score	0.2	-0.0 –0.5	**0.055**	0.2	-0.0 – 0.5	0.087
Age	-0.0	-0.0 – 0.0	0.642	-0.0	-0.0 – 0.0	0.654
Sex	0.2	-0.5 – 0-8	0.649	0.1	-0.6 – 0.8	0.702
ASA	0.2	-0.4 – 0.8	0.469	0.2	-0.5 – 0.9	0.584

[1] = Unstandardized Coefficients B, [2] = The models are adjusted for group (depression/no depression), age, sex and ASA classification. All outcomes are also adjusted by their pre-fracture status, e.g. the pre-fracture HHS is used as a co-variate in the model for HHS at 1 year, and the same applies for pre-fracture PRNS and EQ-5D values.

Adverse events

The occurrence of patient-reported AEs and SAEs during the study period was higher in the depression group compared to the control group but did not reach statistical significance. The AE rate for the depression group compared to the control group were 40.0% (14 of 35) versus 33.1% (42 of 127), p= 0.445. The pattern was similar for SAEs, with 45.7% (16 of 35) in depression group suffering at least one SAE compared to 33.9% (43 of 127) in the control group, p= 0.197.

Mortality

The 1-year mortality was 6.2% (10 of 162) and was higher in the depression group 11.4% (4 of 35), compared to the control group, 4.7% (6 of 127), (Chi-square test). This difference was not statistically significant (p=0.145).

7 METHODOLOGICAL CONSIDERATIONS

In study I, a prospective cohort design was used. When comparing two groups or a new intervention, a randomised clinical trial (RCT) would be considered a better alternative but because of the clinical situation, a randomized clinical trial design was not a viable option for us. Data was collected prospectively and a record review was carried out to identify AEs and SAEs.

The methodology used for data collection for AEs in studies I, II and III was retrospective record review. This is a well-recognized methodology, but it has some limitations; it relies heavily on the quality of the documentation and is both time and labour intensive. If the documentation is poor then the results will reflect this. Previous research has shown a discrepancy can exist between what is documented compared to the actual clinical situation[129]. There is potential for under-reporting, but despite this, it is considered to be a dependable, reliable and valid method to use for the identification of AEs[115,130,131] and is used widely.

The record reviews, in studies II and III were carried out by only one of the authors, which could incorporate observational bias. To control for any potential observational bias in the identification of AEs and SAEs in these studies, the inter-rater reliability was tested by a double check of a random sample of 20 medical records in each study. The Cohen's kappa value (κ) was calculated to assess the level of consensus achieved between pairwise reviewers when identifying AEs and SAEs. A monitoring process was used in study III. This ensured that the data was checked for correctness with respect to judgements about AEs, their severity and preventability.

For studies III and IV, the patient cohort was the same. These patients were asked to sign a consent form giving written consent for their participation. For study IV, patient-reported outcomes measures (PROM) were used for data collection and the patients completed questionnaires (PRNS, HHS, EQ-5D, HADS (D subscale)) at baseline, 3 and 12 months after surgery. Using PROM questionnaires allows for assessment of outcome from the patients' perspective. Their use excluded some patients from participation, for example, those unable to read or understand Swedish and patients with cognitive impairment. When we exclude patients from participation in studies, it is important to keep in mind that the results of the study are only applicable for the group studied. We cannot generalize our results to include the general hip-fracture population.

There is always a risk of recall bias when conducting research with questionnaires in the acute trauma setting. In contrast to elective surgery, where the patient can complete questionnaires prior to their surgery, patients included in trauma studies are required to recall their baseline information from before the fracture or event. There is no way of avoiding this, but it is important to be aware of the problem.

The use of questionnaires can present other methodological challenges. Questionnaires normally have a span within the alternatives. Questionnaires with specific alternatives have the inherent problem of ceiling and floor effects. These occur when a large proportion of the respondents in a study either have the maximum or minimum scores. This can limit the range of the data reported. The EQ-5D-3L used in study IV had 3 alternatives, but since then a new version of the instrument with 5 levels, EQ-5D-5L has been developed with a wider range of alternatives in order to increase the sensitivity and reduce the ceiling effect[106,132].

In studies I and II, logistic regression analyses were carried out to determine predictors. This is appropriate when the dependant variable is dichotomous or with nominal data. In study IV a linear regression analysis was conducted. This type of regression is normally reserved for scale or continuous data but here we have used it on ordinal data. The results of EQ-5D, HHS and PRNS are normally treated as scale data.

Directed acyclic graphs (DAG)[133] were created for both studies II and IV and used as tools to visually illustrate our interpretation of how the data is interconnected and which variables are potential confounders (**Figure 5**). Although the DAG is an over simplification, it can be useful. It was designed to help when identifying confounding variables, and show which variables have been adjusted for and which have not. It provides a graphic illustration of the underlying causal assumptions of the study.

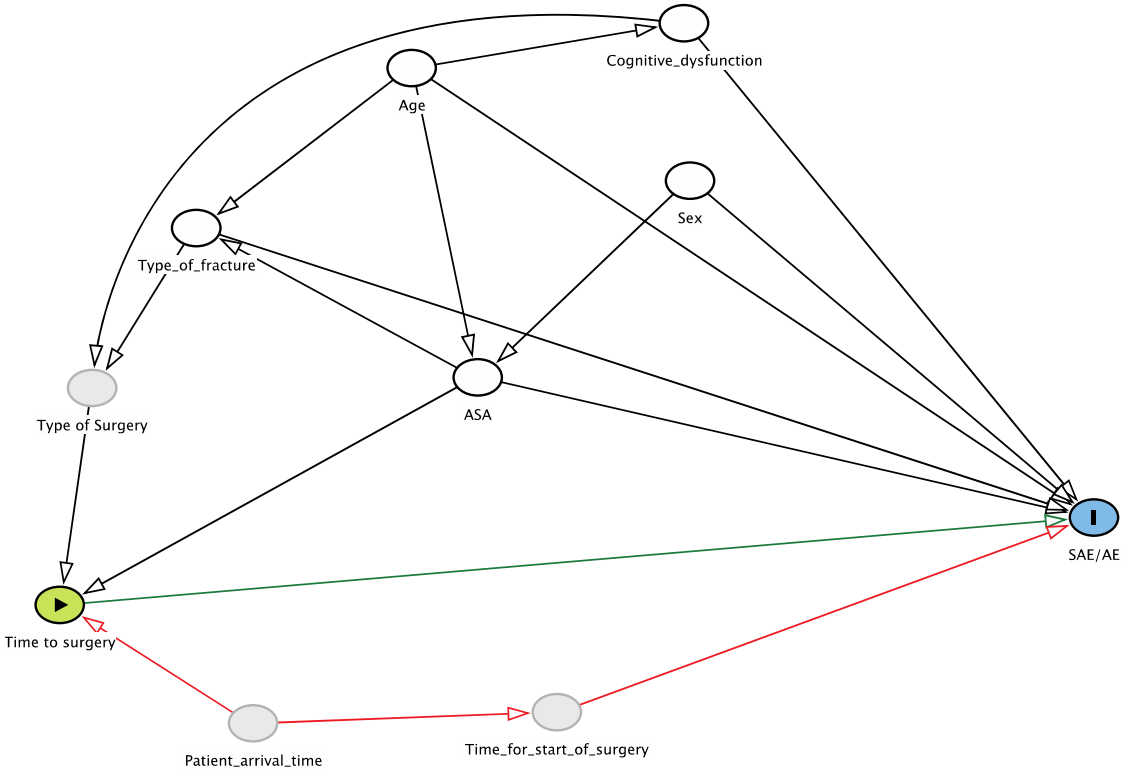

Figure 5. Directed acyclic graphs (DAG) diagram for study II.

A power calculation was done for study I to ensure that sufficient patients were included to be able to show if there was a significant difference between the groups. We did not calculate power for study IV. Having had previous experience of inclusion in studies where informed consent was required, the assumption was that the inclusion period of 2 years duration would be an adequately long period to allow inclusion of a sufficiently large sample size in each group. In hindsight, it would have been more prudent to have calculated power prior to starting the study. Though, it is difficult to assume a clinically relevant difference to be able to calculate for power.

Over the course of these studies, we have used accepted adverse events definitions in an attempt systematize our data collection. When the first two studies were conducted, we had a number of randomised clinical trials in progress at the Orthopaedic Department at Danderyd Hospital. These clinical trials used standardized internationally accepted stringent definitions of AE and SAEs. Coupled with this, there was an ambition at this time from the governing bodies within research that academic research should adopt the same stringent approaches as those used in clinical trials and we took inspiration from these. The World Health Organization (WHO) definitions within patient safety for an adverse event (AE) and serious adverse event (SAE) were used in study I and in study II a modified version of the International Conference on Harmonisation-Good Clinical Practice (ICH-GCP)[89] definition for an SAE was adopted. In study III, the emphasis was to identify those adverse events experienced by patients, where harm was caused by healthcare and to examine their preventability; therefore the AE definition from the Swedish version of Global Trigger Tool (GTT) methodology was chosen as it incorporates evaluation of preventability.

8 DISCUSSION

8.1.1 Study I

Fast-track compared to conventional admission

In study I, we were able to show that with the introduction of an improved fast-track system for hip-fracture patients operating concurrently with an already existing system, it was possible to decrease waiting time to surgery. Mean time to surgery was 20 hours and time to surgery was reduced by a mean 3 hours for the fast-track intervention group. A greater proportion of patients in the fast-track group underwent surgery within 24 hours, 88% versus 75%, compared to the control group.

These results, showing reduced time to surgery, are consistent with findings from other studies[134 135] but a recent randomized study of pre-hospital fast-track care found no significant difference in time to surgery, although time to radiology was significantly reduced[136]. In the randomised study, patients were randomised to either fast track or conventional admission and similar exclusions criteria as in our study disqualified patients from admission via the fast-track system. One possible explanation that may account for the divergent results is that in our study we excluded patients who incurred long delays in the diagnosis of their hip fracture, for example, where magnetic resonance imaging (MRI) or computer tomography (CT) were required. It is unclear if the same exclusion criteria were used in the randomised study. The care and management of these patients is a multi-disciplinary, multi-departmental effort. It could be argued that the fast-track patients may have had an advantage, but in our patients, except for their transportation to and admission on the ward, the care and pre-operative routines for both groups were the same.

Other studies have been able to show that fast-track systems can reduce the length of stay and complication rate after hip fracture[134 137]. We were unable to find any difference in the length of stay between the groups. There was a trend toward fewer AEs in the fast-track group at 3 months, but this difference was not statistically significant. Age and ASA-class were the factors associated with increased risk for AEs.

The logistic regression for probability of surgery within 24 hours was more favourable for the intervention fast-track group even after adjustment for age, gender, cognitive function, ASA-class and surgical method with an odds ratio (OR) of 2.2 (95% CI 1.1-4.5). The greater majority of delays to surgery over 24 hours were administrative delays as opposed to delays for medical reasons (67% compared to 33%). Other studies[58,138] have had comparable findings. Vidán et al[138] found that administrative reasons, particularly lack of operating room availability, caused 60.7% of delays while medical problems accounted for 33.1% of delays.

It has been shown previously, that mortality is significantly higher for medically fit patients with administrative delays compared to no delay [58].

From the literature, we know that the mortality rate after hip fracture is high[30,32,33], and it has been reported that surgery within 12 hours can significantly reduce the risk of the in-hospital mortality[42]. Early surgery has a positive effect on the in-hospital[139], three-month[140] and one-year mortality[40,141]. A recent study[142] reports that patients undergoing early surgery receive an advantage in regard to the one year mortality. Each 10-hour delay to surgery increases the risk of death within one year by 5%. We examined the 3-month mortality rate and found that it was similar in both groups. Age and ASA-classification were significantly associated with increased risk of mortality at 3-months which is consistent with findings from other studies[143,144]. In contrast we found no correlation between early surgery within 24 hours and the 3-month mortality.

Initially, there were fears that with focus on fast tracking hip-fracture patients this would negatively affect other fracture patients. These fears, however, proved to be unfounded, as the results of a concurrent study investigating the effects of process change was able to show[145]. There were knock-on effects that possibly benefited other patient groups, as there was a heightened awareness and vigilance among staff to actively reduce waiting time to surgery for fracture patients.

One of the strengths of this study is that it is a large prospectively and consecutively included cohort of 415 patients. The data obtained is reliable as it was prospectively collected. Studying two parallel fast-tracking systems had not been described previously in the literature. The potential for confounding factors caused by evolving methods of care or data collection was lessened because we were able to study two concurrent fast-track systems. We excluded patients who, due to long delays verifying fractures with methods other than x-rays, for example, MRI and CT as these were not routinely available on a 24-hour basis. Patients who were diagnosed only after failed attempts at mobilization were also excluded, as well as those, who were fast-tracked but it was later discovered they did not have hip fractures. There may have been some selection bias, but we have tried to adjust for this and three fast-track patients with hip-fractures and other life-threatening medical conditions requiring intensive care pre-operatively were excluded. These would not have been candidates for fast-track process if the checklist had been followed correctly.

In conclusion, we have been able to show that using a fast-track system in hip-fracture patients can reduce waiting time to surgery and increase the proportion of patients undergoing surgery within 24 hours.

8.1.2 Study II

The effects of waiting time to surgery

In study II, we found that waiting time to surgery was correlated with an increased risk for the occurrence of SAEs during the hospital stay in hip-fracture patients. There are no safe cut-off times for surgery as the risk increases linearly over time.

After hip-fracture surgery, 20.6% of the patients had been affected by at least one SAE during their hospital stay. A comparable overall medical complication rate after hip fracture was reported by Roche et al[21]. The definition of outcome varies widely in published literature[21,40,41] and this makes comparisons between studies regarding the incidence of SAEs difficult.

We found that waiting time to surgery, male sex, sustaining a subtrochanteric fracture or an ASA classification in the higher range significantly increased the risk of SAEs. That patients with coexisting medical conditions have a higher risk of negative outcomes after surgery is well known and consistent with results from previous studies[21,146,147]. The variables of age and the presence of cognitive impairment were found to have no significant bearing on the SAE occurrence in this study. With regard to the age variable, one explanation may be that the sample size is limited with regard to the number of outcomes studied. The low number of SAEs during the hospital stay among patients with cognitive impairment is explained by their routine early discharge back to their usual place of residence, normally within one to two days after surgery. Our results also showed that there was no impact of waiting time on the one-year mortality rate. In our study, SAEs did not occur within specific time constraints, the progression of risk was linear indicating that every hour counts.

This is a well-described cohort of 577 consecutively admitted patients with hip fractures and this can be seen as one of its strengths. The study was carried out at a large acute hospital and, with the exception of those with pathological and peri-prosthetic fractures, all patients with hip fractures who were admitted during the time period of the study were included. This helps to eliminate selection bias. The study directly reflects the normal clinical setting, which would indicate that our data is valid for the general clinical situation. This implies that the external validity of the study may be regarded as good. Few studies have examined the correlation between time to surgery and the occurrence of SAEs during the hospital stay in hip-fracture patients. Although a study of hip-fracture patients had investigated AEs after surgery, the small sample size (n=39) makes the results difficult to interpret[148].

Retrospective record review has the limitation that it is only as good as the documentation available, but it is considered to be a reliable method for the identification of adverse patient outcomes[115,130]. The medical record review was carried out by only one of the authors, which could incorporate an observational bias. This was controlled for by three senior authors reviewing a random sample of 20 medical records for the identification of AEs and for assessing the severity of these events i.e. SAEs. Statistical testing in the form of Cohen's kappa value was calculated to assess the level of inter-rater consensus, which in this case proved to be substantial.

Caring for hip-fracture patients and reducing waiting time to surgery presents challenges for nursing staff and other health professionals. This is an elderly and fragile patient group and giving optimal care requires not only close inter-professional co-operation between different staff categories e.g. nursing staff, doctors, physiotherapists but also a close collaboration between the relevant hospital departments responsible for these patients' treatment. In recent years, acute care facilities have introduced dedicated processes such as integrated care pathways[149] and fast-track systems[59] to streamline and co-ordinate the management of the care of hip-fracture patients. Reducing waiting time to surgery can be achieved by staff involvement in improvement measures and by active management of acute surgical procedures[145,150]. The use of a multidisciplinary team approach has proved effective in the care of hip-fracture patients, in areas such as reducing waiting time to surgery and lowering the complication rate post-operatively[134,151]

Nurses, as members of an inter-professional team and by virtue of their close proximity to patients, have an important role to play in the co-ordination[152] of the pre-operative patient care and preparation of hip-fracture patients for surgery. They have the potential to help decrease waiting time to surgery. This may lead to a decrease in AEs post-operatively as well diminishing patient suffering as research has shown that patients' experiences of the waiting time to surgery are associated with increased stress, anxiety and fear[153]. More recently ortho-geriatric pathways[61,62,154,155] for hip-fracture patients have been implemented in some hospitals where there is collaborative management between orthopaedics surgeons and gerontologists in the acute care of these patients. As the majority of these patients are elderly and often have pre-existing health issues this should prove to be beneficial.

8.1.3 Study III

Adverse events

In the preface of her volume, Notes on Hospitals, published in 1863, Florence Nightingale had the clear sightedness to note the following "It may seem a strange principle to enunciate as the very first requirement in a Hospital that it should do the sick no harm"[156] and the sentiment holds true even today. The purpose of study III was to identify those adverse events experienced by patients, where harm was caused by healthcare and to examine their preventability. We used the definitions an AE and preventable AE from the Swedish version of Global Trigger Tool[90] (GTT), which incorporate the concept of preventability. We found that 38% of patients admitted with a hip fracture experienced at least one AE related to their index admission, and in just over 60% of cases these AEs were assessed to be preventable. Merten et al[157] conducted a similar study in the Netherlands, using an alternative type of structured RRR methodology, and found that around 20% of hip-fracture patients had suffered an AE related to the hospital admission and that almost 40% of these were potentially preventable. The results in our study show a higher AE rate. We found varying types of AEs in our material, for example, there was a large proportion of nursing-related AEs, which were not identified in the study by Merten et al.

According to the literature, the rate of AEs in the surgical disciplines is high[158-161] compared to others. AEs are common in orthopaedic care in Sweden[162-164]. No studies were found where the global trigger tool methodology was used to examine AEs in hip-fracture patients. The complication rate in hip-fracture patients is high[21,165,166]. In this study, compared to previous studies, we have made a distinction between complications, which may be dependent on the patient's pre-existing comorbidities and AEs, which are specifically related to or caused by healthcare. Our findings are in agreement with the results of other studies that have shown that there is a higher percentage of AEs and preventable AEs in older patients with pre-existing health conditions [161,167].

The most frequently occurring AEs were healthcare-associated infections, e.g. urinary tract infections and pneumonia, these accounted for 19.6% of the AEs identified and 65.0% of these were judged to be preventable. Pressure ulcers (18.6%), all of which were deemed preventable, were the next most common AE, followed by AEs related to surgery such as reoperation and fracture/fissure (14.7%) and acute confusional states (7.8%). Distension of the urinary bladder was also common AE and 57% of these were judged to be preventable.

Adverse events are common in elderly patients [168]. After hip fracture pneumonia [40 169], urinary tract infections and urinary retention [166,170] pressure ulcers[171-173] and confusional

states[174] are common. Our findings are comparable with the results from other research. We found a high proportion of the AEs identified were preventable.

The majority of adverse events 84 (82.4%) were judged to have either caused temporary harm (n=58, 56.9%) or required outpatient care, hospitalization or prolonged an existing hospitalisation (n=26, 25.5%) (NCC MERP categories E and F). The remaining 18 AEs were judged to have caused permanent patient harm in 11 (10.8 %) cases, required an intervention to sustain life in 3 (2.9%) cases and in 4 (3.9%) cases contributed till patient death. In NCC MERP category H, all AEs were judged to be preventable. Most of the AEs occurred in the post-operative period and the AEs identified in this study were estimated to generate 185 extra hospital days.

Our research indicates that AEs identified using GTT methodology are common in hip-fracture patients and a large proportion of these are preventable. From a patient-safety perspective, this research gives new insights into types of preventable AEs. If the focus is on improving healthcare, we should be concentrating our efforts on reducing the number of preventable AEs, with a particular emphasis on improving the care of older patients with pre-existing health conditions who have sustained a hip fracture.

We have chosen to use a stringent definition of what constitutes an AE. Therefore conditions that the patient may have been admitted with or those judged to be related to an underlying disease or condition were excluded. If we want to improve the quality of treatment and care, it is of value to know what harm healthcare is causing patients and if this is preventable.

To control for observational bias, a double check of a random sample of 20 medical records by an independent reviewer was carried out. Cohen's kappa was calculated and the agreement between reviewers was substantial. The study was also monitored to check the reliability and validity of the data. If there were uncertainties about preventability or if an AE was related to a pre-existing condition, a consultant physician in internal medicine and an orthopaedic surgeon could be consulted.

As has been discussed in previously, a well-known limitation of RRR methodology is its dependence on the quality and completeness of the documentation. The review process is only as good as the documentation on which it is carried out. There is a risk for an under-reporting of events. We only included AEs detected in the admission hospital, so we may have missed AEs. However, an earlier AE study [130] conducted at the Orthopaedic Department showed that examining the patients' records of inpatient and outpatient care in the entire Health Authority District identified very few AEs that had not already been detected.

This cohort is small and no patients with cognitive impairment were included. The mean age of the participants is younger than the average hip-fracture patient in Sweden, which should imply that there would be fewer AEs occurring in this cohort, as age is a known risk factor for AEs. Despite this 38% of patients had at least one AE during their hospital stay and up to 90 days post-operatively.

8.1.4 Study IV

Depression and hip fracture

Study IV focused on examining the influence depression has on functional outcome and quality of life one year after hip fracture. The findings in the literature are inconclusive, as some studies have found a correlation between depression and poorer functional outcome after hip fracture [76,79-83] while other studies have not established this link.[84-87] They suggest that comorbidity[86], as well as cognitive function and fear of falling[85] affect functional outcome more than depression. In our study, we found no significant differences in functional outcome between the depression and the control group. One factor which may have influenced our findings, was the relatively low mean age of the participants, 76 years in our study compared to 82 years which is the average age of hip-fracture patients in Sweden[8]. Our cohort was younger than the average patient with hip fracture. One possible explanation for this is that in the acute setting after a traumatic fracture the frail elderly are less likely to want to participate in activities that have the potential to further complicate their lifestyle.

The quality of life scores were significantly higher in the control group at baseline. Both the depression and control group experienced a decline in their quality of life over the duration of the study. These results are consistent with others studies that have shown decline after hip fracture[175,176]

Those patients included with depressive symptoms had mild to moderate symptoms (HADS – D score 8-14, none had severe symptoms 15-21). This was surprising, as the literature tells us that depression is common among hip-fracture patients[72,73]. There may be selection bias here as, those patients with severe depressive symptoms would be less likely to agree to participate in studies, due to the inherent nature of the illness. In our study, patients with depression had an increased mortality rate at one year but the difference was not statistically significant. Other studies have shown depression is associated with an increased mortality[74,75].

In the literature, the patient follow-up times vary widely, ranging from the short-term in days up to discharge to the long term up to 2 years after surgery. Our patients were followed up for 12 months after their fracture, as one can typically expect post-operative recovery by 3 months but there is scope for improvement in hip function up to 12 months after surgery[177].

The cohort was meticulously followed up with visits to, or telephone interviews with, a research RN and apart from those who died, few patients were lost-to follow up during the study. In addition, we have examined depression in hip-fracture patients in relation to functional outcome using a disease-specific assessment instrument HHS. Patient-reported outcome measure questionnaires were used making the patient the primary source of

information and giving them the opportunity to relate their perceived experiences of their treatment and care without incorporating any observational bias from investigators.

Although HADS has not been validated specifically for hip fracture, it has been widely used. In a Swedish population sample has been found to be useful in gauging the presence of depression and anxiety symptoms[112,113]. In addition, a large meta-analysis of 747 articles examining the validity of the instrument showed it to perform well in the assessment of symptom severity for both depression and anxiety states in the general population as well as for patients assessed in medical, psychiatric and primary care settings[114].

There are some limitations to this study. No formal power calculation was done and we were therefore unable to detect small significant statistical differences, but on the other hand these small differences may not be clinically relevant. In addition, a large group of hip-fracture patients was excluded from the study, those with dementia or a cognitive impairment. Cognitive impairment in patients with hip-fracture is common[28]. However, correctly estimating their pre-fracture status is difficult, as it has to be done by a relative or care giver. Our results are therefore applicable to hip-fracture patients without cognitive dysfunction.

All the studies were cohort studies and a quantitative approach was used. The first two studies are large cohort studies. The first study was a prospective observational cohort study with 415 patients while the second was an observational cohort study of 576 patients. Patients included in these studies were consecutively admitted which helped to reduce any selection bias. No age limits were imposed and patients with cognitive impairment were eligible for inclusion in the first two studies. Patients with pathological fractures were excluded, as the aetiology of the hip fracture is different: malignancy as opposed to bone fragility. The patients are representative of the average patient who sustains a hip fracture and therefore the results are applicable to the general hip-fracture population. These two studies directly reflect the normal clinical setting, which would indicate that our data is valid in general. The third and fourth studies were smaller cohorts and the results of these studies are applicable for hip-fracture patients without cognitive impairment.

The intention over the course of the first three studies was to use a more structured, systematized approach to detection of adverse events. Whether this was prudent or not remains to be seen. There are merits in each definition but in hindsight, the global trigger tool definition and methodology, which includes evaluation of preventability and thereby allows possibility for change, is perhaps the most appropriate if we want to improve patient care.

9 CONCLUSIONS AND CLINICAL APPLICATIONS

Study I

The introduction of a fast-track system for the management of patients with hip fracture can reduce waiting time to surgery and increase the proportion of patients undergoing surgery within 24 hours without influencing mortality or length of stay.

Study II

Approximately 20% of hip-fracture patients suffer an SAE during their hospital stay, the risk increases linearly over time and there are no safe time limits. We recommend implementation of routines for prioritizing this patient group with an emphasis on male patients, those with higher ASA-classification and those suffering subtrochanteric fractures.

Study III

Healthcare-related injuries are common in hip-fracture patients and a large proportion of these are preventable. From a patient-safety perspective, in the clinical setting efforts should be made to reduce the number of preventable adverse events.

Study IV

Depression pre-fracture does not have a bearing on functional outcome one year after fracture for patients without cognitive impairment.

10 IMPLICATIONS FOR FUTURE RESEARCH

The studies in this thesis have examined some aspects of the management and care of patients with hip fracture, but can have implications for other areas of orthopaedic care

Although difficult to co-ordinate, further randomized clinical trials examining the effect of fast-track systems on waiting time to surgery for hip-fractures patient are warranted.

Further research and development of the fast-track concept to include other high volume fracture types within the orthopaedic sphere, for example, fractures of the lower extremities.

Research studies into the impact of psychological factors on outcome after revision surgery of the hip and patients with peri-prosthetic fractures of the hip are needed. Even studies to examine reasons for patient dissatisfaction with outcome after knee and hip arthroplasty would be of benefit.

Research studies using global trigger methodology to examine the incidence and preventability of adverse events in other acute fracture patients, as well, extending this to include patients undergoing revision surgery of the hip.

Qualitative studies to elucidate the patient perspective regarding aspects of their treatment, care and rehabilitation in patients with hip fracture, as well as, patients undergoing revision surgery of the hip are needed.

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13 APPENDICES

13.1 APPENDIX 1. CHECKLIST FOR THE AMBULANCE PROCESS

Pre-hospital checklist for hip fractures

Used in conjunction with leaving report
If patient is excluded, checklist is to be left at the A&E

Name : Call out no.

ID no. Ambulance no.

Gender:

Female ☐ Male ☐

Suspected Fracture, side:

Right ☐ Left ☐

History:

.....

.....

.....

Fall on same level

Indoors ☐ Outdoors ☐

Pulse ☐

Systolic BP ☐

Saturation ☐

Known blood infection? ☐ No ☐ Yes

Which? _____

Hospital stay abroad during last 6 months

No ☐ Yes ☐ Where? _____

Inclusion criteria:

☐ Fall on same level with pain i hip/groin (= Suspected hip fracture)

Exclusion criteria:

☐ Other suspected acute illness/injury which has higher priority, e.g..

☐ Heart attack, Stroke

☐ Circulation or breathing problems

☐ Skull trauma with change in level of consciousness

☐ Patient fainted / Syncopy

☐ Compromised distal-status on injured side

☐ Suspicion of multiple fractures or previous surgery same hip

☐ Unable to contact person at hospital per telephone

☐ Patient who cannot be identified

13.2 APPENDIX 2. HARRIS HIP SCORE QUESTIONNAIRE (HHS)

Datum: Initial: Patientnr:

Nedanstående frågor gäller din skadade höft innan frakturen

Ringa in den bokstav för påståendet som stämmer bäst

1. Beskriv om du haft någon smärta i höften

Ingen	A
Obetydlig smärta, ingen begränsning i aktivitet, känner vid enstaka tillfällen av höften	B
Lätt smärta, ej påverkan av dagliga aktiviteter, men smärta vid större ansträngning, använder ibland smärtstillande	C
Måttlig smärta, begränsning i dagliga aktiviteter, Använder regelbundet smärtstillande mediciner	D
Uttalad smärta, stark begränsning av aktiviteter, tar starka smärtstillande regelbundet	E
Invalidiserad, vilosmärtor	F

2. Använder du något gånghjälpmedel?

Inget	A
Käpp vid långa promenader	B
Nästan alltid käpp	C
1 krycka	D
2 käppar eller rollator	E
Går inte alls	F

3. Har du hälta efter en promenad med det gånghjälpmedel du använder?

Ingen hälta	A
Lätt hälta	B
Måttlig hälta	C
Uttalad hälta	D

Datum: Initial: Patientnr:

4. Hur långt kan du gå med det gånghjälpmedel du använder?

Över 2 kilometer	A
1 – 2 kilometer	B
½ - 1 kilometer	C
Mindre än ½ kilometer eller endast inomhus	D
Kan inte gå	E

5. Trappgång?

Jag går i trappa utan stöd	A
Jag använder ledstång eller räcke vid trappgång	B
Jag går i trappa med stora svårigheter	C
Jag kan inte gå i trappa	D

6. Ta på sig skor och strumpor

Utan svårighet	A
Med svårighet	B
Jag kan inte ta på mig skor och strumpor själv	C

7. Sitta

Jag kan sitta bekvämt på en vanlig stol	A
Jag sitter endast bekvämt i en hög stol, jag kan endast sitta bekvämt i en halvtimme på grund av höftsmärta	B
Jag kan inte sitta bekvämt i en halvtimme på grund av höftsmärta	C

8. Tunnelbana/Buss

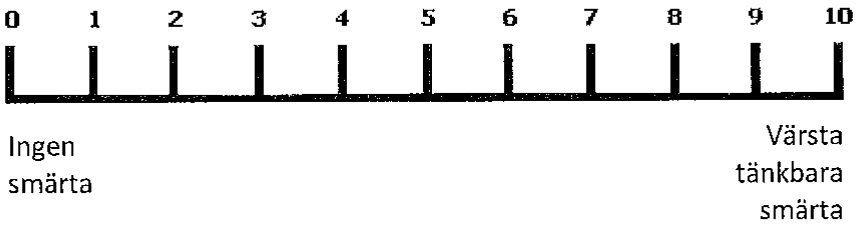
Jag kan åka tunnelbana eller buss	A
Jag kan inte åka tunnelbana eller buss	B

13.3 APPENDIX 3. PAIN NUMERICAL RATING SCALE (NRS)

Datum: Initial: Patientnr:

PAIN NUMERICAL RATING SCALE (NRS)

På nedanstående skala, ringa in det nummer som bästa motsvarar din GENOMSNITTLIGA nivå för din höft/bensmärta i det skadade benet, under de sju senaste dagarna.



13.4 APPENDIX 4. EQ-5D-3L AND EQ-5D VAS

EQ - 5D

Hälsoenkät

Svensk version
(Swedish version)

Markera, genom att kryssa i en ruta i varje nedanstående grupp (så här ☑), vilket påstående som bäst beskriver Ditt hälsotillstånd i dag.

Rörlighet

Jag går utan svårigheter	❑	A
Jag kan gå men med viss svårighet	❑	B
Jag är sängliggande	❑	C

Hygien

Jag behöver ingen hjälp med min dagliga hygien, mat eller påklädning	❑	A
Jag har vissa problem att tvätta eller klä mig själv	❑	B
Jag kan inte tvätta eller klä mig själv	❑	C

Huvudsakliga aktiviteter *(t ex arbete, studier, hushållssysslor, familje- och fritidsaktiviteter)*

Jag klarar av mina huvudsakliga aktiviteter	❑	A
Jag har vissa problem med att klara av mina huvudsakliga aktiviteter	❑	B
Jag klarar inte av mina huvudsakliga aktiviteter	❑	C

Smärtor/besvär

Jag har varken smärtor eller besvär	❑	A
Jag har måttliga smärtor eller besvär	❑	B
Jag har svåra smärtor eller besvär	❑	C

Oro/nedstämdhet

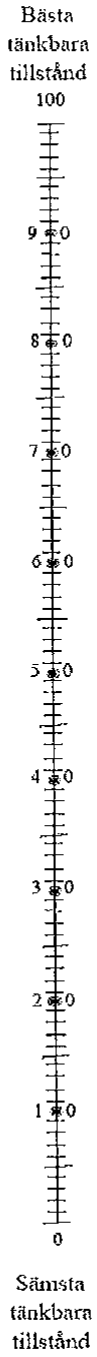
Jag är inte orolig eller nedstämd	❑	A
Jag är orolig eller nedstämd i viss utsträckning	❑	B
Jag är i högsta grad orolig eller nedstämd	❑	C

Datum: Initial: Patientnr:

Till hjälp för att avgöra hur bra eller dåligt ett hälsotillstånd är, finns den termometer-liknande skalan till höger. På denna har Ditt bästa tänkbara hälsotillstånd markerats med 100 och Ditt sämsta tänkbara hälsotillstånd med 0.

Vi vill att Du på denna skala markerar hur bra eller dåligt Ditt hälsotillstånd är, som Du själv bedömer det. Gör detta genom att dra en linje från nedanstående ruta till den punkt på skalan som markerar hur bra eller dåligt Ditt nuvarande hälsotillstånd är.

Ditt nuvarande hälsotillstånd



13.5 APPENDIX 5 THE HOSPITAL ANXIETY AND DEPRESSION SCALE (HADS)

Datum: Initial: Patientnr:

5. **Oroande tankar kommer för mig**
   - ☐ Mycket ofta
   - ☐ Ofta
   - ☐ Då och då men inte så ofta
   - ☐ Bara någon enstaka gång

6. **Jag känner mig glad**
   - ☐ Inte alls
   - ☐ Inte ofta
   - ☐ Ibland
   - ☐ För det mesta

7. **Jag kan sitta i lugn och ro och känna mig avspänd**
   - ☐ Absolut
   - ☐ Oftast
   - ☐ Inte ofta
   - ☐ Inte alls

8. **Jag känner mig som om jag gick på "lågt varv"**
   - ☐ Nästan jämt
   - ☐ Mycket ofta
   - ☐ Ibland
   - ☐ Inte alls

9. **Jag får en slags känsla av rädsla som om jag hade "fjärilar i magen"**
   - ☐ Inte alls
   - ☐ Någon gång
   - ☐ Rätt ofta
   - ☐ Mycket ofta

10. **Jag har tappat intresset för mitt utseende**
    - ☐ Absolut
    - ☐ Jag bryr mig inte så mycket om det som jag borde
    - ☐ Jag kanske inte bryr mig om det riktigt så mycket
    - ☐ Jag bryr mig precis lika mycket om det som förut

Datum: Initial: Patientnr:

11. Jag känner mig rastlös som om jag måste vara på språng

- ☐ Verkligen mycket
- ☐ En hel del
- ☐ Inte så mycket
- ☐ Inte alls

12. Jag ser fram emot saker och ting med glädje

- ☐ Lika mycket som förut
- ☐ Något mindre än jag brukade
- ☐ Klart mindre än jag brukade
- ☐ Nästan inte alls

13. Jag får plötsliga panikkänslor

- ☐ Verkligen ofta
- ☐ Rätt ofta
- ☐ Inte så ofta
- ☐ Inte alls

14. Jag kan njuta av en bra bok, ett bra radio- eller TV-program

- ☐ Ofta
- ☐ Ibland
- ☐ Inte så ofta
- ☐ Mycket sällan

KONTROLLERA ATT DU HAR SVARAT PÅ ALLA FRÅGOR

TACK FÖR DIN MEDVERKAN!

13.6 APPENDIX 6. GLOBAL TRIGGER TOOL (GTT) 38 TRIGGERS

Care module	Transfusion of blood
	In-hospital stroke
	Cardiac arrest or deterioration in vital signs
	Unplanned dialysis
	Deep venous thrombosis or pulmonary embolus
	Fall
	Pressure ulcer
	Distended urinary bladder
	Thrombophlebitis or skin impairment
	Neurological impairment
	Abnormal temperature
	Positive blood culture
	Healthcare-associated infection
	Transfer to higher level of care
	Acute visit within 2 days after discharge from in-hospital care
	Readmission within 90 days
	Documentation of mistake
	Other
Laboratory module	Low haemoglobin value
	Low glucose value
	Increased creatinine value
	Abnormal potassium value
	Abnormal sodium value
Surgical and other invasive procedure module	Reoperation
	Change in procedure/organ harm
	Unplanned ventilation treatment
	Intra- or Post-Operative Death
	Post-operative increase of troponin
	Post-operative complication
	Anaesthesia related impairment/harm
Medication module	Increased risk for haemorrhage
	Anaphylactic reaction
	Adverse drug event/adverse drug reaction
Intensive care module	Ventilator-associated pneumonia
	Readmission to the intensive care unit or other higher level of care
	Treatment within intensive care
	Intubation, re-intubation, tracheotomy or coniotomy
	Intensive care unit syndrome