

Understanding and Improving Morbidity and Mortality after Hip Fracture

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for the Degree Master of Science

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ABSTRACT

Hip fractures are common injuries with devastating consequences, including high rates of morbidity and mortality. The purpose of my thesis was to lay the foundation for further research which can fully explore: i) the epidemiology of morbidity and mortality following hip fracture; ii) risk factors for poor outcomes following hip fracture; iii) causes and pathways to mortality following hip fracture; iv) secondary prevention of morbidity and mortality following hip fracture; and v) potential interventions to improve outcomes following hip fracture.

To this end, I will first detail the design, execution, results, and ‘lessons learned’ of a prospective observational pilot cohort study that recruited 100 consecutive patients aged ≥ 18 years presenting with a hip fracture to the Juravinski Hospital and Cancer Centre of the Hamilton Health Sciences. The primary aim of this pilot study was to assess the feasibility of a larger prospective international cohort study.

Second, I will present a systematic review and meta-analysis of a promising intervention that consisted of multi-disciplinary (specifically geriatrician-led) co-management of hip fracture patients. This intervention has previously been shown to reduce mortality and length of stay following hip fracture. The meta-analysis presented will determine the effectiveness of this intervention in reducing the incidence, duration, and severity of delirium—a common condition following hip fracture.

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CHAPTER 1: INTRODUCTION

BACKGROUND AND RATIONALE

Magnitude of the Problem

In Canada, approximately 30,000 individuals incur a hip fracture annually [1]. Estimates indicate that the number of hip fractures will continue to increase as the ‘baby boomer’ generation enters its elderly years in historic numbers [1]. The economic impact of hip fractures in Canada is substantial, with direct and indirect patient care costs projected to rise from \$650 million in the mid-1990s, to \$2.4 billion by 2041 [2]. This is a trend that is being observed throughout the developed world [3,4]. Furthermore, as longevity increases in the developing world and populations continue to age, global projections estimate that more than 6.5 million people will suffer a hip fracture annually by 2050 [5].

Mortality after Hip Fracture

In addition to pain and dysfunction in the acute setting, hip fractures are considered sentinel events, associated with considerable short and long-term mortality. One-month mortality following hip fracture approaches 10%, and rises to between 14% and 36% at one year, despite aggressive management with surgery and rehabilitation [6-9].

Unfortunately, these rates have been fairly stagnant over time, demonstrating only marginal decreases, at best [3,10]. Mundi et al performed a systematic review of mortality rates in randomized controlled trials published between 1981 and 2012, inclusive [11]. Overall, they found similar mortality rates in the 1980s (24%), 1990s (23%), and 2000s (21%), with no significant decreases over time. In contrast, mortality rates secondary to acute myocardial infarction have fallen precipitously since the 1960s—from a high greater than 30% to less than 5%—and continue to demonstrate substantial declines in recent years [12,13]. In this age of rapid

advances in healthcare and medical technology, allowing hip fracture mortality rates to persist is unacceptable. Unfortunately, despite a plethora of data indicating excessive mortality associated with hip fractures, we still do not fully understand what causes these patients to die. Without fully comprehending the clinical course of hip fracture patients, intervening to circumvent this excessive mortality will be difficult.

Quality of the Available Evidence

Although many studies have evaluated hip fractures and mortality, these data have substantial limitations regarding understanding the causal pathways for mortality. Several large retrospective administrative database reviews have aimed to correlate "risk factors" or "predictors" with subsequent all-cause mortality [14-17]. Others have attempted to identify actual causes of mortality as reported on death certificates. Table 1 summarizes retrospective population-based studies that reported cause-specific mortality along with the most common causes of death. However, administrative databases have known limitations which limit their interpretability, including retrospectively collected data, frequency of errors in the primary data sources, and limits in the availability of relevant information [18]. Therefore, although many of these studies have been large, they are clearly unable to establish causal pathways and cannot adequately answer the question of why hip fracture patients die.

Published prospective studies have typically had underpowered sample sizes, been limited in scope, or failed to use active surveillance to detect early pathological events [19-23]. Active and systematic surveillance is fundamental to accurately identifying and quantifying incident morbidity in the post-operative population as events can be missed during routine clinical practice. For instance, the use of opioid narcotics post-operatively can veil chest pain which

would otherwise trigger investigations for myocardial infarction, thereby leading to missed events that may precipitate death.

The most comprehensive prospective study to date on this topic was published by Roche and colleagues [23]. This was a moderate-sized observational study which followed 2448 patients with a diagnosis of a hip fracture to identify causes of 30-day and 1-year mortality. The authors reported that amongst post-operative complications, the strongest predictors of 30-day and 1-year mortality were cardiac failure (65% at 30 days, 92% at 1 year) and chest infection (43% at 30 days, 71% at 1 year), which accounted for 73% of all deaths in this study.

Thromboembolic disease and myocardial infarction were also strong predictors of death (Hazard ratio 5.1 and 4.6, respectively, for 30-day mortality), but were detected in a smaller fraction of the study sample (1% and 2%, respectively).

The greatest limitation of using the aforementioned findings to conclude causes of mortality is that the findings were based on routine clinical practice. Specifically, the study did not employ proactive day-to-day clinical surveillance and investigations and therefore may have either misclassified or missed pathological events entirely. For instance, it is plausible that cardiac failure—the strongest correlate with death in this study—could have been secondary to acute myocardial injury which was simply not recognized. Such missed acute events were especially probable given that a medical consultant or internist was not formally involved in patient care except at the request of the anaesthesia service, which the authors acknowledged was a rare occurrence. Furthermore, the 1% rate of myocardial infarction is substantially lower than the results of more recent large international studies that have employed active surveillance in consecutive patients undergoing noncardiac surgery [24,25]. Detecting early events is imperative

to both identify the etiologic pathway to death and, more importantly, identify where to target early interventions in order to circumvent the poor prognosis of these patients.

A few studies have attempted to systematically follow perioperative blood work, namely troponin levels, of hip fracture patients. Only four such studies have been conducted in the past decade, and they were relatively small, with sample sizes ranging from 75 to 238 patients [26-29]. These findings, although informative, must be corroborated with a larger more generalizable study that employs an adequate sample size. Following other investigations systematically alongside troponin measurements may also provide a comparison of relative and absolute impact of myocardial damage on mortality; information which has the potential to inform appropriate interventions.

It is noteworthy to define two further issues which have been poorly explored in the prior literature. The first is the clinical course of non-operatively managed hip fracture patients. This subpopulation has been largely neglected as nearly all studies in the literature have focused on surgically managed hip fracture patients. However, in addition to the moral and ethical imperative to study these patients, these patients provide a unique window into understanding why hip fracture patients die. Many of these patients tend to be more acutely ill than those that are managed operatively. After they arrive at the hospital and experience complications prior to a planned surgical intervention (such as an acute myocardial infarction or pulmonary embolism) surgery may be delayed indefinitely as they deteriorate clinically and die. Studying the clinical course of these patients would provide insight into some of the pathological processes experienced by all hip fracture patients.

The second major issue involves events that are poorly detected unless actively screened for. For instance, pulmonary embolism is a life-threatening event which requires a high index of

suspicion [22]. Risk factors and associated mortality are poorly captured in the literature because studies have not been able to detect a sufficient number of thromboembolic events to analyze them in a meaningful way. A larger study capturing a larger number of events would help better elaborate the pathways and consequences of these events.

Summary Background

Given the limitations of the available evidence, there is uncertainty pertaining to the cause of excessive mortality observed in hip fracture patients. Without defining the causal pathway, intervening appropriately becomes difficult, if not impossible. We propose a large prospective observational study of a national scope that follows consecutive hip fracture patients with systematic clinical surveillance and investigations. This will not only capture the pathological events which lead to eventual mortality, but also identify such events at an early phase to allow for targeted intervention. Further, the large trial will determine the optimal risk estimation model for short-term mortality and morbidity in hip fracture patients. Prior to undertaking this large study, we will first undertake a pilot study to demonstrate feasibility of recruitment, monitoring strategies, follow-up, and resource requirements.

TABLES

Table 1: Cause-specific Mortality after Hip Fracture in Population-Based Studies

Study	Country	Number of Cases	Top 4 Causes of Death within 1 year
Farahmand et al., 2005	Sweden	1,327	<ol style="list-style-type: none"> 1. Circulatory diseases 2. Cancer 3. Injuries & poisoning 4. Respiratory diseases
Vestergaard et al., 2007	Denmark	169,145	<ol style="list-style-type: none"> 1. Cardiovascular 2. Cancer 3. Cerebrovascular diseases 4. Infectious diseases
Panule et al., 2011	Finland	428	<ol style="list-style-type: none"> 1. Circulatory system disease 2. Malignant neoplasm 3. Respiratory system disease 4. Dementia
Wang et al., 2013	Taiwan	143,595	<ol style="list-style-type: none"> 1. Malignancy 2. Diabetes 3. Heart disease 4. Cerebrovascular disease
Koh et al., 2013	Singapore	63,257	<ol style="list-style-type: none"> 1. Cancer 2. Coronary heart disease 3. Pneumonia 4. Stroke
Klop et al., 2014	Britain	31,495	<p>Males:</p> <ol style="list-style-type: none"> 1. Cardiovascular diseases 2. Respiratory infections 3. Non-infectious respiratory diseases 4. Dementia <p>Females:</p> <ol style="list-style-type: none"> 1. Cardiovascular diseases 2. Injuries 3. Dementia 4. Respiratory infections

CHAPTER 2: STUDY PROTOCOL

Objectives

Primary objectives were:

1. To determine the feasibility of recruiting hip fracture patients in a timely manner.
2. To determine the feasibility of obtaining follow up data and outcome information in-hospital and at 30 days and 6 months.
3. To determine the resource requirements to achieve recruitment and follow up goals.

Secondary objectives were:

1. To determine the incidence of short-term (30-day and 6-month) all-cause and cause-specific mortality in hip fracture patients aged ≥ 18 years.
2. To determine short-term (within 30 day and 6 months) major complications.
3. To determine the incidence of medical and surgical complications in hip fracture patients.
4. To determine the incidence of delirium during hospitalization for hip fracture.
5. To determine change in functional independence following hip fracture.

Study Setting and Design

This study employed a prospective observational cohort design. It was conducted at the Hamilton Health Sciences, Juravinski Hospital site. This hospital site has been established as a centre of excellence for hip fractures within the hospital corporation. As such, all patients, with few exceptions, presenting with hip fracture to the Hamilton Health Sciences hospital group are transferred to the Juravinski Hospital for definitive management and care.

ELIGIBILITY CRITERIA

Inclusion Criteria

1. Patients aged ≥ 18 years admitted to the hospital with hip fractures [i.e. fractures involving the femoral head, subcapital, femoral neck, trochanteric, or subtrochanteric (≤ 5 cm below the lesser trochanter) regions], treated either operatively or non-operatively.
2. Mechanism of injury consistent with either:
 - a. A fall from a standing height or;
 - b. Another mechanism of injury which, in the clinical judgment of an orthopedic surgeon, would impart the same or less traumatic energy as a fall from a standing height.

Exclusion Criteria

1. Patients with fractures isolated to the femoral diaphysis.
2. Patients with periprosthetic hip fractures (i.e. fractures around a previous hip implant or orthopaedic hardware).
3. Patients with bilateral hip fractures.
4. Patients with hip fractures resulting from high energy mechanisms, such as motor vehicle accidents or falls from a substantial height.
5. Patient who refuse 30-day follow-up.
6. Patients who refused to consent either by themselves or through a substitute decision-maker (for patients unable to consent, we will use a deferred consent process, as described below).

SAMPLE SIZE

We recruited a convenience sample of 100 patients for this pilot study. This sample size would enable us to estimate an 85% recruitment rate within a confidence interval of $\pm 7\%$, and a 95% follow-up rate within a confidence interval of $\pm 4\%$.

TIMELINE

A priori we decided that a full study would be feasible if we could achieve a recruitment rate of at least 85%. With an average of one hip fracture admission per day (from Juravinski Hospital data), we anticipated meeting our recruitment target within 4 months.

PATIENT RECRUITMENT AND INFORMED CONSENT

All orthopaedic surgeons at the Juravinski Hospital were provided with this protocol as well as a detailed orientation session of the study. Orthopedic surgeons/residents referred to research personnel all patients diagnosed with a hip fracture. Patients admitted during the nighttime were seen in the morning by the study personnel.

The study personnel confirmed eligibility and obtained written informed consent. If a patient was unable to consent, study personnel contacted the substitute decision maker to obtain consent for participation. This study was a low risk observational study which relied on the timeliness of investigations of consecutive patients to ensure valid results. As such, we used a deferred consent process if we were not able to immediately contact the substitute decision maker within 24 hours. In this process, patients who were unable to consent were enrolled for systematic surveillance and blood work as per our protocol until such time that study personnel were able to contact the substitute decision maker. At that point, if there was refusal to provide consent, we immediately ceased our protocol investigations. Such deferred consent processes have been used previously, such as in the VISION Study [24], where timeliness of investigations is important to ensure validity and limit bias, and where risk of study participation is low.

PATIENT REGISTRATION

All patients aged ≥ 18 years diagnosed with a hip fracture who provided informed consent to participate were registered into the study using a central web based registration system (IWRS). The IWRS is a 24-hour computerized registration internet system maintained by the coordinating centre at the Population Health Research Institute (PHRI).

FOLLOW UP

In-Hospital Follow up

All patients participating in this study were monitored closely throughout their hospital stay. Study personnel followed each participant daily to ensure protocol compliance and to record results of investigations. The following investigations were conducted until the time of hospital discharge:

1. Troponin I level at admission and days 1 through 10, and once every second day thereafter.
 - a. All elevations resulted in an ECG being obtained and two more troponin levels spaced 8 hours apart. If there was no indication of ischemia on the ECG and the patient had no ischemic symptoms we then recommended obtaining an echocardiogram.
2. Complete blood counts and creatinine levels at admission and days 1 through 10, and once weekly thereafter.
3. Confusion Assessment Method (CAM) Instrument at admission and once daily post admission day 1 through 10, and once weekly thereafter (ceased if positive on any occasion).
4. Episodes of fever (temperature $>38^{\circ}\text{C}$) resulted in the measurement of blood cultures (x2), urine analysis and culture, and a portable chest radiograph. Repeats of these

investigations were only undertaken if there was resolution of the fever for a complete 48-hour interval prior to recurrence.

5. The Functional Independence Measure (FIM) Instrument was administered within 72 hours of admission to establish pre-fracture functional independence and disability.

When the patient was unable to provide this information, it was obtained from a knowledgeable informant.

All patients participating in this study were monitored daily by the research team throughout the duration of their hospitalization. This team co-ordinated additional investigations and imaging based on the protocol.

Nutritional Status

Patients' nutritional intake may serve as an important prognostic variable, and may possibly represent an early marker of clinical deterioration. We assessed each patient's nutritional status on a daily basis. Specifically, we collected the type of intake (e.g. clear fluids only, non-meal-replacement thick fluid, meal-replacement thick fluid, or solid food) as well as the approximate amount of food consumed as a categorical variable.

Mobility Assessment

Patients with hip fracture experience on average more than five days of immobility in the hospital [30]. Delayed ambulation after hip fracture surgery is related to the development of post-operative medical complications, increased length of hospital stay, and increased mortality at 6 month [30,31]. We assessed the weight-bearing status and mobility of each patient on a daily basis. We recorded the duration of time each patient spent sitting and standing as well as their daily walking distance.

Autopsy

We encouraged consideration of obtaining an autopsy for all participants who died in hospital. Autopsies were encouraged when the cause of death was unclear and were only conducted if fully informed consent was obtained from patients' substitute decision makers. All autopsies were conducted at the Hamilton General site of the Hamilton Health Sciences following established institutional protocol.

Follow-up

Patients were contacted by research personnel in person or by telephone (if the patient was discharged) 30 days and 6 months after study registration. In addition to clinical outcomes, the FIM Instrument was administered to determine post-fracture functional independence and disability. Petrella and coworkers have validated the administration of the FIM motor domain by phone interview in hip fracture patients [32]. For reported outcomes study personnel obtained the relevant hospital records, and the source documents were forwarded to the project office for adjudication.

STUDY OUTCOMES

Primary outcomes

1. Feasibility of recruiting 100 hip fracture patients at Juravinski Hospital, Hamilton ON while achieving an inclusion rate of 85% of all eligible patients.
2. Feasibility of obtaining 95% follow-up at 30 days and 6 months.
3. The time and resources requirements to achieve complete in-hospital, 30 day and 6 month follow-up.

Sub-classification of mortality

Mortality was further sub-classified based on cause of death based on the judgment of an adjudication committee. The adjudication committee received all source documentation, including the results of the aforementioned investigations as well as the patient's /progress notes when available. They classified cause of death into one of the following categories; vascular (vascular cardiac, vascular noncardiac, vascular of unknown cause) and nonvascular (See Appendix 3).

Secondary Outcomes

1. Total and cause specific mortality in hip fracture patients at 30 days and 6 months.
2. Major complications within 30 days and 6 months. This was a composite outcome of all-cause mortality, nonfatal MI, nonfatal stroke, nonfatal PE, infection with sepsis, and life-threatening bleeding (Appendix 3). A second composite was also used, which included all MINS (in addition to nonfatal MI).
3. Incidence of individual outcomes including; myocardial infarction, myocardial injury after noncardiac surgery (MINS), pulmonary embolism, infection, major bleeding, life-threatening bleeding, stroke, new congestive heart failure, new atrial fibrillation, cardiac arrest, deep vein thrombosis, new AKI, new AKI receiving dialysis, cardiac catheterization, PCI, CABG, ileus, bowel perforation, pressure ulcer, fall, delirium, implant failure, prosthetic hip dislocation, periprosthetic fracture, re-operation, critical care admission, length of critical care unit stay, length of hospital stay, length of rehabilitation stay, new nursing home residence, first mobilization, and FIM (motor).

Adjudication of Outcomes

The following outcomes were adjudicated: MI, MINS, non-fatal cardiac arrest, stroke, DVT, PE, and death. All adjudication were performed by a committee of clinicians who were independent

of the study design and conduct. The clinicians on this committee were individuals with expertise in perioperative outcomes.

Statistical Analysis

Feasibility outcomes were reported as descriptive statistics, including data pertaining to rate and proportion of patients recruited, data completeness, and required staff time. A priori we decided that a large study would be feasible if study personnel could recruit 100 patients within 12 months, while obtaining $\geq 85\%$ inclusion rate, and completing $\geq 95\%$ of follow-up at both 30 days and 6 months.

We used descriptive statistics for the baseline patient characteristics, incidence of all-cause and cause-specific mortality, incidences of both the primary and secondary outcomes along with the incidences of individual clinical events. For each patient who has died, we determined the date and time of each of the clinical events preceding the death in order of occurrence.

A two-tailed t test was used to determine any difference between pre-fracture and post-fracture function based on results from the FIM instrument. An a priori significance level of $p < 0.05$ was established. Statistical analyses were performed using SAS Statistical Software.

ETHICAL STANDARDS

Good Clinical Practice (GCP)

The procedures set out in this protocol were designed to ensure that the investigator abided by the principles of the Declaration of Helsinki and Good Clinical Practice Guidelines (ICH-GCP) in the latest version, in conduct, evaluation and documentation of the study.

Informed consent of the patient

Patients who meet all inclusion criteria and none of the exclusion criteria were deemed eligible.

Before registration into the clinical study occurred, all patients, or their proxy decision-makers, were explained the details of the study protocol, and were asked to sign a consent form for participation after the nature, scope and possible consequences of the study were explained both orally and in writing.

Approval of study protocol

The Hamilton Health Sciences Research Ethics Board (REB) approved the study protocol and consent form before this site was activated to enroll patients.

Confidentiality

All patient names will be kept confidential. Patients were identified by the patient ID number allotted to them by the study. The patients were assured that all findings will be stored on computer and handled in the strictest confidence.

CHAPTER 3: RESULTS

FEASIBILITY

From December 2013 to March 2014 (i.e., 4 months), we recruited 100 consecutive adult hip fracture patients from a single centre. One patient declined participation over this time period (>99% recruitment rate). Consent was obtained within 24 hours of their hip fracture diagnosis for 61 patients and after 24 hours for 39 patients. Eight patients were initially enrolled using the deferred consent process (written consent was eventually obtained for all).

We obtained 30-day and 6-month follow-up for all enrolled patients (100% follow-up rate). A mean of 166 minutes of research assistant time was required for each patient enrolled, comprising means of 19 minutes for eligibility and baseline assessment, 23 minutes for follow-up during hospitalization, 88 minutes for daily assessments, 15 minutes for 30-day follow-up, and 21 minutes for 6-month follow-up (Table 2). The completeness of daily troponin measurements (one of our protocol measures) was variable. While all patients except one had one or more troponin measures while in hospital, only 11 patients had troponins measured every day (up to the first 10 days, and taking into account length of stay) as per our protocol. Completeness of data for troponin, complete blood counts (CBCs), creatinine, and Confusion Assessment Method (CAM) administration are found in Appendix 1. Autopsies were not obtained for either of the two patients who died in hospital.

PATIENT, INJURY, AND TREATMENT CHARACTERISTICS

Patient Characteristics

The majority of enrolled patients were female (60%), White/Caucasian (97%), and were fluent in English (88%). Mean age was 76.8 (SD 12.8) years. Fifteen patients resided in a nursing home prior

to fracture, 23 required assistance with Activities of Daily Living, and 51 required the use of a walking aid prior to the hip fracture (Table 3). Hypertension was the most common baseline medical co-morbidity (65 patients). Twenty patients had dementia (Table 4).

Injury and Treatment Characteristics

Fifty-eight patients had an intracapsular hip fracture, 41 had an intertrochanteric/trochanteric hip fracture, and one had a subtrochanteric fracture. Ninety-six patients had surgery for their hip fracture, while four were treated non-operatively. Forty-seven patients were treated with open reduction and internal fixation, 47 were treated with arthroplasty, and one each was treated with resection arthroplasty and a complex reconstruction/tumour-type prosthesis (Table 5). The median time from fracture to emergency was 2.2 hours, from emergency department to diagnosis was 2.5 hours, and from diagnosis to surgery, was 23.9 hours (Table 6).

OUTCOMES

Mortality and Subclassification

In total, 2 patient died at the 30-day follow-up (both while in hospital), and 13 additional patients had died at the 6-month follow-up. Of the 15 patients who died, 8 were female and 7 were male. Causes of death were sub-classified into 3 respiratory failures, 2 liver failures, 2 cancers, 1 sepsis, 1 vascular (cardiac), 3 'other' non-vascular, and 3 'other' vascular. One or more of troponin elevation, new delirium, infection, or major bleeding represented early clinical events preceding deaths in all patients.

Composite Outcomes

At 30 days, 19 patients experienced the composite outcome (i.e., including only from MINS), including two patients that had died. If all MINS were included in the composite (i.e., not only MIs

meeting the third universal definition), the number of patients experiencing the composite increased to 47. At 6 months, 35 patients had experienced composite 1 (i.e., only MI from MINS), including 13 additional patients that had died. The composite outcomes, as well as individual components of the composites are reported in Table 7.

Sequence of Events for In-Hospital Mortality

There were two in-hospital deaths during initial hospitalization for hip fracture. These two cases were deconstructed based on sequence of clinical events leading up to death. Both deaths were preceded by cardiac arrest, and pneumonia was the most recent clinical event preceding both deaths (Figure 1). The 13 deaths that occurred between 30 days and 6 months were also deconstructed based on temporal sequence of clinical events preceding each death (Appendix 2).

Medical/Surgical Outcomes

MINS/MI, delirium, infection, major bleeding, and death were the most common clinical events following hip fracture. Post-operative orthopaedic/surgical complications were uncommon (Table 8).

Function Outcomes

There was a decrease in FIM scores from mean 82.5 (standard deviation [SD] 15.6) pre-fracture to a mean of 70.1 (SD 23.3) at 30 days. This increased slightly to a mean of 76.1 (SD 20.5) at 6 months. Among patients that did not come from a nursing home (n=85), 6 (7.1%) resided in a nursing home at 6 months.

Medications

Medications related to secondary preventative efforts for osteoporosis and fall-related injuries were poor overall. At 6 months, only 58% of patients alive for follow-up were taking Vitamin D, 34%

were taking calcium, and 25% were taking osteoporosis medication (i.e., bisphosphonates).

Eighteen percent of patients were on benzodiazepines at 6 months (Table 9).

TABLES

Table 2: Research Assistant Workload Per Patient

Workload For:	Mean (Minutes)	Standard Deviation (Minutes)
Baseline Assessment	18.7	10.5
Daily Assessment	88.4	67.0
Hospital Discharge	23.3	31.5
30-Day Follow-up	14.6	20.4
6-Month Follow-up	21.4	35.5

Table 3: Baseline Patient and Enrollment Characteristics

Characteristic	Number/Percentage of Patients
Patients Enrolled	100
<u>Written Consent</u>	
Less than or equal to 24 hours	61
Greater than 24 hours	39
Deferred Consent	8
Female	60
<u>Ethnicity</u>	
White/Caucasian	97
Asian	2
Hispanic/Latino	1
<u>English Language</u>	
Fluent	88
Limited	12
<u>Frailty Measures</u>	
Assistance with ADLs	23
Walking Aid	51
Nursing Home Residence	15
Previous Hip Fracture	8

Table 4: Baseline Patient Medical Histories

Medical History	Number/Percentage of Patients
Hypertension	65
Stroke or TIA	18
Stroke	10
TIA	10
Coronary Artery Disease	28
Recent High-Risk CAD	3
Coronary Revascularization	13
Previous Atrial Fibrillation	18
Current Atrial Fibrillation	11
Congestive Heart Failure	8
Aortic Stenosis	3
Cardiac Arrest	2
Peripheral Vascular Disease	5
DVT/PE	6
Diabetes (requiring OHA or Insulin)	16
Chronic Kidney Disease or transplant	0
COPD	9
Obstructive Sleep Apnea	5
Dementia	20
Active Cancer	9
Osteoporosis	23
On anti-osteoporotic agent	15
History of Tobacco Use	57

Table 5: Injury and Treatment Characteristics

Variable	Number/Percentage of Patients
Side of Hip fracture	
Left	44
Right	56
Type of Hip Fracture	
Intracapsular	58
Intertrochanteric	41
Subtrochanteric	1
Type of Surgery	
Open reduction and internal fixation	47
Arthroplasty	47
Resection Arthroplasty/Girdlestone	1
Complex Reconstruction	1
Type of Anesthesia	
General	30
Spinal	66
Regional	3
Surgery delay > 6 hours	97

Table 6: Injury and Treatment Timelines

Timeline	Min	Q1	Median	Q3	Max
Fracture to Emergency (hours)	0.2	1.4	2.2	5.4	3004.5
Emergency to Diagnosis (hours)	0	1.6	2.6	3.8	164.3
Diagnosis to Surgery (hours)*	7.5	18.3	23.9	42.4	113.4
Surgery to Hospital Discharge (days)	3	6	8	13	30
Length of Hospital Stay (days)	6	8	10	15	31
CCU Stay (days)	2	3	3	5	9

*** among patients who went to surgery**

Table 7: Number and Percentage of Patients Experiencing Composite and Major Outcomes

Outcome	30-Day Follow-up	6-Month Follow-up
Composite 1 (including all MINS)	47	63
Composite 2 (including only MI but not MINS that did not fulfill the MI definition)	19	35
Death	2	15
MINS	42	42
MI	12	13
Stroke	1	1
Sepsis	6	12
Life-Threatening Bleeding	1	2
Non-Fatal Cardiac Arrest	2	2

Table 8: Number and Percentage of Patients Experiencing Clinical Events In-Hospital, within 30 days, and within 6 months

Clinical Event	During Hospitalization	Discharge to 30 days	31 days to 6 months
Death	2	0	13
Troponin elevation	41	7	3
Critical care unit admission	21	3	4
Non-fatal cardiac arrest	2	0	0
Stroke	0	1	0
TIA	0	0	0
Leg or arm DVT	0	0	1
Pulmonary embolism	0	0	0
Major bleeding	9	4	2
Life-threatening bleeding	0	0	1
Cardiac catheterization	1	0	1
PCI	0	0	0
CABG	0	0	0
New congestive heart failure	1	1	2
New clinically important atrial fibrillation	6	1	1
Infection	12	13	10
New acute kidney injury requiring dialysis	5	0	2
Ileus/bowel perforation	2	0	2
Delirium	16	3	1
Fall	0	10	5
Pressure ulcer	1	0	1
Post-op orthopaedic complication (all)	1	2	0
Periprosthetic fracture	0	1	0
Hip re-operation	0	1	0

Table 9: Medications Taken at Baseline and Follow-Up

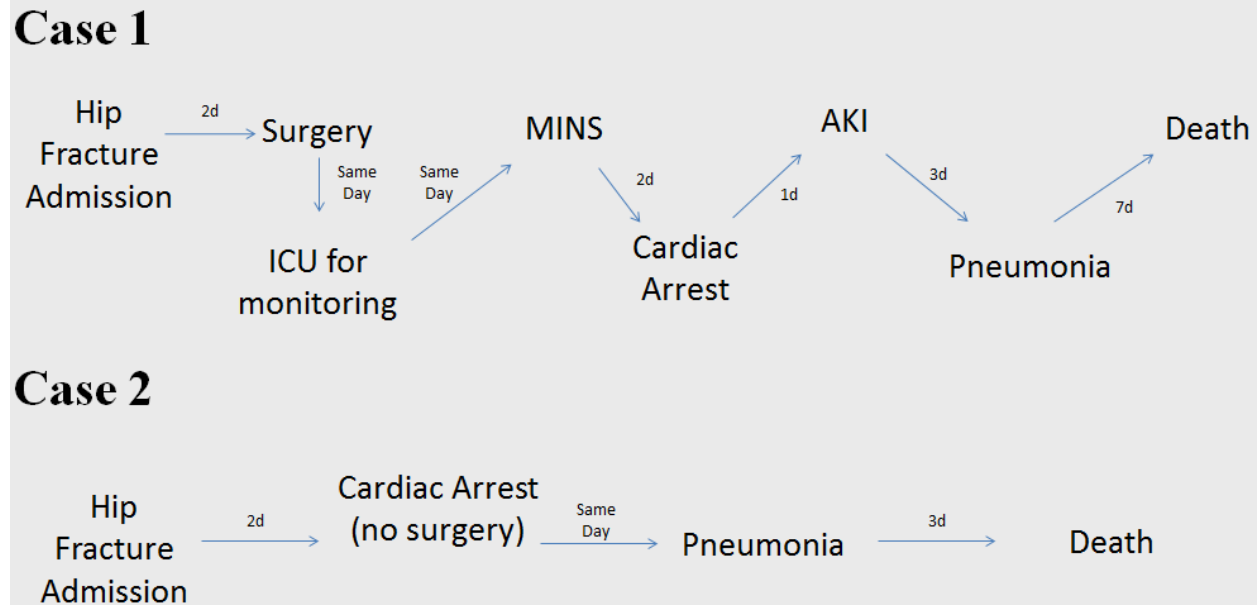
Medication	Baseline ¹ , %	30-Day Follow-Up, %	6-Month Follow-up, %
Aspirin	26	36	38
Other antiplatelet agent	2	1	4
Vitamin K antagonist	8	8	6
Long-acting nitrate	2	3	1
Ace-I/ARB	43	47	48
Beta-Blocker	25	39	33
Digoxin	5	4	4
Non-Dihydropyridine (Rate-controlling) CCB	5	8	9
Dihydropyridine CCB	15	13	9
Alpha-2-antagonist	0	0	0
Statin	41	47	44
Non-statin cholesterol lowering agent	1	2	2
Cholinesterase inhibitor	2	2	1
Insulin	5	6	4
Oral hypoglycemic agent	9	11	11
Prophylactic antithrombotic agent	0	50	4
Therapeutic antithrombotic agent	6	8	7
Corticosteroid	4	4	4
Proton pump inhibitor	28	36	42
Benzodiazepene	15	8	18
Anti-psychotic agent	11	11	12
COX-2 Inhibitor	1	0	2
NSAID/non COX-2 Inhibitor	6	6	6
Diuretic	28	19	33
Calcium	8	31	34
Vitamin D	20	49	58
Anti-osteoporotic agent ²	15	17	25
Hormone replacement therapy	1	3	0

¹Medications taken between 1 and 7 days prior to fracture

²Taken at any time prior to fracture

FIGURES

Figure 1: Sequence of events leading to death during initial hip fracture hospitalization by patient



CHAPTER 4: DISCUSSION

Hip fractures are common injuries and occur predominantly in the elderly. As the population continues to age, we can expect at least a stable, if not increasing, number of hip fractures throughout both the developed and developing worlds [1-4]. These injuries are important in that they not only lead to the acute consequences of pain and immobility, but that there are substantial long-term consequences as well, such as functional decline, and high rates of morbidity and mortality [23]. Unfortunately, rates of mortality have not changed substantially over the past several decades, and the causes of mortality after hip fracture are poorly understood [3,10,11]. In this pilot study, we have demonstrated the feasibility of obtaining high rates of recruitment and follow-up of hip fracture patients. We have also explored some of the preliminary clinical findings, which are fairly consistent with those in the literature. The aim of the definitive trial will be to explore the causes of mortality in hip fracture patients in a large international cohort study.

Summary of Results

Feasibility

We achieved all of our primary feasibility objectives. Specifically, only a single patient declined participation (>99% recruitment rate), 30-day and 6-month follow-up was completed for all patients, and resources requirements were quantified and were reasonable despite the requirement for daily in-hospital assessment and follow-up of each enrolled patient. Both recruitment and follow-up have been considered a major challenge in prospective study designs involving patients with dementia [33,34]. There is a high prevalence of dementia in the hip fracture population, and indeed 20% of patients in our pilot study had baseline dementia. However, using strategies that were used to obtain high rates of follow-up in previous studies such as VISION [24]

and POISE [25], we were able to obtain near-perfect follow-up. We would similarly expect this to translate into excellent follow-up at the international stage, as has been the case for previous studies.

High Rates of Medical Complications

Complications after hip fracture were common, and were comprised predominantly of medical complications. Orthopaedic/surgical complications were minimal during the follow-up period, with a total of three (one in-hospital and two at 30 days). In contrast, 63 patients experienced the composite outcome (i.e., any of MINS, stroke, sepsis, life-threatening bleeding, non-fatal cardiac arrest, or death). Infections (35 events), Delirium (20 events), and major bleeding (15 events) were also common clinical events after hip fracture. These high rates of medical complications are consistent with existing literature [15,22,23]. The use of a larger sample size will enable us to determine how these clinical events relate to and/or cause mortality and functional decline. It will also enable us to develop a comprehensive risk-estimation model for patients who sustain hip fracture.

Poor Secondary Preventative Efforts

In addition to acute management, a hip fracture presents an opportunity—and indeed an obligation—to initiate efforts to mitigate risks of future falls, fractures, and medical complications. Overall, in our small cohort, our observations suggested that this was being performed less than optimally. For instance, a hip fracture is considered diagnostic for osteoporosis. However, only 49% of patients were taking Vitamin D, 30% of patients were taking calcium, and 21% of patients were taking an anti-osteoporotic agent (i.e., bisphosphonate) at 6 months. Vitamin D and, in certain situations, calcium supplementation are considered mainstays of osteoporosis management. Further, bisphosphonates have been shown to have a mortality benefit after hip fracture. Although there may be instances where certain contra-indications exist, the sheer number of patients not taking these

medications suggests there is some degree of mismanagement occurring following hip fracture. Another example includes benzodiazepine use, which has been associated with falls and subsequent fractures [35]. We found that 15% of patients were taking benzodiazepines at 6 months despite having sustained a hip fracture. There was also a general trend noted of medication changes across all types of medications after hip fracture. The universality and appropriateness of these medication changes can and must be further explored in a large international cohort.

Considerations for Large International Cohort Study

Strengths

Our pilot study—and the large international study that this pilot will inform—has several unique strengths in comparison to existing studies evaluating hip fracture outcomes. First, this study utilises a prospective study design with systematic investigation and daily assessments by research staff. A systematic search of the literature reveals that the largest prospective follow-up of hip fracture patients was conducted in the United Kingdom by Roche et al [23]. However, this study relied predominantly on medical records based on routine care and did not employ systematic surveillance for occult conditions. Certain conditions, such as MINS and delirium, cannot be detected reliably without systematic surveillance. Our pilot study was able to detect these conditions at much higher rates than Roche et al reported [23].

Second, our pilot study employs broad eligibility criteria. Although the benefits of this are less clear in the pilot phase given the small sample size, a larger international study will be able to capture data on a diversity of patients. This will enable us to analyze and explore effects of hip fracture in various subgroups within the broader hip fracture population, including younger patients, high- and low-energy injuries, and pathologic fractures (e.g. malignancy-related fractures). Given the relative low proportion of these subgroups among the vast number of hip fractures that occur

every day, high quality studies have not typically evaluated these patients. For instance, Roche and colleagues deliberately excluded patients under the age of 60 [23]. However, these subgroups may have differing outcomes and prognoses following hip fracture, which is important to identify and understand.

Further, in addition to enabling the detailed study of these various subgroups, inclusion of a breadth of patients will have pragmatic implications as well. One of the main difficulties in executing a large, prospective observational study is that it is difficult to obtain sufficient support in terms of financial resources and participating centers. By including many subgroups, a diversity of interests may be piqued, resulting in participation of more centers and opportunities for more funding. For example, inclusion of pathologic hip fractures resulting from bony malignancy may interest orthopaedic oncologists, who will subsequently push their centers to participate in the study. Furthermore, a substudy or subgroup analysis on patients with metastatic hip fractures opens the door to more funding opportunities from cancer foundations (e.g., Cancer Care Ontario). Ultimately, this is good for both patient care and science, as we will obtain data on subgroups of patients for which there is presently a dearth of data. These approaches have been previously described in orthopaedics [36]. Further, the original VISION study relied on more than 60 sources of funding (a combination of both peer reviewed and industry grants), a proportion of which were obtained for proposed substudies within the larger international cohort.

Finally, the high proportion of patients recruited and followed to six months is a major strength of our study as described in the feasibility section above. One of the difficulties we anticipated in achieving this goal was the recruitment of patients who had both hip fracture and either an acute or chronic cognitive condition, such as delirium or dementia. Recruitment of such patients into clinical studies presents both practical and ethical challenges [33,34,37]. We were able

to overcome these issues in the pilot study by obtaining consent by proxy (e.g., Power of Attorney) or (barring that) using a deferred consent process whereby the patient was enrolled into the study until such time that consent could be obtained from either the patient or a proxy (e.g. Power of Attorney). Our deferred consent process was justified owing to a low risk to participants (i.e., there was no intervention and negligible additional risk of the study protocol as compared to usual clinical care). Further, the design of the deferred consent process included an eventual requirement for explicit consent (by patient or proxy) or, barring that, a time-out period after which consent would be withdrawn. These are factors that have been previously described and are generally well-accepted in the literature [37-39]. Eight patients were enrolled in this pilot study using the deferred consent process, and all of these patients had written consent obtained within 48 hours. It will be crucial to ensure that we are able to obtain a deferred consent process at all participating centers in the international study.

Limitations

The main limitation to the interpretation of the results of this study is that the sample size does not have sufficient power to make any definitive conclusions on clinical endpoints (i.e., the secondary outcomes). This is especially true for rarer outcomes, such as mortality, and may explain the relative low rate of in-hospital and 30-day mortality that we observed (i.e., 2% mortality in-hospital and 30 days). More common clinical events, such as MINS and delirium, may be closer to the average population value; however, these too must be confirmed within a larger sample. Moreover, the single centre design of this pilot study does not allow us to make any conclusions pertaining to the broader population, as only a local population (i.e., Hamilton, Ontario, Canada) has been represented. Hence inclusion of multiple centres in multiple countries throughout the world for the definitive study is crucial.

There are also further limitations to our pilot study that need to be considered in the design of a large international multi-center cohort study. The first issue was one of protocol compliance (i.e., compliance with the daily protocol-mandated investigations was less than 100%). For instance, the protocol mandated daily bloodwork for troponin measurement for each of the first 10 days of admission or until discharge (whichever occurred first). Although the vast majority of patients had initial troponin measurements, the compliance with this decreased with each subsequent day of admission. Ultimately, the majority of patients had at least 5 (or at least 50%) of troponin measurements while in hospital. The number of patients that did not meet this threshold was 11, and only a single patient did not have any troponins drawn. Based on our data, we were unable to determine whether the reason for less than perfect compliance was attributable to provider, patient, or research staff factors. Therefore, non-compliance with the protocol is an issue that will need to be proactively monitored throughout the duration of a larger trial. This will require encouragement and reiteration of the rationale for routine and systematic monitoring to healthcare providers, enrolled patients, and local research staff. Protocol compliance will also need to be closely monitored by a Central Co-ordination Center with weekly and monthly reports in order to provide real-time feedback to each participating international center.

From the aforementioned issue, the other consideration that arises is whether the protocol should exclude patients that are deemed to be at high risk of non-compliance with protocol-mandated investigations. There are two main reasons why we have not chosen this approach. The first is that it is difficult to accurately identify patients that will eventually decline protocol-mandated investigations. This is because during the course of active treatment for an acute condition (i.e., hip fracture +/- associated morbidity), each patient's condition is continuously changing. As such, a stable patient may develop an acute medical condition necessitating many investigations;

alternatively, an initially unwell patient initially requiring many investigations may become palliative and subsequently decline every investigation. Determining this at the time of admission is very difficult, if not impossible. Secondly, by excluding patients that may be high risk of non-compliance with protocol-mandated investigations, there is the risk of either biasing outcomes or missing important epidemiological information. For instance, a patient who chooses to decline investigations may be more likely to have dementia and, therefore, develop delirium (because dementia is a risk factor for delirium) [40]. By excluding these patients, not only will we underrepresent patients with dementia—which is a known issue in the orthopaedic literature [41]—we will also be missing important information pertaining to the epidemiology and prognosis of patients with delirium. Therefore, the lesson learned from the pilot is that we must both monitor and encourage strict adherence to the protocol, although acknowledging we may end up with less than such.

Another limitation of this pilot study stems from the limited experience establishing causes and pathways to deaths, which is attributable to only two deaths occurring within 30 days. However, despite the limited experience with this issue, some important lessons were learned. First, it became apparent that determining the cause of death is a challenging task given the multiple processes that occur in close proximity or simultaneously (see Figure 1 and Appendix 2). It has become evident that precisely defining cause of death—as well as root causes where intervention may be beneficial—will require a team of experts assessing all collected data along with source documentation. Specifically, the establishment and appropriate training of a Mortality Adjudication Committee will be integral to achieving the main objective of this study (i.e., determining causes and root causes of mortality in hip fracture patients). Ideally, this committee will be trained in the use of ‘root-cause analysis’, with methodology gleaned mainly from the patient safety literature,

prior to adjudication [42]. Committee members will need to combine this training with their clinical expertise to provide meaningful and reliable mortality outcome adjudication. Clinical research experience with root-cause analysis outside the patient safety literature is limited [43], and our international study will provide a further opportunity to develop this field of study.

Given the multiple competing events, autopsy information would also be very informative in assisting an adjudication committee in determining a precise cause of death. Indeed, there is a strong ethical case to be made for obtaining autopsies on hip fracture cases predicated on the persistently high mortality rates and unknown causes of mortality. Indeed, we were able to obtain institutional ethics board approval as well as pathology departmental buy-in to conduct autopsies for this pilot study. Unfortunately, we were unable to obtain consent for autopsy from the two patients that died in hospital. Given the low numbers, it is difficult to know whether difficulty obtaining autopsies will be a major issue in a large international cohort. However, given the potential information that might be gleaned from autopsies, attempting to obtain autopsies on any patient that dies in-hospital is a potentially useful strategy, which may be reconsidered in the larger study once a sufficient number of experiences with this process are obtained.

We were able to obtain the most comprehensive assessments of mortality for patients that died in hospital (Figure 1), and indeed the potential addition of autopsy information would further facilitate this. Accuracy of adjudication of mortality that occurs after hospital discharge will be more limited, as we rely more heavily on routine clinical notes, patient records, and telephone follow-up. Nevertheless, as demonstrated in Appendix 2, the information that we glean will still be very detailed and certainly more informative than the existing literature, which comprises predominantly retrospective administrative database studies. Further, we will be able to correlate events that occurred in hospital, as well as function, medications, and outcomes at 30 days, 6 months, and 1

year with mortality. This will enable us to develop far more insight into risk factors and possible causes of long-term mortality after hip fracture than are currently available.

Conclusions

High rates of mortality after hip fracture have persisted, with little to no improvement, for decades. Medical complications and decline in function are other devastating consequences following a hip fracture. The case for a large international cohort to explore causes of mortality, identify root causes for intervention, and opportunities for improvement in care is compelling. Our pilot study has demonstrated that such a large prospective observational cohort of hip fracture patients is feasible. The findings of this study also suggests that the rate of medical complications and mortality is disproportionately high, and suggest that secondary prevention efforts for falls, fractures, and medical conditions are very poor in the hip fracture population. These are issues that will need to be further explored in a large international cohort.

CHAPTER 5: An Intervention to Improve Outcomes – Geriatric Co-Management

Systematic Review and Meta-Analysis

Introduction

Over 320,000 individuals suffer a hip fracture in North America each year, and the incidence is forecasted to increase as the population continues to age [44,45]. By the year 2050, the global incidence of hip fracture is expected to surpass 6 million [45]. One of the most common complications following hip fracture is an acute state of cognitive dysfunction known as delirium. Elderly patients are particularly prone to delirium, and the physiologic and environmental stresses following hip fracture further increase this risk [40]. By some estimates, up to 50% of all hip fracture patients will develop delirium at some point following a hip fracture [46].

Delirium is characterized by certain cardinal features including an acute and fluctuating course, decreased level of consciousness, inattentiveness, and perceptual disturbances [40,47]. Although transient in nature, several longitudinal studies have demonstrated that incident delirium is prognostic of long-term cognitive decline, functional impairment, and mortality [48-51]. Further, delirium also results in lengthier hospital stays and increased associated economic costs [52]. Unfortunately, the evidence to date has not convincingly demonstrated an effective treatment for delirium, either pharmacologic or non-pharmacologic [53]. Therefore, management efforts have largely focused on delirium prevention.

Pharmacologic prophylaxis has not been particularly effective at preventing delirium, and most clinical practice guidelines and systematic reviews recommend a multi-component approach to the management of delirium [53,54]. Multi-component management generally

consists of a diversity of non-pharmacologic measures, including prevention and treatment of medical complications, ensuring fluid and electrolyte balance, orientation, adequate pain management, medication review and minimization, supplemental oxygen, and adequate bowel/bladder care [53,54]. Such a multi-component intervention is most likely best administered by a specialized individual (or team of individuals), such as that which can be achieved through orthogeriatric co-management of hip fracture patients.

Orthogeriatric collaborative models of care are becoming increasingly recognized for their effectiveness in improving outcomes after hip fracture. A systematic review and meta-analysis found that orthogeriatric collaborative care of hip fracture patients reduced in-hospital mortality, long-term mortality, and lengths of hospital stay [55]. A recent randomized trial also found that comprehensive geriatric care resulted in better mobility four months after hip fracture as compared to usual orthopaedic care [56]. Given that prevention of delirium requires a detailed and complex multi-modal approach, we hypothesized that orthogeriatric co-management would be particularly beneficial for delirium.

We therefore conducted a systematic review and meta-analysis of comparative clinical studies to determine if orthogeriatric co-management compared to orthopedic care alone reduces the incidence, duration, and severity of delirium in patients with hip fracture.

Methods

Our systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [57].

Inclusion Criteria

We included all comparative study designs (i.e. Randomized/Quasi-Randomized Controlled Trials and Observational Studies). We chose not to exclude observational study designs because preliminary manual electronic searches revealed that the number of randomized controlled trials (RCTs) was sparse. It has been argued that observational studies may add important information to meta-analyses, especially if RCT level evidence is lacking [58].

We only included studies in which the sample population consisted of patients with an acute hip fracture. Intervention groups had to receive co-management by a geriatrician or geriatric team. The control group had to receive usual care that did not include routine co-management with a geriatric team and come from a similar population to the intervention group. Incidence of delirium had to be reported as an outcome (either primary or secondary).

Exclusion Criteria

Studies that did not systematically screen all enrolled patients in both groups for delirium were excluded. Failure to screen in a systematic manner could lead to an artificially higher incidence in the intervention group owing to increased surveillance for the condition. We also excluded studies in which the intervention occurred in the post-acute care, rehabilitation, or community setting.

Literature Search and Full Text Review

We performed a comprehensive search of MEDLINE (1990 to December 2014, inclusive), EMBASE (1990 to December 2014, inclusive), and the Cochrane Central Register of Controlled Trials (1990 to December 2014, inclusive) using broad search terms (Appendix 6). We also manually searched Google Scholar, PubMed, and reference lists of relevant articles for eligible studies. Titles and abstracts were initially screened to exclude studies that clearly did not meet eligibility criteria. Subsequently, a full text review of all potentially eligible studies was undertaken. Pairs of authors performed the article screening and full text review in duplicate. Disagreements were resolved by consensus, and any irreconcilable disagreements were to be resolved by a third adjudicator. Agreement was calculated using Cohen's Kappa statistic. The search was managed using Reference Manager 12.0 Software (Thomson Reuters, Philadelphia, PA, USA).

Risk of Bias

Risk of bias was described for each study. Randomized/Quasi-randomized trials were evaluated using the Cochrane Risk of Bias tool. Observational studies were evaluated using the Methodological Index for Non-Randomized Studies (MINORS) [59]. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) criteria were used to grade the quality of each pooled outcome measure, and were summarized using GradePro software [60].

Data Extraction

Descriptive data from each included study were collected in duplicate using standardized data collection forms. These data included study design, location of study, publication date, total number of enrolled participants, delirium screening method/instrument and frequency of administration, and details of the intervention and control. Outcome data included number of

cases, duration, and severity of delirium (along with severity-measuring method) in each group. For continuous data, means and measures of variance were recorded (i.e., standard deviations, confidence intervals). If only medians and ranges/interquartile ranges were reported, these were converted into means and standard deviations, respectively, using appropriate methodology [61].

Sensitivity and Subgroup Analysis

A sensitivity analysis of randomized versus non-randomized/observational study designs was planned *a priori* to explore any potential sources of heterogeneity. We also planned a subgroup analysis of patients with dementia.

Statistical Analysis

As orthogeriatric co-management was hypothesized to reduce delirium incidence, duration, and severity, we felt pooling outcomes across all studies was warranted. We made an *a priori* decision to conduct a random effects analysis because we expected some heterogeneity in the interventions between studies (i.e., the specific components of each intervention were not expected to be entirely uniform). Selecting a model of analysis *a priori* has been considered more methodologically robust than basing this decision on a post-hoc test of heterogeneity [62]. Using the reported incidence of delirium, forest plots were created and pooled estimates of the mean with risk ratios (RR) and 95% confidence intervals (CIs) were calculated. We inferred statistical significance based on a p-value less than 0.05. Data analysis was conducted with RevMan 5.3 (The Cochrane Collaboration, Copenhagen, Denmark) [63].

Results

Our electronic database search yielded 4110 articles, and our manual search yielded an additional 3 (for a total of 4113 articles screened). Of these, 880 duplicates were excluded. We excluded 3192 articles after screening titles and abstracts. There was good agreement between reviewers ($\kappa = 0.79$, 95% CI 0.69 to 0.89). We undertook full text review of 41 of these articles, of which 33 were subsequently excluded. A total of 8 studies were included in this systematic review (Figure 2) [64-71]. In total, 2515 participants were included in the meta-analysis. The overall incidence of delirium was 30.5% (48.5% in the RCTs and 19.5% in the observational studies). The relatively lower incidence in the observational studies was mainly attributable to a large study which did not employ a validated delirium screening instrument [66]. Removal of this study resulted in an incidence of 36.5% in the observational studies.

Study Characteristics

Four of the included studies were RCTs (Table 10) and four were observational studies (Table 11). All studies were published in 2001 or later. Study sample sizes ranged from 99 to 951. Five studies were conducted in European countries, two studies were conducted in Australia, and one study was conducted in the United States. Delirium screening was performed by the Confusion Assessment Method (CAM) in six studies, the modified Organic Brain Syndrome (OBS) scale in one study, and blinded physician judgment in one study.

Risk of Bias

Among the four randomized trials, none were able to blind caregivers or patients, but all made a reasonable attempt at blinding outcome assessors. Only two trials had descriptions of adequate random sequence generation and allocation concealment. There were no biases associated with incomplete outcome or selective reporting in any of the trials. Among the four

observational studies, MINORS scores ranged from 20 to 22 (out of a possible 24). Three observational studies used non-contemporary (i.e., historical) control groups, two had serious baseline discrepancies between the study groups, one did not include consecutive patients and one had serious bias in the assessment of the study endpoint. Sample size calculation was inadequate in one study and not reported in two observational studies.

Delirium Incidence

Orthogeriatric co-management decreased the risk of developing delirium in the pooled estimate across all studies (RR 0.74, 95% CI 0.64-0.87, $p < 0.001$). A greater magnitude of effect was observed with observational study designs (RR 0.63, 95% CI 0.46-0.87, $p = 0.005$) as compared to RCTs (RR 0.81, 95% CI 0.69-0.94, $p = 0.007$), although the test for subgroup differences was not significant ($p = 0.18$). Statistical heterogeneity was low for RCTs only ($I^2 = 27\%$), and moderate for observational studies only ($I^2 = 58\%$) and across all studies ($I^2 = 47\%$) (Figure 3). There was moderate confidence in the RCT estimate and low confidence in the observational study estimate based on GRADE criteria (Table 12).

Duration of Delirium

Duration of delirium was reduced by a mean of 1.48 days in patients that received geriatric co-management as compared to patients who received usual care (95% CI 0.28-2.68, $p = 0.002$) (Figure 4). Four studies (3 RCTs and 1 observational study) reported duration of delirium for each group. This effect was not significant in the RCTs (mean reduction of 1.33 days, 95% CI -0.13-2.80, $p = 0.07$), and only a single observational study reported duration of delirium in each group as an outcome. There was substantial statistical heterogeneity in the RCT subgroup ($I^2 = 82\%$) and overall pooled comparisons ($I^2 = 80\%$). There was very low confidence in both the RCT estimate (owing to serious imprecision, heterogeneity, and risk of bias) and the

observational study estimate (owing to study design and potential for publication bias) based on GRADE criteria.

Severity of Delirium

Severity of delirium was reported in three studies, but there was insufficient information to allow for pooled analysis. The Memorial Delirium Assessment Scale (MDAS) was used to assess delirium severity in two RCTs. One RCT quantified the number of patients in each group with an MDAS score greater than or equal to 18 (out of a possible 24) and found less patients met this criteria in the intervention group (7 vs 18, RR=0.40, 95% CI 0.18-0.89, p=0.02) [68]. Another RCT reported median scores between the two groups, and did not find substantial differences between the intervention and control (21.5 days [IQR 15-25] vs 20 days [IQR 14-26]) [70]. The Delirium Index was used in one observational study, and no differences were found at any of the five time points when it was administered (i.e., days 1, 3, 5, 8, and 15) [62].

Dementia Subgroup

Data on patients with dementia were available for two studies (both RCTs) [67,68]; in one of these, data on the dementia subgroup was published as a separate article [72]. There was no detectable reduction in delirium with geriatric co-management in the subgroup of patients with dementia (RR 0.22, 95% CI 0.03-1.85, p=0.16). However, the sample size was small (n=164) and the CI was wide. GRADE confidence in this estimate was rated very low owing to very serious imprecision and heterogeneity.

TABLES

Table 10: Characteristics of Included Randomized Trials

Study	Location	Number (mean age±SD) of patients receiving intervention	Number (mean age±SD) of patients in control group	Intervention Details	Delirium Assessment
Lundstrom et al [67]	Sweden	102 (82.3±6.6)	97 (82.0±5.6)	Post-operative admission to a specialized geriatric orthopaedic ward employing multi-disciplinary team care	Modified OBS Scale
Marcantonio et al [68]	USA	62 (78±8)	64 (80±8)	Post-operative geriatric consultation and use of a structured delirium prevention protocol on orthopaedic ward	CAM
Vidan et al [69]	Spain	155 (81.1±7.8)	164 (82.6±7.4)	Multi-disciplinary geriatric evaluation and co-management on orthopaedic ward	CAM
Watne et al [70]	Norway	163 (median 84, range 55-99)	166 (median 85, range 46-101)	Admission to acute geriatric ward and multi-disciplinary geriatric care	CAM

Table 11: Characteristics of Included Observational Studies

Study	Location	Number (mean age±SD) of patients receiving intervention	Number (mean age±SD) of patients in control group	Intervention Details	Delirium Assessment
Boddaert et al [64]	France	131* (85±6)	203 (86±6)	Post-operative admission to dedicated geriatric unit	CAM
Deschodt et al [65]	Belgium	94 (80.4±7.0)	77 (81.1±7.2)	Routine consultation by a multi-disciplinary geriatric team	CAM
Fisher et al [66]	Australia	447 (81.9±8.0)	504 (81.3±8.2)	Routine co-management with a geriatric medicine physician	No instrument, systematic physician assessment
Wong Tin Niam et al [71]	Australia	71 (82.3±9.8)	28 (81.3±9.3)	Daily review of each hip fracture case by a geriatric medicine physician for adherence to delirium prevention recommendations	CAM

* Delirium outcomes only available for 118 patients

Table 12: GRADE Summary of Findings for Delirium Incidence

Orthogeriatric Co-Management compared to Usual Care for Hip Fracture Care

Patient or population: Hip Fracture
Setting: Hospital
Intervention: Orthogeriatric Co-Management
Comparison: Usual Care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	n of participants (Studies)	Quality of the evidence (GRADE)	Comments
	Risk with Usual Care	Risk with Orthogeriatric Co-Management				
Delirium Incidence - RCT	Study population		RR 0.81 (0.69 to 0.94)	973 (4 RCTs)	⊕⊕⊕○ MODERATE ¹	
	525 per 1000	426 per 1000 (363 to 494)				
Delirium Incidence - Observational	Study population		RR 0.63 (0.46 to 0.87)	1542 (4 observational studies)	⊕⊕○○ LOW ²	
	219 per 1000	138 per 1000 (101 to 190)				

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio; OR: Odds ratio;

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Inconsistency: Two (i.e., half) of the RCTs demonstrated no significant effect despite low statistical heterogeneity
2. Study design

FIGURES

Figure 2: Search Strategy

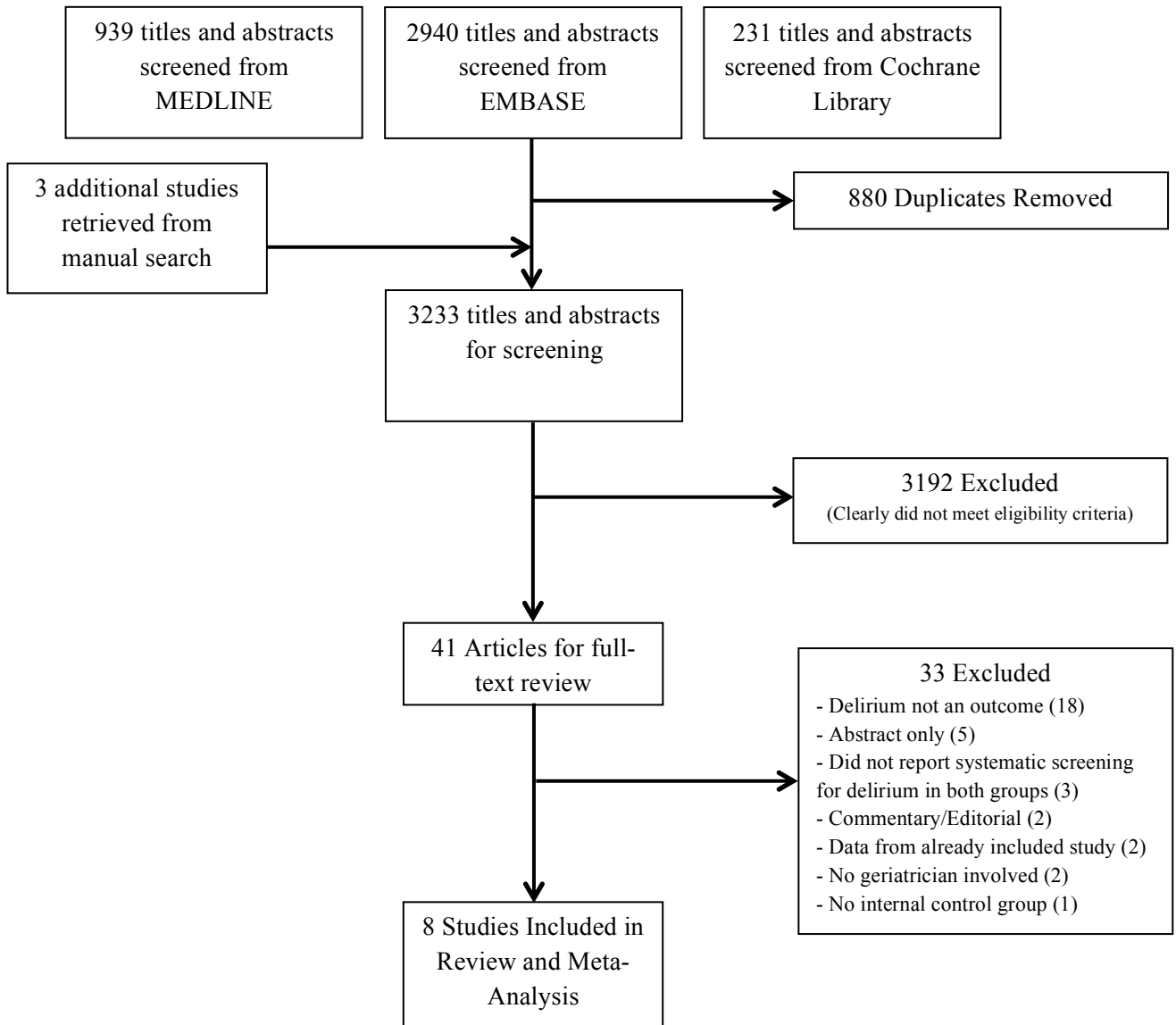


Figure 3: Forest Plot for Delirium Incidence

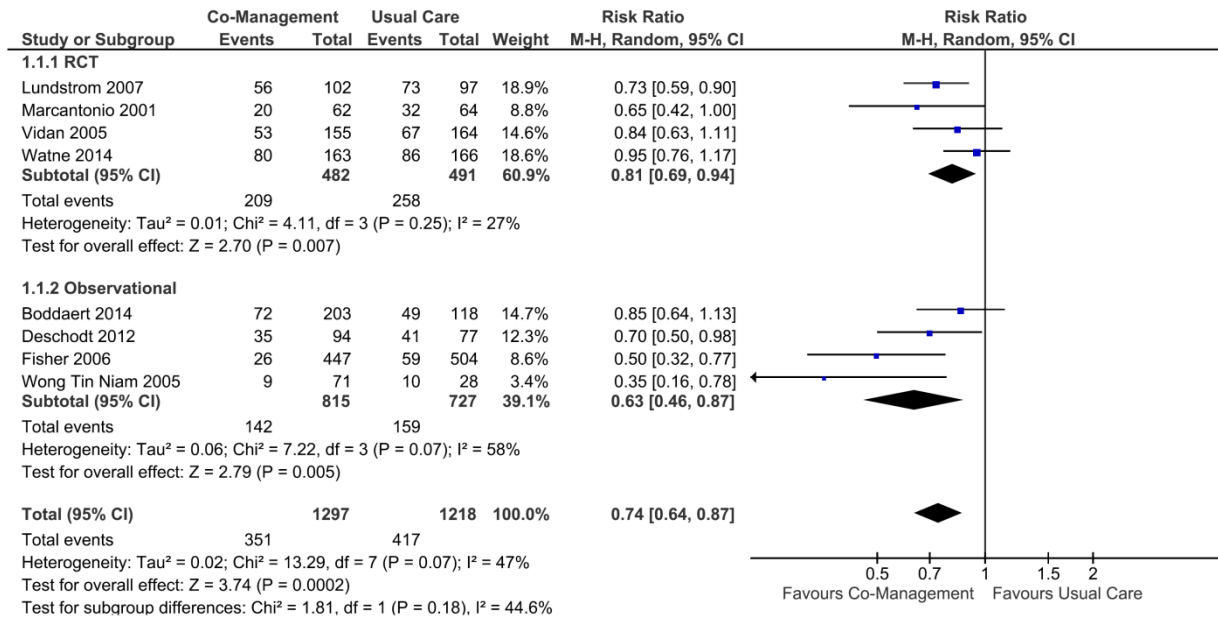
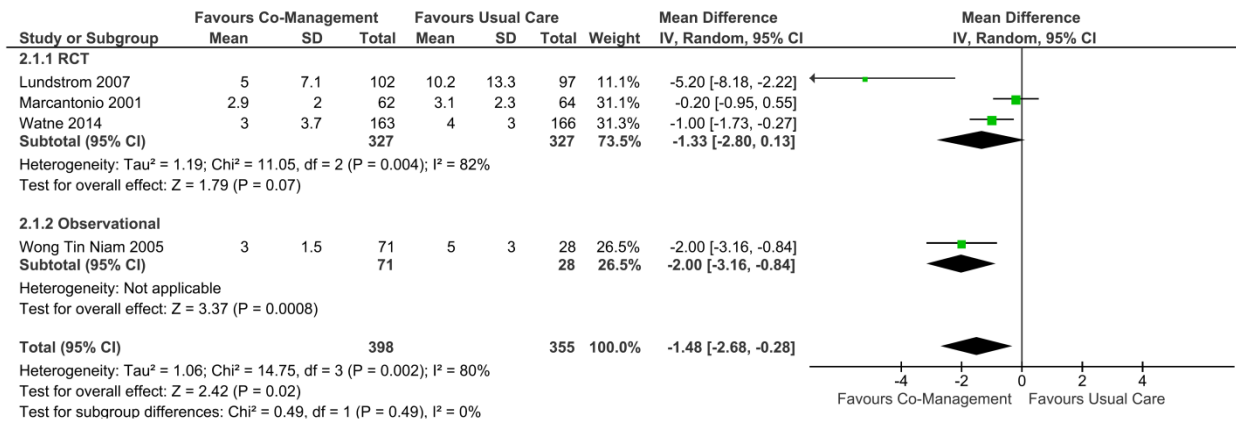


Figure 4: Forest Plot for Duration of Delirium



Discussion

The results of this systematic review and meta-analysis demonstrate, with moderate confidence, that hip fracture patients receiving orthogeriatric co-management have a 19% (95% CI 6% to 31%) lower risk of developing in-hospital delirium than those receiving usual orthopaedic care. With a control group event rate of 52.5% in the highest quality (i.e., RCT) subgroup, this represents a substantial absolute reduction in delirium cases. Delirium is a serious medical condition, and has been associated with long-term declines in function and cognition, increased lengths of hospital stay, and a possible increase in the risk of mortality [40]. Therefore, the effectiveness of this intervention in preventing delirium has important clinical and public health implications.

The finding that geriatric co-management is beneficial in preventing delirium is consistent with previous literature. Grigoryan and colleagues demonstrated that orthogeriatric collaboration substantially reduced the risk of in-hospital and long-term mortality in hip fracture patients, but there was insufficient data to make conclusions pertaining to delirium [55]. A systematic review by Inouye and colleagues summarized delirium prevention studies in both hip fracture and non-hip fracture patient populations, and found that the bulk of the evidence favours multi-component prevention strategies [53]. Reston and Schoelles systematically reviewed studies of in-facility delirium prevention programs, and found that all but one study demonstrated effectiveness [73]. Our findings add to this literature by demonstrating and quantifying the benefit of orthogeriatric co-management in preventing incident delirium specifically in the hip fracture population.

Our review also suggests that the duration of delirium may be reduced by over a day through orthogeriatric co-management. This is important because longer duration of delirium has

been associated with higher risk of mortality [74]. However, evidence generally suggests that treatment following the development of delirium does very little to change its course or natural history [40,53]. An exception to this may be in cases where there is an acutely correctable underlying medical condition [40]. It is plausible that there was a substantial subset of patients with acute medical conditions that were identified and treated earlier by an involved geriatrician or geriatric team, thereby leading to more prompt resolution of delirium. However, given the conflicting literature, and low confidence in our estimates of effect, further research is required to corroborate this conclusion.

Our meta-analysis also demonstrates that observational study designs provide higher estimates of treatment effects and explain a substantial amount of the heterogeneity between studies. Further, observational studies underestimated the incidence of delirium, likely owing to use of non-validated screening methods and historical control groups. The limitations of observational study designs are well-described, specifically the tendency to overestimate estimates of treatment effects owing methodological limitations, residual confounding, and higher likelihood of publication of bias [75]. In order to remain comprehensive, and with the limited number of available studies in this topic area, we chose to include observational studies in our review. However, our findings reaffirm the importance of employing high quality randomized controlled trial designs to answer important clinical questions accurately.

Limitations

Our review has several limitations. First, as mentioned, only four of eight studies were RCTs, of which only two attempted to blind outcome assessors. Lack of blinding may have led to a potential overestimation of the treatment effect in these trials and, therefore, in the RCT pooled estimate. Second, there was a degree of clinical heterogeneity in the details of the

interventions. Studies varied in their use or encouragement of standardized protocols, location of co-management (e.g., orthopaedic ward versus specialized ward), and degree of involvement of the geriatric physician, among other factors. This makes it difficult to determine the specific aspects of co-management that are most important to reproduce when implementing these models.

We were also limited in coming to conclusions on severity—and to a lesser extent duration—of delirium. This was owing to inconsistent reporting among trials, as well as use of varying methodologies and outcome instruments. Use of a validated and common outcome instrument will be important for future delirium studies to enable meta-analysis and meaningful conclusions. Similarly, outcomes for patients with dementia (although well-represented), were not independently reported in all studies, thereby limiting our meta-analysis of this subgroup. Dementia patients may have differing effects (i.e., either greater or lesser) from those observed in patients without dementia [41]. Future studies must aim to determine whether the effects of orthogeriatric co-management are reproducible in patients with dementia.

Conclusion

This systematic review and meta-analysis demonstrates that ortho-geriatric co-management of hip fracture patients may lead to a substantial reduction in the incidence of delirium in this population. Along with benefits demonstrated in the existing literature, this conclusion supports implementation of collaborative models of care for all hip fracture patients. Future research must strive to determine the benefit of these models in specific subgroups (e.g., patients with dementia), as well as determine the most important elements of an optimal orthogeriatric co-management model.

CHAPTER 6: Thesis Conclusions and Future Directions

Hip fractures are common and devastating injuries. In this thesis, I have attempted to lay the foundation and assess the feasibility for further work in understanding and improving outcomes after hip fracture. In a pilot study of 100 consecutive hip fracture patients, we were able to demonstrate that a prospective observational cohort of patients with hip fracture was feasible in terms of recruitment, follow-up, and resource requirements. Furthermore, secondary clinical results confirmed our hypothesis of poor medical outcomes after hip fracture, while also alerting us to the possibility of poor secondary prevention efforts following hip fracture.

Conducting this pilot study provided insight into various factors that we will consider moving forward. Among our major lessons learned were:

- The clinical findings of the pilot study are preliminary. These findings are prone to biases resulting from random error, and it is impossible to determine the effect in various subgroups given limited number included in the pilot. A larger sample size is needed.
- Our study addresses two types of questions—one is epidemiological (e.g., to determine the incidence and prevalence of various conditions among hip fracture patients) and the second is exploratory (e.g., to determine causes of death). Therefore, broad eligibility criteria are important to ensure we do not miss any subgroups of hip fracture patients. Further, broad eligibility criteria have important practical advantages, such as site recruitment and funding.
- Deferred consent processes are important and useful when studying a patient population with a high incidence/prevalence of cognitive dysfunction.

- Routine and systematic surveillance is important in detecting occult conditions, but certain elements of the protocol are more prone to non-compliance and will need to be more closely monitored throughout the full trial.
- The pathways to mortality are complex and involve multiple preceding events. The need to establish and train a Mortality Adjudication Committee will be important in accurately identifying each ‘cause of death’ and potential areas for intervention after hip fracture.

Ultimately, the knowledge that will be gleaned from the definitive prospective cohort study can be used by clinicians involved in the care of hip fracture patients to improve outcomes. The second part of my thesis dealt with the question of whether such expert clinicians (i.e., geriatricians dedicated to the *medical* care of hip fracture, in addition to the *surgical* care performed by the orthopaedic surgeon) could improve delirium outcomes. The findings of this systematic review and meta-analysis demonstrated that the incidence of delirium can indeed be reduced with such co-management. This fits well into the existing literature, which has shown length of stay and mortality may also be reduced with geriatric co-management. As the question answered in this meta-analysis was one of a pragmatic nature, we were not able to explore the individual components of the intervention that led to improvement in outcomes. However, it is highly likely that individual components of this intervention could be improved. Therefore, the findings of the international HIP VISION study integrated into these multi-disciplinary models of care have the potential to improve mortality and morbidity of hip fracture patients worldwide. I hope that this thesis has provided the foundation for this exciting future.

REFERENCES

1. Leslie WD, O'Donnell S, Jean S, Legace C, Walsh P, Bancej C, et al. Trends in hip fracture rates in Canada. *JAMA* 2009;302:883-889.
2. Wiktorowicz ME, Goeree R, Papaioannou A, Adachi JD, Papadimitropoulos E. Economic implications of hip fracture: health service use, institutional care and cost in Canada. *Osteoporos Int* 2001;12:271-278.
3. Brauer CA, Coca-Perrillon M, Cutler DM, Rosen AB. Incidence and mortality of hip fracture in the United States. *JAMA* 2009;302:1573-1579.
4. Icks A, Haastert B, Wildner M, Becker C, Meyer G. Trend of hip fracture incidence in Germany 1995-2004: a population-based study. *Osteoporos Int*. 2008;19(8):1139-1145.
5. Cooper C, Campion G, Melton LJ III. Hip fractures in the elderly: a world-wide projection. *Osteoporos Int* 1992;2:285-289.
6. Alzahrani K, Gandhi R, Davis A, Mahomed N. In-hospital mortality following hip fracture care in Southern Ontario. *Can J Surg* 2010;53:294-298.
7. Leblanc ES, Hillier TA, Pedula KL, Rizzo JH, Cawton PM, Fink HA, et al. Hip fracture and increased short-term but not long-term mortality in healthy older women. *Arch Intern Med* 2011;171:1831-1837.
8. Haentjens P, Magaziner J, Colon-Emeric CS, Vanderschueren D, Milisen K, Velenkeniers B, Boonen S. Meta-analysis: excess mortality after hip fracture among older women and men. *Arch Intern Med* 2010;152:380-390.
9. Simunovic N, Devereaux PJ, Sprague S, Guyatt GH, Schemitsch E, DeBeer J, Bhandari M. Effect of early surgery after hip fracture on mortality and complications: systematic review and meta-analysis. *CMAJ* 2010;182:1609-1616.

10. Giverson IM. Time trends of mortality after first hip fractures. *Osteoporos Int* 2007;18:721-732.
11. Mundi S, Pindiprolu B, Simunovic N, Bhandari M. Similar mortality rates in hip fracture patients over the past 31 years: a systematic review of RCTs. *Acta Orthop*. 2014;85:54-59.
12. Fox KAA, Steg PG, Eagle KA, Goodman SG, Anderson FA, Granger CB, et al. Decline in rates of death and heart failure in acute coronary syndromes, 1999-2006. *JAMA* 2007;297:1892-1900.
13. de Vreede JJ, Gorgels AP, Verstraaten GM, Vermeer F, Dassen WR, Wellens HJ. Did prognosis after acute myocardial infarction change during the past 30 years? A meta-analysis. *J Am Coll Cardiol* 1991;18:698-706.
14. Vestergaard P, Rejnmark L, Mosekilde L. Increased mortality in patients with hip fracture-effect of pre-morbid conditions and post-fracture complications. *Osteoporos Int* 2007;18:1583-1593.
15. Lawrence VA, Hilsenback SG, Noveck H, Poses RM, Carson JL. Medical complications and outcomes after hip fracture repair. *Arch Intern Med* 2002;2053-2057.
16. Shoda N, Yasunaga H, Horiguchi H, Matsuda S, Ohe K, Kadono Y, Tanaka S. Risk factors affecting in-hospital mortality after hip fracture: retrospective analysis using the Japanese diagnosis procedure combination database. *BMJ Open* 2012;2:e000416.
17. de Luise C, Brimacombe M, Pederson L, Sorensen HT. Chronic obstructive pulmonary disease and mortality following hip fracture: a population-based cohort study. *Eur J Epidemiol* 2008;23:115-122.
18. Sedgwick P. Retrospective cohort studies: advantages and disadvantages. *BMJ*. 2014;348:g1072.

19. Bhaskar D, Parker MJ. Haematological indices as surrogate markers of factors affecting mortality after hip fracture. *Injury* 2011;42:178-182.
20. Lee K-H, Ha Y-C, Lee Y-K, Kang H, Koo K-H. Frequency, risk-factors, and prognosis of prolonged delirium in elderly patients after hip fracture surgery. *Clin Orthop Relat Res* 2011;469:2612-2620.
21. Furlaneto ME, Garcez-Leme L-E. Impact of delirium on mortality and cognitive and functional performance among elderly people with femoral fractures. *Clinics* 2007;62:545-552.
22. Rosencher N, Vielpeau C, Emmerich J, Fagnani F, Samama CM. Venous thromboembolism and mortality after hip fracture surgery: the ESCORTE study. *J Thromb Haemost* 2005;3:2006-2014.
23. Roche JJW, Wenn RT, Sahota O, Moran GG. Effect of comorbidities and postoperative complications on mortality after hip fracture in elderly people: prospective observational cohort study. *BMJ* 2005;331:1374.
24. VISION Study Investigators. Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. *JAMA* 2012;307:2295-2304.
25. POISE Study Group, Devereaux PJ, Yang H, Yusuf S, Guyatt G, Leslie K, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet* 2008;371:1839-47.
26. Fisher AA, Southcott EN, Goh SL, Srikusalanukul W, Hickman PE, Davis MW, et al. Elevated serum cardiac troponin I in older patients with hip fracture: incidence and prognostic significance. *Arch Orthop Trauma Surg* 2008;128:1073-1079.

27. Dawson-Bowling S, Chettiar K, Cottam H, Worth R, Forder J, Fitzgerald-O'Connor I, et al. Troponin T as a predictive marker of morbidity in patients with fractured neck of femur. *Injury* 2008;39:775-780.
28. Ausset S, Minville V, Marquis C, Fourcade O, Rosencher N, Benhamou D, Auroy Y. . Age and Ageing 2009;38:473-476.
29. Spurrier E, Wordsworth D, Martin S, Norris R, Parker MJ. Troponin T in hip fracture patients: prognostic significance for mortality at one year. *Hip Int* 2011;21:757-761.
30. Siu AL, Penrod JD, Boockvar KS, Koval K, Strauss E, Morrison RS. Early ambulation after hip fracture: effects on function and mortality. *Archives of internal medicine*. 2006; 166(7); 766-71. Epub 2006/04/12.
31. Kamel HK, Iqbal MA, Mogallapu R, Maas D, Hoffmann RG. Time to ambulation after hip fracture surgery: relation to hospitalization outcomes. *The journals of gerontology Series A, Biological sciences and medical sciences*. 2003, 58(11):1042-5. Epub 2003/11/25.
32. Petrella RJ, Overend T, Chesworth B. FIM after hip fracture: is telephone administration valid and sensitive to change? *American journal of physical medicine & rehabilitation / Association of Academic Physiatrists* 2002;81:639-44.
33. Roberts J, Waddy S, Kaufmann P. Recruitment and retention monitoring: facilitating the mission of the National Institute of Neurological Disorders and Stroke (NINDS). *J Vasc Interv Neurol*. 2012;5:14-19.
34. Grill JD, Karlawish J. Addressing the challenges to successful recruitment and retention in Alzheimer's disease clinical trials. *Alzheimers Res Ther*. 2010; 2: 34.

35. Wagner AK1, Zhang F, Soumerai SB, Walker AM, Gurwitz JH, Glynn RJ, Ross-Degnan D. Benzodiazepine use and hip fractures in the elderly: who is at greatest risk? *Arch Intern Med.* 2004;164:1567-1572.
36. Tornetta P 3rd, Pascual M, Godin K, Sprague S, Bhandari M. Participating in multicenter randomized controlled trials: what's the relative value? *J Bone Joint Surg Am.* 2012;94:107-111.
37. Karlawish JHT. Research involving cognitively impaired adults. *N Engl J Med.* 2003;348:1389-1392.
38. Coats TJ. Ethical and practical issues in trauma care research. *Br J Surg.* 2012;99:6-7.
39. Jansen TC, Kompanje EJO, Druml C, Menon DK, Wiedermann CJ, Bakker J. Deferred consent in emergency intensive care research: what if the patient dies early? Use the data or not? *Intensive Care Med.* 2007;33:894-900.
40. Chaudhry H, Devereaux PJ, Bhandari M. Cognitive dysfunction in hip fracture patients. *Orthop Clin North Am.* 2013;44:153-62.
41. Mundi S, Chaudhry H, Bhandari M. Systematic review on the inclusion of patients with cognitive impairment in hip fracture trials: a missed opportunity? *Can J Surg.* 2014;57:e141-145.
42. Wu AW, Lipshutz AK, Pronovost PJ. Effectiveness and efficiency of root cause analysis in medicine. *JAMA.* 2008;299:685-687
43. Vollmer CM Jr, Sanchez N, Gondek S, McAuliffe J, Kent TS, Christein JD, Callery MP; Pancreatic Surgery Mortality Study Group. A root-cause analysis of mortality following major pancreatectomy. *J Gastrointest Surg.* 2012;16:89-102; discussion 102-113.

44. Leslie WD, O'Donnell S, Jean S, Legace C, Walsh P, Bancej C, et al. Trends in hip fracture rates in Canada. *JAMA*. 2009;302:883-889.
45. Bhandari M, Sprague S, Schemitsch E, et al. Resolving controversies in hip fracture care: the need for large collaborative trials in hip fractures. *J Orthop Trauma*. 2009;23:479-84.
46. Bruce AJ, Ritchie CW, Blizard R, Lai R, Raven P. The incidence of delirium associated with orthopaedic surgery: a meta-analytic review. *Int Psychogeriatr*. 2007;19:197-214.
47. Kaplan NM, Palmer BF. Etiology and management of delirium. *Am J Med Sci*. 2003;325:20-30.
48. Gruber-Baldini AL, Zimmerman S, Morrison RS, Grattan LM, Hebel JR, Dolan MM, et al. Cognitive impairment in hip fracture patients: timing of detection and longitudinal follow-up. *J Am Geriatr Soc*. 2003;51:1227-36.
49. Pandharipande PP, Girard TD, Jackson JC, Morandi A, Thompson JL, Pun BT, et al. Long-term cognitive impairment after critical illness. *N Engl J Med*. 2013;369:1306-16.
50. Bickel H, Gradinger R, Kochs S, Forstl H. High risk of cognitive and functional decline after postoperative delirium. A three year prospective study. *Dement Geriatr Cogn Disord*. 2008;26:26-31.
51. Witlox J, Eurelings LS, de Jonghe JF, Kalsivaart KJ, Eikelenboom P, van Gool WA. Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: a meta-analysis. *JAMA*. 2010;304:443-51.
52. McCusker J, Cole MG, Dendukuri N, Belzile E. Does delirium increase hospital stay? *J Am Geriatr Soc*. 2003;51: 1539-46.

53. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. *Lancet*. 2013; Aug 27. doi:pii: S0140-6736(13)60688-1. 10.1016/S0140-6736(13)60688-1. [Epub ahead of print].
54. National Collaborating Centre for Acute and Chronic Conditions. Delirium: diagnosis, prevention and management. London (UK): National Institute for Health and Clinical Excellence (NICE);2010 Jul 29 p. (Clinical guideline; no. 103).
55. Grigoryan KV, Javedan H, Rudolph JL. Ortho-geriatric care models and outcomes in hip fracture patients: a systematic review and meta-analysis. *J Orthop Trauma*. 2013;Aug 1 [Epub ahead of print].
56. Prestmo A, Hagen G, Sletvold O, Helbostad JL, Thingstad P, Taraldsen K, Lydersen S, Halsteinli V, Saltnes T, Lamb SE, Johnsen LG, Saltvedt I. Comprehensive geriatric care for patients with hip fractures: a prospective, randomised, controlled trial. *Lancet*. 2015;[Epub Ahead of Print].
57. Moher D, Liberati A, Tetzlaff J, Altman DG; the PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 2009;338:b2535.
58. Shrier I, Boivin J-F, Steele RJ, Platt RW, Furlan A, Kakuma R, et al. Should meta-analysis of interventions include observational studies in addition to randomized controlled trials? A critical examination of underlying principles. *Am J Epidemiol*. 2007;166:1203-1209.
59. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (MINORS): development and validation of a new instrument. *ANZ J Surg*. 2003;73:712-716.

60. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol*. 2011;64:383-394.
61. Higgins JPT, Deeks JJ. Chapter 7: Selecting studies and collecting data. In: *Cochrane handbook for systematic reviews of interventions (Version 5.1.0) [updated March 2011]*. Higgins JPT, Green S [Eds.].
62. Field AP, Gillett R. How to do a meta-analysis. *Br J Math Stat Psychol*. 2010;63:665-94.
63. Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012.
64. Boddaert J, Cohen-Bittan J, Khiami F, Le Manach Y, Raux M, Beinis JY, Verny M, Riou B. Postoperative admission to a dedicated geriatric unit decreases mortality in elderly patients with hip fracture. 2014;9:e83795.
65. Deschodt M, Braes T, Flamaing J, Detroyer E, Broos P, Haentjens P, et al. Preventing delirium in older adults with recent hip fracture through multidisciplinary geriatric consultation. *J Am Geriatr Soc*. 2012;60:733-9.
66. Fisher AA, Davis MW, Rubenach SE, Sivakumaran S, Smith PN, Budge MM. Outcomes for older patients with hip fractures: the impact of orthopedic and geriatric medicine cocare. *J Orthop Trauma*. 2006;20:172-8; discussion 179-80.
67. Lundstrom M, Olofsson B, Stenvall M, Karlsson S, Nyberg L, Englund U, et al. Postoperative delirium in old patients with femoral neck fracture: a randomized intervention study. *Aging Clin Exp Res* 2007; 19: 178-86.
68. Marcantonio ER, Flacker JM, Wright RJ, Resnick NM. Reducing delirium after hip fracture: a randomized trial. *J Am Geriatr Soc*. 2001;49:516-22.

69. Vidan M, Serra JA, Moreno C, Riquelme G, Ortiz J. Efficacy of a comprehensive geriatric intervention in older patients hospitalized for hip fracture: a randomized, controlled trial. *J Am Geriatr Soc.* 2005;52:1476-82.
70. Watne LO, Torbergsen AC, Conroy S, Engedal K, Frihagen F, Hjorthaug GA, Juliebo V, Raeder J, Saltvedt I, Skovlund E, Wyller TB. The effect of a pre- and postoperative orthogeriatric service on cognitive function in patients with hip fracture: randomized controlled trial (Oslo Orthogeriatric Trial). 2014;12:63.
71. Wong Tin Niam DM, Bruce JJ, Bruce DG. Innovations in aged care: quality project to prevent delirium after hip fracture. 2005;24: 174-77.
72. Stenvall M, Berggren M, Lundström M, Gustafson Y, Olofsson B. A multidisciplinary intervention program improved the outcome after hip fracture for people with dementia-- subgroup analyses of a randomized controlled trial. *Arch Gerontol Geriatr.* 2012;54:e284-289.
73. Reston JT, Schoelles KM. In-facility delirium prevention programs as a patient safety strategy: a systematic review. *Ann Intern Med.* 2013;158:375-80.
74. Bellelli G, Mazzola P, Morandi A, Bruni A, Carnevali L, Corsi M, Zatti G, Zambon A, Corrao G, Olofsson B, Gustafson Y, Annoni G. Duration of postoperative delirium is an independent predictor of 6-month mortality in older adults after hip fracture. *J Am Geriatr Soc.* 2014 Jul;62:1335-1340.
75. Simunovic N, Sprague S, Bhandari M. Methodological issues in systematic reviews and meta-analyses of observational studies in orthopaedic research. *J Bone Joint Surg Am.* 2009;91 Suppl 3:87-94.

APPENDIX 1: Data Completeness

		CAM		Troponin		Creatinine		CBC	
Assessment (Day*)	# patients in hosp	Done	Not done	Done	Not done	Done	Not done	Done	Not done
1	100	65	35	34	66	86	14	86	14
2	100	86	14	50	50	46	54	59	41
3	100	84	16	93	7	92	8	94	6
4	100	82	18	93	7	93	7	97	3
5	96	79	17	83	13	89	7	91	5
6	89	68	21	69	20	71	18	80	9
7	79	60	19	52	27	58	21	64	15
8	67	48	19	43	24	50	17	54	13
9	52	39	13	34	18	42	10	42	10
10	49	38	11	33	16	37	12	38	11

APPENDIX 2: Clinical Events Preceding Deaths in HIP VISION

Patient	Sequence of Events	Cause of Death
1	Infection Sepsis Pneumonia Infection Sepsis Pneumonia	Non Vascular: Septic Shock/Sepsis
2	Troponin Elevation CCU Admission Bleeding Non-fatal Cardiac Arrest New Acute Kidney Injury Infection Sepsis Infection Sepsis Pneumonia	Non Vascular: Other
3	CCU Admission Troponin Elevation Troponin Elevation Troponin Elevation Fall Troponin Elevation Infection Sepsis Pneumonia CCU Admission	Non Vascular: Respiratory Failure
4	CCU Admission Infection Infection Sepsis Bleeding CCU Admission Bleeding CCU Admission CCU Admission Infection Sepsis New Delirium CCU Admission	Non Vascular: Respiratory Failure
5	Troponin Elevation New Delirium	Non Vascular: Liver Failure

	Infection Pneumonia	
6	Troponin Elevation New Delirium Infection	Vascular: Other
7	Troponin Elevation Troponin Elevation New Acute Kidney Injury Infection Pneumonia Pressure Ulcer	Vascular: Cardiac
8	Troponin Elevation New Delirium Troponin Elevation Fall Infection Sepsis Pneumonia CCU Admission Bleeding New Acute Kidney Injury	Non Vascular: Other
9	Troponin Elevation New Delirium New Clinically Important Atrial Fibrillation New Congestive Heart Failure Pressure Ulcer Infection Pneumonia	Non Vascular: Other
10	Troponin Elevation	Vascular: Other
11	Bleeding Troponin Elevation New Delirium	Vascular: Other
12	-	Non Vascular: Cancer
13	Troponin Elevation Troponin Elevation CCU Admission	Non Vascular: Cancer
14	New Delirium	Non Vascular: Liver Failure

	Bleeding CCU Admission	
15	Non-fatal Cardiac Arrest Pneumonia	Non Vascular: Respiratory Failure

Appendix 3: Event Definitions Used in HIP VISION Pilots

*The following definitions were used in the HIP VISION Pilot study. These definitions are taken and/or adapted from previous studies and trials conducted by Dr. PJ Devereaux at the Population Health Research Institute.

Sub-classification of Death

Judicial outcome assessors will classify all deaths as either vascular or non-vascular. Vascular death is defined as any death with a vascular cause including; vascular cardiac death following myocardial infarction, congestive heart failure, cardiac arrest, cardiac revascularization procedure (i.e., percutaneous coronary intervention [PCI] or coronary artery bypass graft [CABG] surgery), vascular noncardiac death following a cerebrovascular event, pulmonary embolus, hemorrhage, or other vascular deaths due to an unknown cause. Non-vascular death is defined as any death due to a clearly documented non-vascular cause (e.g. trauma, infection, malignancy, gastrointestinal complications and renal failure).

Myocardial Infarction (MI) prior to surgery, MI if no surgery and MI beyond 30 days after surgery

The diagnosis of MI prior to surgery or MI in patients who do not undergo surgery or MI occurring beyond 30 days after surgery requires any one of the following criteria:

1. Detection of a rise or fall of a cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile of the upper reference limit (URL) together with evidence of myocardial ischemia with at least one of the following:
 - a. Ischemic signs or symptoms (i.e. chest, arm, neck, or jaw discomfort, shortness of breath, pulmonary edema) within 24 hours of Troponin elevation.
 - b. Development of pathologic Q waves present in any two contiguous leads that are > 30 milliseconds.
 - c. ECG changes indicative of ischemia (i.e. ST elevation [\geq 2mm in leads V1, V2, or V3 and \geq 1mm in the other leads], ST segment depression [\geq 1mm], or symmetric inversion of T waves \geq 1mm in at least two contiguous leads, or development of new LBBB).
 - d. Coronary artery intervention (i.e. PCI or CABG surgery) within 2 weeks of Troponin elevation or ischemic symptoms.
 - e. New or presumed new cardiac wall motion abnormality on echocardiography or new or presumed new fixed defect on radionuclide imaging.
2. Cardiac death, with symptoms suggestive of myocardial ischemia and presumed new ischaemic ECG changes or new LBBB, but death occurred before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased.
3. Percutaneous coronary intervention (PCI) related myocardial infarction is defined by elevation of a troponin value (>5 x 99th percentile URL) in patients with a normal baseline troponin value (\leq 99th percentile URL) or a rise of a troponin measurement $>20\%$ if the baseline values are elevated and are stable or falling. In addition, either (i) symptoms suggestive of myocardial ischaemia or (ii) new ischaemic ECG changes or (iii) angiographic findings consistent with a

procedural complication or (iv) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality are required.

4. Stent thrombosis associated with myocardial infarction when detected by coronary angiography or autopsy in the setting of myocardial ischaemia and with a rise and/or fall of cardiac biomarker values with at least one of value above the 99th percentile URL.
5. Coronary artery bypass grafting (CABG) related myocardial infarction is defined by elevation of cardiac biomarker values ($>10 \times$ 99th percentile URL) in patients with a normal baseline troponin value (\leq 99th percentile URL). In addition, either (i) new pathological Q waves or new LBBB, or (ii) angiographic documented new graft or new native coronary artery occlusion, or (iii) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

MINS (Myocardial Injury after Noncardiac Surgery)

The diagnosis of myocardial injury after noncardiac surgery requires one of the following criteria:

1. Within the first 30 days after noncardiac surgery, peak Troponin T ≥ 0.03 ng/mL, peak Troponin I ≥ 0.04 ng/mL or, elevation of Troponin or CK-MB measurement with one or more of the following defining features:
 - a. Ischemic signs or symptoms (i.e., chest, arm, neck, or jaw discomfort; shortness of breath, pulmonary edema);
 - b. Development of pathologic Q waves present in any two contiguous leads that are >30 milliseconds;
 - c. Electrocardiogram (ECG) changes indicative of ischemia (i.e., ST segment elevation [>2 mm in leads V1, V2, or V3 OR >1 mm in the other leads], ST segment depression [>1 mm], OR symmetric inversion of T waves >1 mm) in at least two contiguous leads;
 - d. New LBBB;
 - e. New or presumed new cardiac wall motion abnormality on echoardiography or new or presumed new fixed defect on radionuclide imaging; or
 - f. Identification of intracoronary thrombus on angiography or autopsy
2. Within the first 30 days after noncardiac surgery, peak Troponin T ≥ 0.03 ng/mL or, elevation of Troponin or CK-MB measurement with no alternative explanation (e.g., pulmonary embolism, sepsis, cardioversion, a known troponin antibody or known chronically elevated troponin measurements, or another known non ischemic etiology) to myocardial injury.

Myocardial Infarction after MINS within 30 days of surgery

Myocardial infarction after MINS and within 30 days of surgery requires the following criteria:

1. Detection of a rise or fall of a cardiac biomarker (preferably troponin) with at least one value above the 99th percentile of the upper reference limit (URL) and 20% higher than the last troponin measurement related to the preceding event together with evidence of myocardial ischemia with at least one of the following:
 - a. Ischemic signs or symptoms (i.e., chest, arm, neck, or jaw discomfort; shortness of breath, pulmonary edema);

- b. Development of pathologic Q waves present in any two contiguous leads that are > 30 milliseconds;
- c. New or presumed new ECG changes indicative of ischemia (i.e., ST segment elevation [> 2 mm in leads V1, V2, or V3 OR > 1 mm in the other leads], ST segment depression [> 1mm], or symmetric inversion of T waves > 1 mm) in at least two contiguous leads;
- d. New LBBB;
- e. New cardiac wall motion abnormality on echocardiography or new fixed defect on radionuclide imaging; or
- f. Identification of intracoronary thrombus on angiography or autopsy.

Nonfatal cardiac arrest

Nonfatal cardiac arrest is defined as successful resuscitation from either documented or presumed ventricular fibrillation, sustained ventricular tachycardia, asystole, or pulseless electrical activity requiring cardiopulmonary resuscitation, pharmacological therapy, or cardiac defibrillation.

New atrial fibrillation

ECG demonstrates absence of P waves with irregular ventricular rate. Clinically important atrial fibrillation is defined as new atrial fibrillation that results in angina, congestive heart failure, symptomatic hypotension, or that requires treatment with a rate controlling drug, antiarrhythmic drug, or electrical cardioversion.

Stroke

Stroke is defined as a new focal neurological deficit thought to be vascular in origin with signs or symptoms lasting more than 24 hours. Stroke should be classified according to the following:

Ischemic (Non-hemorrhagic): a stroke caused by an arterial obstruction due to either a thrombotic (e.g., large vessel disease/atherosclerotic or small vessel disease/lacunar) or embolic etiology.

Hemorrhagic: a stroke due to a hemorrhage in the brain as documented by neuroimaging or autopsy. This category will include strokes due to primary intracerebral hemorrhage (intraparenchymal or intraventricular), primary subarachnoid hemorrhage, and subarachnoid and parenchymal hematoma as a complication of primary ischemic stroke except for petechial hemorrhagic transformation of a primary ischemic stroke

Type Unknown: the stroke type could not be determined by imaging or other means (i.e., lumbar puncture, neurosurgery, or autopsy), or no imaging was performed.

Pulmonary embolus (PE)

The diagnosis of PE requires any one of the following:

1. A high probability ventilation/perfusion lung scan
2. An intraluminal filling defect of segmental or larger artery on a helical CT scan
3. An intraluminal filling defect on pulmonary angiography

4. A positive diagnostic test for DVT (e.g. positive compression ultrasound or venogram) and one of the following:
 - a. Non diagnostic (i.e. intermediate probability) ventilation/perfusion lung scan
 - b. Non-diagnostic (i.e. sub segmental defects) helical CT scan

New congestive heart failure

The diagnosis of congestive heart failure requires at least ONE of the following clinical signs i.e., any of elevated jugular venous pressure, respiratory râles/crackles, crepitations, or presence of S3 **AND**, at least ONE of the following radiographic findings: vascular redistribution, interstitial pulmonary edema, or frank alveolar pulmonary edema.

Infection

Infection is defined as a pathologic process caused by the invasion of normally sterile tissue or fluid or body cavity by pathogenic or potentially pathogenic organisms.

Pneumonia [adapted from CDC definition of nosocomial respiratory infection]

Diagnosis requires one of the following:

1. At least two clinical signs of the following:
 - a. New onset purulent sputum, change in character of sputum or increased respiratory secretions
 - b. New onset or worsening cough, dyspnea, or tachypnea
 - c. Crackles, râles, or bronchial breath sounds
 - d. Clinical indication of worsening gas exchange
2. New or progressive radiographic infiltrate, consolidation, or cavitation
3. Fever with no other recognized cause OR leukocytes <4 OR leukocytes >12 OR altered mental status with no other apparent cause

Sepsis

Sepsis diagnosis requires two or more signs of systemic inflammatory response syndrome present along with infection.

- a. Core temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$
- b. Heart rate >90 beats/min
- c. Respiratory rate >20 breaths/min **OR** $\text{PaCO}_2 <32\text{mmHg}$
- d. White blood cell count $>12 \times 10^9/\text{L}$ **OR** $4 \times 10^9/\text{L}$ **OR** $>10\%$ bands

Acute Kidney Injury

Acute kidney injury postoperatively is defined as an increment of serum creatinine of $\geq 26 \mu\text{mol/L}$ or $\geq 50\%$ increase within any 48-hour interval.

Acute Kidney Injury receiving dialysis

Defined as a new requirement for dialysis (i.e., use of dialysis machine or peritoneal dialysis apparatus in patients without dialysis prior to study registration).

Life-threatening Bleeding

Life-threatening bleeding is bleeding that is fatal, or leads to: significant hypotension that requires inotrope therapy/vasopressor therapy, urgent (within 24 hours) surgery (other than superficial vascular repair), or intracranial hemorrhage.

Major Bleeding

Major bleeding is defined as bleeding that is not specified under “life- threatening bleeding” above, and

- results in a postoperative hemoglobin ≤ 70 g/L and the patient receiving a transfusion of ≥ 2 units of red blood cells
- results in a hemoglobin drop of ≥ 50 g/L and the patient receiving a transfusion of ≥ 2 units of red blood cells
- results in the patient receiving a transfusion of ≥ 4 units of red blood cells within a 24 hour period
- leads to one of the following interventions: embolization, superficial vascular repair, nasal packing **OR**
- is retroperitoneal, intraspinal, or intraocular (confirmed clinically or on imaging).

Deep venous thrombosis (DVT) of leg or arm

The diagnosis of DVT requires any one of the following:

1. A persistent intraluminal filling defect on contrast venography,
2. Noncompressibility of one or more venous segments on B mode compression ultrasonography, or
3. A clearly defined intraluminal filling defect on contrast enhanced computed tomography.

Ileus

Obstipation and intolerance of oral intake due to non mechanical factors that disrupt the normal coordinated propulsive motor activity of the gastrointestinal tract.

Bowel perforation

Complete penetration of the wall of the stomach, small intestine or large bowel, resulting in intestinal contents flowing in the abdominal cavity.

New delirium

Defined as acute onset of confusion fulfilling the diagnostic criteria of the Cognitive Assessment Method (CAM) for delirium.

Pressure ulcer

Pressure ulcers are lesions caused by unrelieved pressure that results in damage to the underlying tissue.

Fall

An event which results in a person coming to rest unintentionally on the ground or other lower level, not as a result of major intrinsic event (such as stroke) or overwhelming hazard.

Periprosthetic Fracture

Periprosthetic fracture refers to a fracture through any part of either the femur and/or acetabulum to which a hip implant used for hip repair/reconstruction was fixed.

Prosthetic Hip Dislocation

Prosthetic hip dislocation refers to any acute dislocation of a prosthetic femoral head from within its intended concentric location within the acetabulum. The acetabulum may or may not be resurfaced/replaced.

Implant Failure

Implant failure refers to any mechanical issue related to the integrity of any component of the hip implant which requires a surgical procedure to correct. This includes:

1. Loss of implant fixation to bone (either with or without associated periprosthetic fracture); or
2. Broken, disassociated, or dislocated implant components

Hip Re-operation

Hip re-operation refers to any second surgical procedure undertaken on the fractured hip being followed in the study, for any reason, after it has been initially repaired and the patient has left the operating room (e.g. infection, implant failure, periprosthetic fracture, wound dehiscence, etc.)

APPENDIX 4: The FIM Instrument

FIM[®] INSTRUMENT
Motor Function Component

Scale:

- 1 Total Assistance (\geq 75% helper effort, can't, doesn't, or won't do task)
- 2 Maximal Assistance (50% - 74% helper effort)
- 3 Moderate Assistance (26% - 49% helper effort)
- 4 Minimal Contact Assistance (Requiring incidental hands-on help only [\leq 25% helper effort])
- 5 Supervision or Setup (Requiring only standby assistance or verbal cueing, prompting, or coaxing)
- 6 Modified Independence (Requiring the use of a device or extra time, but no physical help)
- 7 Complete Independence (Fully independent)

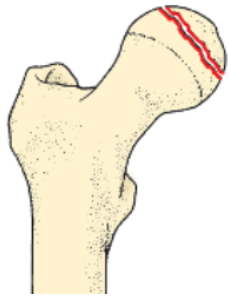
A. FIM ASSESSMENT (Please see CRF Manual for scoring instructions)

1. Assessed by: Self Family Member Nurse Other

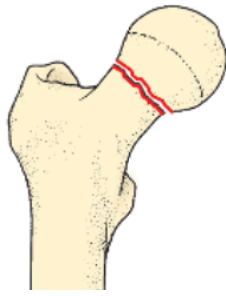
	<i>Total Assistance</i>				<i>Complete Independence</i>		
	1	2	3	4	5	6	7
2. <u>SELF CARE ITEMS</u>							
a) Eating	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b) Grooming	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c) Bathing	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d) Dressing Upper Body	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e) Dressing Lower Body	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f) Toileting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. <u>SPHINCTER CONTROL</u>							
a) Bladder Management	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b) Bowel Management	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. <u>TRANSFERS</u>							
a) Bed, Chair, Wheelchair	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b) Toilet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c) Tub or Shower	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. <u>LOCOMOTION</u>							
a) <input type="checkbox"/> Walking OR <input type="checkbox"/> Wheelchair	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b) Stairs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. MOTOR FUNCTION SCORE:	<input style="width: 20px; height: 20px;" type="text"/> <input style="width: 20px; height: 20px;" type="text"/>						

APPENDIX 5: Types of Hip Fractures

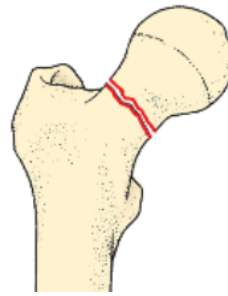
Intracapsular Fractures



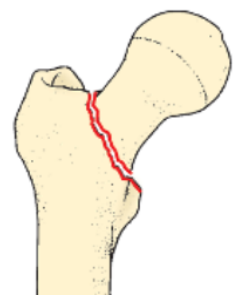
Femoral Head^a



Subcapital^a

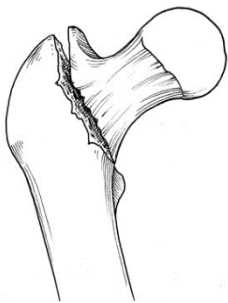


Femoral Neck^a

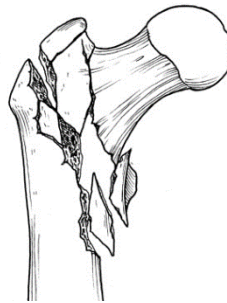


Basicervical^a

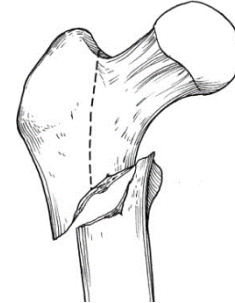
Extracapsular Fractures



Intertrochanteric^b



Comminuted
Intertrochanteric^b



Intertrochanteric –
Reverse Oblique
Pattern^b



Subtrochanteric^c

Image Sources:

a. Greenspan A, Ed. Orthopedic Imaging: A Practical Approach, 5th Ed. Lippincott Williams and Wilkins;2010.

b. Lindskog D, Baumgaertner MR. Unstable intertrochanteric hip fractures in the elderly. JAAOS. 2004;12:179-90.

c. Haidukewych GJ, Langford J. Subtrochanteric fractures. In: Buscholz R et al, Ed. Rockwood and Green's Fractures in Adults, 7th Ed. Lippincott Williams and Wilkins;2010.

APPENDIX 6: Systematic Search Terminology

MEDLINE

1. Delirium/
2. Delirium, Dementia, Amnestic, Cognitive Disorders/
3. delirium.mp
4. Geriatric Assessment/
5. geriatric*.mp
6. Patient Care Team/
- 7.1 OR 2 OR 3 OR 4 OR 5 OR 6
8. exp Hip Fractures/
9. hip fracture.mp
10. 8 AND 9
11. 7 AND 10
12. limit 11 to yr="1990-2014", English

EMBASE

1. delirium/
2. postoperative delirium/
3. geriatric assessment/
4. geriatric care/
5. geriatrician/
6. geriatr*.mp
7. patient care team/
8. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7
9. exp hip fractures

10. hip fracture.mp
11. 9 AND 10
12. 8 AND 11
13. limit 12 to yr="1990-2014", English

Cochrane Library

ID	Search
#1	MeSH descriptor: [Delirium] explode all trees
#2	delirium
#3	MeSH descriptor: [Hip Fractures] explode all trees
#4	hip fracture
#5 trees	MeSH descriptor: [Geriatric Assessment] explode all 1128
#6	geriatric*
#7	(#1 or #2 or #5 or #6) and (#3 or #4)
	Publication Year from 1990 to 2014, in Trials